The Urinary Tract and Adrenal Glands

Normal Anatomy of the Urinary Tract

Embryology

The three embryonic kidneys are the pronephros, mesonephros, and metanephros. The first two degenerate during fetal life but are important inducers of the development of the third. The ureteral bud, derived from the wolffian duct, grows toward the metanephros and induces differentiation of the nephrogenic blastema into renal parenchyma. The actively growing part of the ureteral bud, the ampulla, undergoes multiple divisions, induces the development of nephrons, and establishes communications with them. This activity continues throughout gestation until the 32d to 36th weeks. The ureteral bud gives rise to the renal pelvis, calyces, papillae, and collecting tubules, whereas the metanephric blastema gives origin to the nephron (glomeruli, proximal and distal convoluted tubules, and Henle's loop). The differentiation, elongation, and maturation of the components of the nephron continue even after birth.[6]

The metanephros is originally located in the fetal pelvis. Rapid growth of the caudal portion of the embryo results in displacement of the kidneys cephalad until they reach their normal position in the lumbar fossae. Abnormalities in this process result in ectopic kidneys. The renal pelves are initially directed anteriorly. They rotate so that the hilum of the kidney and calyces are directed medially at the end of
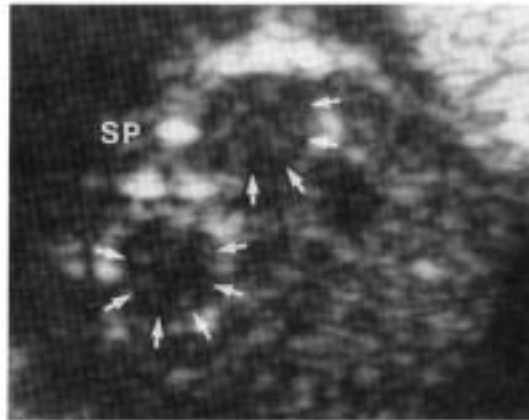

Figure 8-1. Transverse section of the fetal abdomen at 16 weeks. Arrows delineate kidneys. Sp, spine.

Figure 8-2. Transverse scan of a 27-weeks fetus. Arrows delineate the two kidneys. The pelvocaliceal system and capsule are visible.
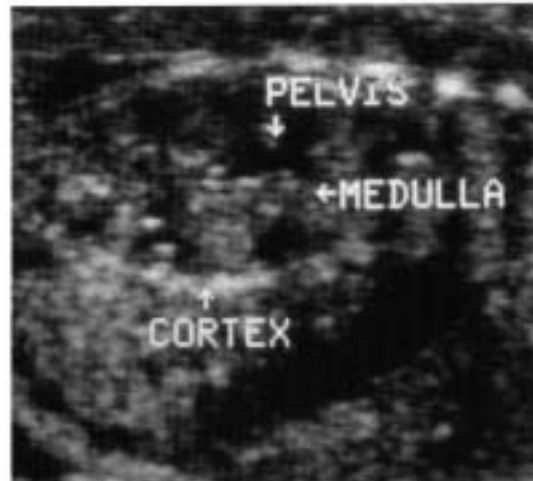

Figure 8-3. Longitudinal scan of a fetal kidney in late third trimester.

TABLE 8–1. NORMAL SIZE VALUES OF KIDNEY DIMENSIONS

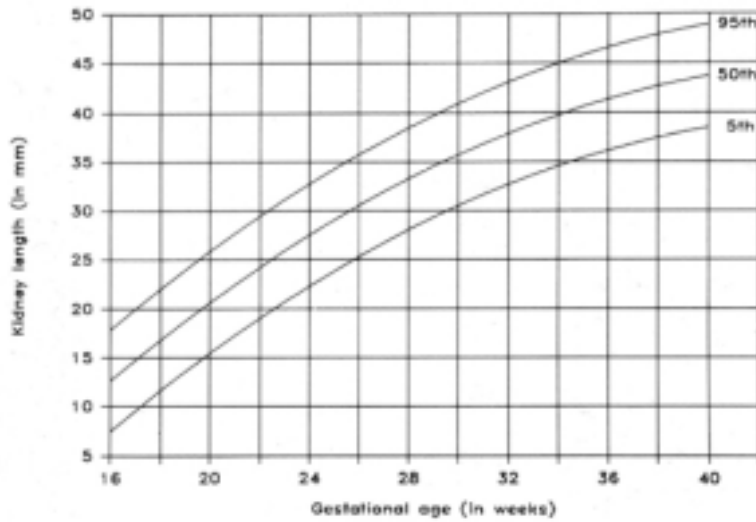| Age (weeks)	Kidney Thickness (mm)			Kidney Width (mm)			Kidney Length (mm)			Kidney Volume (cm³)		
	5th	50th	95th	5th	50th	95th	5th	50th	95th	5th	50th	95th
16	2	6	10	6	10	13	7	13	18	—	0.4	2.6
17	3	7	11	6	10	14	10	15	20	—	0.6	2.8
18	4	8	12	6	10	14	12	17	22	—	0.7	2.9
19	5	9	13	7	10	14	14	19	24	—	0.9	3.1
20	6	10	13	7	11	15	15	21	26	—	1.1	3.3
21	6	10	14	8	12	15	17	22	28	—	1.4	3.6
22	7	11	15	8	12	16	19	24	29	—	1.7	3.9
23	8	12	16	9	13	17	21	26	31	—	2.1	4.3
24	9	13	17	10	14	18	22	28	33	0.3	2.5	4.7
25	10	14	18	11	15	19	24	29	34	0.8	3.0	5.2
26	11	15	19	12	16	19	25	31	36	1.3	3.5	5.7
27	11	15	19	12	16	20	27	32	37	1.9	4.1	6.3
28	12	16	20	13	17	21	28	33	38	2.5	4.7	6.9
29	13	17	21	14	18	22	29	35	40	3.2	5.4	7.6
30	14	18	22	15	19	23	31	36	41	3.9	6.1	8.3
31	14	18	22	16	20	24	32	37	42	4.6	6.8	9.0
32	15	19	23	17	20	24	33	38	43	5.4	7.5	9.7
33	16	20	23	17	21	25	34	39	44	6.1	8.3	10.5
34	16	20	24	18	22	26	35	40	45	6.8	9.0	11.2
35	17	21	25	18	22	26	35	41	46	7.4	9.6	11.8
36	17	21	25	19	23	27	36	41	47	8.1	10.2	12.4
37	18	22	26	19	23	27	37	42	47	8.6	10.8	13.0
38	18	22	26	19	23	27	37	43	48	9.0	11.2	13.4
39	19	23	27	19	23	27	38	43	48	9.4	11.6	13.8
40	19	23	27	19	23	27	38	44	49	9.6	11.8	14.0

Figure 8-4. Relationship between kidney length and gestational age.

embryogenesis. Fusion of the kidneys to form a horseshoe kidney often occurs at the level of the lower pole.

The pathogenesis of renal congenital anomalies is poorly understood. The timing of the insult is responsible for the type of anomaly. For example, if the insult occurs within 5 weeks after conception, failure of communication between the ureteral bud and the metanephric blastema results in renal agenesis. Disturbances occurring immediately after union of these two structures would result in dysplastic cystic kidneys. If the insult takes place

after most of the structural development of the kidney has occurred, a milder form of cystic kidney disease (Potter syndrome type IV) or hydronephrosis will ensue.

Sonographic Anatomy

The kidneys can be imaged as early as 9 1/2 weeks into gestation.[5] In early pregnancy, the kidneys appear as hypoechogenic, oval structures in the posterior midabdomen (Fig. 8-1). As the kidney matures, the pelvocaliceal system appears as an echo-poor structure (Fig. 8-2). The capsule becomes more visible,
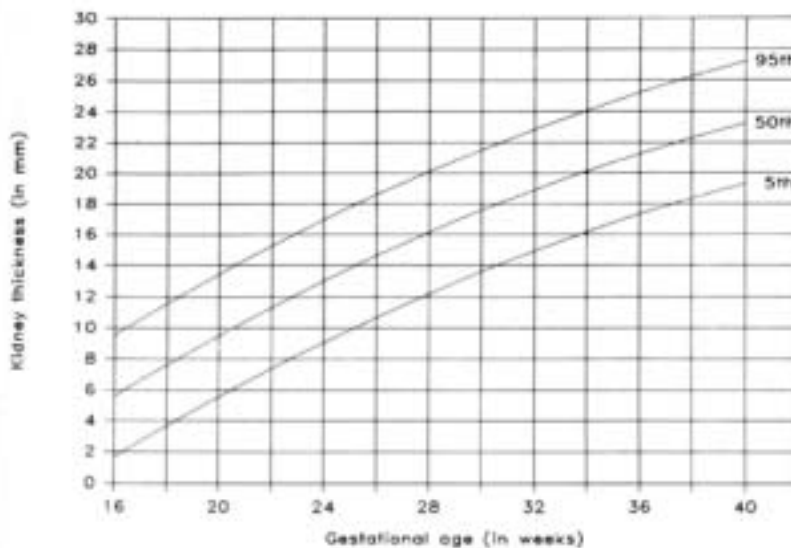

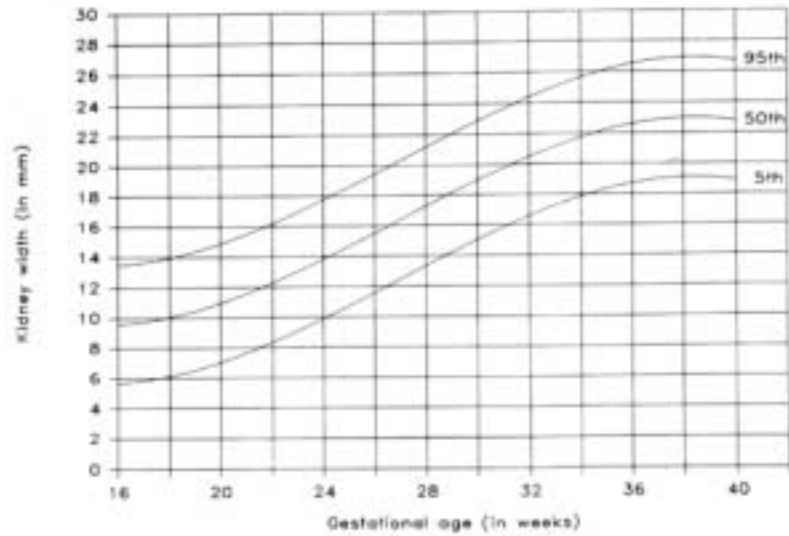**Figure 8-5.** Relationship between kidney thickness and gestational age.

Figure 8-6. Relationship between kidney width and gestational age.

and the distinction between the pyramids and the cortex becomes apparent during the third trimester (Fig. 8-3). With high-resolution equipment, the arcuate arteries can be seen as little, bright echoes that are parallel to the cortex.

Renal biometry can be assessed quite readily.[1,3,4] The renal length is measured from the upper pole to the lower pole of the kidney in a longitudinal section of the fetus in a scan that is parallel to the long axis of the aorta. It is important to avoid using an oblique cut through the kidney. A practical hint is to keep the aorta in the same scan. The thickness, width, and

perimeter of the kidney are measured in a transverse section of the kidney. This section is obtained at level of the renal pelvis, if visible; otherwise, it is obtained at the level where the renal section is the largest. Normal biometry is shown in Table 8-1 (Figs. 8-4 through 8-7). Caliper positioning can be difficult because of the low contrast between the renal parenchyma and the surrounding tissues. Respiratory movements, when present, are extremely helpful in defining the cleavage plane between the kidney and the adrenal glands, spleen, liver, and bowel. The ratio of the kidney perimeter to the abdominal
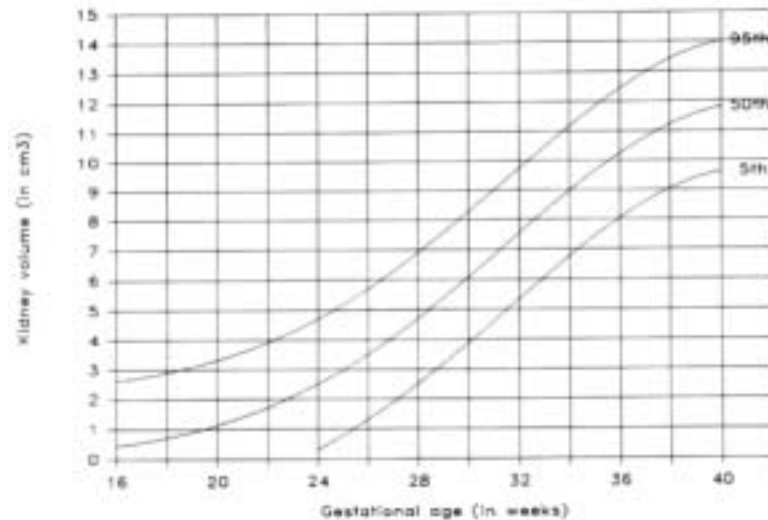

Figure 8-7. Growth of kidney volume through gestational age.

TABLE 8–2. KIDNEY PERIMETER TO ABDOMINAL PERIMETER RATIO

Gestational Age (weeks)	Ratio (%)	Percentile	
		5th	95th
<17	28	24	32
17–20	30	24	36
21–25	30	26	34
26–30	29	24	33
31–35	28	22	34
36–40	27	19	35

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perimeter is a simple screening procedure for renal nomalies.[3] The ratio can be either computed or measured with a digitizer or a map reader.

The computed kidney perimeter to abdominal perimeter ratio is calculated as follows:

$$\text{Ratio} = \frac{(\text{kidney width} + \text{kidney thickness})}{(\text{anteroposterior abdominal diameter} + \text{transverse abdominal diameter})}$$

The normal values for the kidney perimeter to abdominal perimeter ratio are shown in Table 8-2.

The normal fetal bladder can be visualized as early as the 13th week of gestation. Changes in the size of this organ are generally apparent during the course of a monographic examination because the fetus empties its bladder every 30 to 45 minutes. A technique for the calculation of fetal bladder volume has been proposed by Campbell et al.[2,7] They obtained three bladder diameters and use the formula:

$$\text{Bladder Volume} = 4/3 \times \pi \times \text{diameter } a/2 \times \text{diameter } b/2 \times \text{diameter } c/2$$

Diameter a is obtained from the bladder fundus to the bladder neck, diameter b is the maximum transverse diameter, and diameter c is the maximum anteroposterior diameter. Hourly urinary output was calculated

by doing serial examinations at 15 to 30 minute intervals. The urinary output increased with progressive gestational age from a mean of 12.2 ml/hr at 32 weeks to 28 ml/hr at 40 weeks.[7] The bladder walls are normally thin but in the presence of obstruction, they may undergo hypertrophy.

This chapter focuses on the most common renal abnormalities and tumors of the kidney. Bilateral renal agenesis, cystic diseases of the kidney, obstructive uropathies, and tumors will be discussed. Recently, Hill et al. have shown that ultrasound can identify pelvic kidneys in the fetus. Ectopic kidneys are found in 1:1200 autopsies but the frequency reported in clinical studies is 1:10,000. This suggests that they are frequently asymptomatic. Ectopic kidneys should be suspected when both kidneys are not seen in their normal position in a transverse scan of the fetal trunk. They may be associated with an increased incidence of hydronephrosis and other congenital anomalies involving the cardiovascular, skeletal, and gastrointestinal tracts.[3.]

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Bilateral Renal Agenesis

Definition
Bilateral absence of kidneys.

Epidemiology
The incidence of bilateral renal agenesis (BRA) varies between 0.1 and 0.3 per 1000 births.[11,16,45,57,60,74] The male to female ratio is 2.5:1.[17,57,58,74]

Etiology
BRA can be an isolated finding, or less frequently, it can be part of a syndrome. Syndromic BRA can occur in conjunction with the following disorders:

Chromosomal Disorders
1. Familial marker chromosomes involves the pres-

ence of an abnormal, small, extra chromosome, possibly a segment of chromosome [22].

2. Cat's eye syndrome[23] is characterized by iris coloboma, anal atresia, preauricular tags, and renal anomalies. It is probably due to a small, extra acrocentric autosome.

3. 4p-Syndrome[49] is characterized by multiple heterotopies of cells (in adrenals, brain, pancreas, and skin) and BRA. Cardiac, facial, and genital anomalies have been reported as well.

Autosomal Recessive Disorders

1. Fraser syndrome consists of cryptophthalmos (partial or complete absence of eyelid), syndactyly, auditory canal atresia, cleft palate, and malformation of the external genitalia. BRA and laryngeal atresia are less constant findings of the syndrome. [10, 17,19,47,51]

2. Cerebro-oculo-facio-skeletal syndrome is a complex syndrome with some of the following abnormalities: microcephaly, microphthalmia, narrow palpebral fissures, high nasal bridge, large ears, micrognathia, kyphosis, scoliosis, flexion contraction of the extremities, and rocker-bottom foot. The prognosis is poor, and most infants die within the first 3 years of life.[59]

3. Acro-renal-mandibular syndrome[33] is characterized by severe split-hand/split-foot anomaly, renal and genital malformation: bilateral renal agenesis with lens prolapse and cataracts,[8] and syndrome of renal, genital, and middle ear abnormalities.[76]

Autosomal Dominant Disorders

1. Branchio-oto-renal syndrome[14] consists of preauricular pits, bronchial fistulas, and renal anomalies.

2. Müllerian duct anomalies and renal agenesis.[7,6]

Nonmendelian Disorders. Other associations with BRA have been described suggesting a genetic basis. They include agnathia, tracheoesophageal fistula, duodenal atresia and renal agenesis,[65] VATER (vertebral defects, anal atresia, tracheoesophageal fistula, radial and renal dysplasia) association,[20,72] congenital cystic adenomatous malformation,[43] renal agenesis with cardiovascular and skeletal abnormalities,[38] and hypothalamic-hamartoma syndrome.[34]

Sporadic Syndromes. Some teratogenic conditions, such as diabetes mellitus, have been associated with BRA.[30,44,55]

Nonsyndromic BRA. Several patterns of inheritance have been proposed for familial cases of BRA, including autosomal recessive,[12,31,42,61,67,73] X-linked recessive,[54] and multifactorial.[9] In the largest available

series, the risk of a second affected sibling when recognized syndromes are excluded, ranges from 3.5 to 5.9 percent.[4,17,63] This frequency is too high to be explained purely on the basis of a multifactorial inheritance pattern. An alternative explanation is heterogeneity of cases included in the reported series. Indeed, they may have included cases of BRA as isolated malformation sequence inherited with a multifactorial pattern as well as BRA associated with mendelian syndromes (i.e., in families in which individuals have other renal anomalies).[25,66,74,79] In these cases, BRA may be a severe manifestation of an autosomal dominant gene with reduced penetrance and variable expressivity, milder in females and more severe in males.[9,20,52,75]

Risk of Recurrence

The etiology of BRA is not clear. In the presence of chromosomal defects, the risk of recurrence depends on the parents' karyotypes. Autosomal recessive and autosomal dominant syndromes have a 25 and 50 percent risk of recurrence, respectively.

In nonsyndromic cases, parents can be counseled with the following information:

1. The first relatives of a patient with BRA have an increased risk (13 percent) of having silent unilateral renal agenesis. In parents with two affected infants, the risk of silent renal anomalies increases to 30 percent.[63] Therefore, screening parents with ultrasound is indicated.

2. The risk of having another affected child is increased to 3 percent. This risk is higher if either parent has unilateral renal agenesis.[15] When BRA is part of a multiple malformation syndrome, the rate of malformed infants is 12.5 percent, and the risk of BRA is lower.[4] The high frequency of birth defects in this group suggests an autosomal recessive syndrome.

3. Infants of affected families are at risk not only for BRA but also for unilateral renal agenesis and renal dysplasia.[26] The risk for sirenomelia or caudal regression is probably not increased, since these represent a different genetic defect.[26,52]

Embryology

The three embryonic kidneys are the pronephros, mesonephros, and metanephros. The first two degenerate during fetal life but are important inducers of the development of the third. The ureteral bud, derived from the wolffian duct, grows toward the metanephros and induces differentiation of the nephrogenic blastema into renal parenchyma.

Renal agenesis might result from interruption in the normal embryologic sequence from pronephros to metanephros. Alternatively, failure of development of the ureteral bud or lack of stimulation of

nephron formation in the metanephric blastema can also result in renal agenesis.

DuBois[22] has proposed the following classification of the various embryonic defects:

1. Normal ureteric bud growth but defective differentiation of the metanephric blastema results in renal aplasia, in which there is a nubbing of nonfunctional tissue.
2.. Failure of the ureteric duct to reach the nephrogenic blastema results in the ureters ending blindly.
3. Failure of both the ureteral bud and the metanephric blastema results in absence of both kidneys and ureters.
4. Lack of development of the wolffian duct leads to both BRA and severe lower urogenital malformations.

Pathology

Potter[57] has suggested that the term BRA be reserved for those patients in whom both kidneys and ureters are absent (Fig. 8-8). Renal aplasia refers to the presence of ureters and rudimentary fragments of tissue that may have identifiable tubular structures. BRA may change the shape of the adrenal glands, which usually take a discoid configuration, since there is no upward pressure to give them their characteristic shape. This concept is important, since these organs have been confused with kidneys during prenatal [21] and postnatal [69] sonography.

BRA is associated with other anomalies in what has been termed the "Potter sequence," "Potter syndrome," or "oligohydramnios sequence." These anomalies include:

1. Pulmonary hypoplasia. Lungs often weigh less than one-half that expected from the total fetal weight.[1,46] There is a reduction in the number of alveoli and also of conducting airways. This suggests that the responsible insult occurs before the 16th conceptional week.[36]
2. Typical facies. Low set ears, redundant skin, prominent fold arising at inner canthus of each eye, parrot-beak nose, and receding chin.
3. Aberrant hand and foot positioning, bowed legs, clubbed feet, hip dislocation.

Severe oligohydramnios is thought to be responsible for this phenotype. Supporting evidence is that infants with severe oligohydramnios secondary to premature rupture of membranes or intrauterine growth retardation show the same spectrum of anomalies[56] Furthermore, infants with BRA but without significant oligohydramnios and with other anomalies that impair amniotic fluid dynamics (e.g., intestinal obstruction) do not show the elements of the Potter sequence.[71] However, not all the anomalies of the

Figure 8-8. Empty renal fossa of a fetus with bilateral renal agenesis. White arrow points toward renal fossa.

Potter sequence are due to oligohydramnios. A relationship between low set ears and oligohydramnios has not been established.

Amniotic fluid is primarily produced as a dialysate of fetal blood.[53] The fetal kidney begins to produce urine at the 10th conceptional week of gestation. Oligohydramnios in the presence of BRA has been observed as early as the 14th week of gestation [68]

Associated Anomalies

These vary in frequency in the different reports. Buchta et al.[9] suggest that anomalies due to oligohydramnios, such as facial anomalies, anomalies of the extremities, pulmonary hypoplasia, and intrauterine growth retardation, should not be classified as associated anomalies but simply as part of the sequence.

Associated anomalies can be divided into two categories[9,58]: (1) anomalies involving adjacent structures, ranging from mild forms of associated genital malformations to sirenomelia, and (2) multiple unrelated anomalies involving heart, CNS, face, and others. In two studies, anomalies involving adjacent structures occurred in 9 of 16 patients (56 percent)[63]
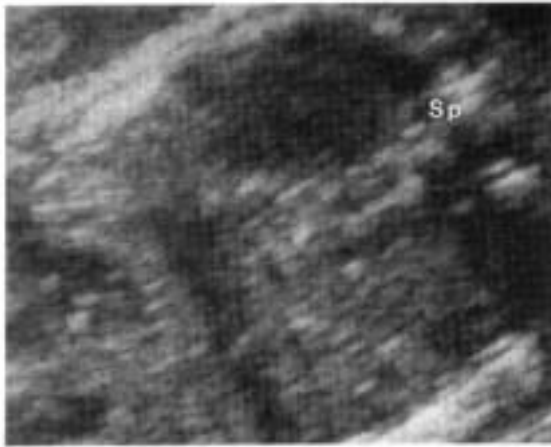
Figure 8-9. Typical sonographic image of a fetus with bilateral renal agenesis. The renal fossa is empty. Note the presence of severe oligohydramnios. Sp, spine.

and 89 of 134 (66 percent).[4] Anomalies of nonadjacent structures occurred in 7 of 16 patients (44 percent)[63] and 45 of 134 (34 percent).[4]

Various organ systems can be involved. Cardiovascular malformations (14 percent)[74] include tetralogy of Fallot, ventricular septal defect, atrial septal defect, hypoplastic left ventricle, coarctation of the aorta, dextrocardia, single ventricle, transposition of the great vessels, total anomalous pulmonary venous drainage, tricuspid atresia, and hypoplastic aorta.

Musculoskeletal malformations (40 percent)[74] include absent radius and fibula, digital anomalies, lumbar hemivertebrae, cleft palate, sacral agenesis, and diaphragmatic hernia.

Central nervous system malformations (11 percent)[74] include hydrocephaly, microcephaly, meningocele, cephaloceles, holoprosencephaly, and iniencephaly.

Gastrointestinal malformations (19 percent)[74] include duodenal atresia, imperforate anus, tracheoesophageal fistula, malrotation, absent stomach or gallbladder, and omphalocele.

Other anomalies include microphthalmia, single umbilical artery, and amnion nodosum.

Diagnosis

Prenatal diagnosis of BRA has been reported several times in the literature.[13,32,37,40,41,50,62] Criteria for a positive diagnosis include the following:

Absence of a Fetal Bladder. The bladder can be seen as early as 10 ½ weeks of gestation but is not consistently imaged until 13 weeks. It is believed that it is never completely empty, with a normal fetus voiding at least once an hour.[13,77] In those cases in which there is poor visualization of this organ, serial exam-

inations at 30-minute intervals should reveal the presence of the bladder. Visualization of the bladder is difficult when the fetus is in breech presentation. The administration of furosemide has been used to induce fetal diuresis.[78] The furosemide test is performed by administering a single intravenous dose of 20 to 60 mg of furosemide to the mother and then monitoring filling of the fetal bladder during the next 2 hours. A distended bladder would obviously indicate the presence of functioning kidneys.

Several authors have reported failure of the furosemide test to reliably identify BRA from other causes of intrauterine renal failure.[35,64] Indeed, a case has been reported in which an infant with severe oligohydramnios that failed to respond to furosemide was found after delivery to have renal failure requiring peritoneal dialysis.[27]

Experimental data in an ovine model suggest that administration of furosemide to the mother at doses of 1 to 2 mg/kg body weight does not induce fetal diuresis. [18] Perhaps this observation can be explained by the poor transplacental passage of furosemide in the ovine model. Indeed, Chamberlain et al. did not find furosemide in the fetal venous plasma using an assay with a sensitivity of 100 ng/ml.[18] Furthermore, direct administration of furosemide to the fetus at doses of > 3 mg/kg body weight were required to induce diuresis in an inconsistent manner.[18] The value of these interesting observations to human pregnancy remains to be established because there are data to support the view that furosemide crosses the human placenta. Beerman et al. have reported cord levels of 330 to 340 µg/ml between 8.5 and 9.5 hours after maternal oral ingestion.[6] In our opinion, a negative test cannot be used to diagnose renal agenesis.

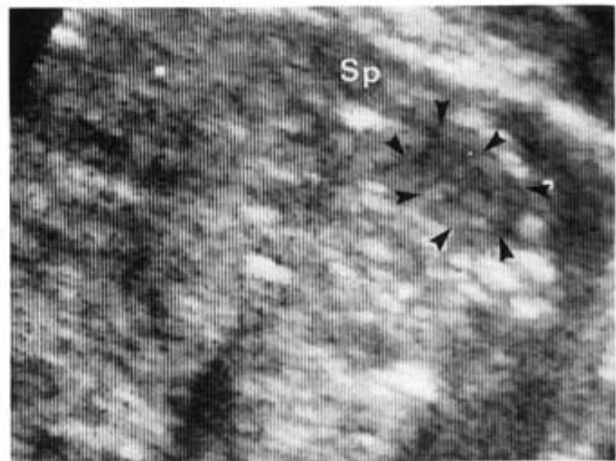The diagnostic value of other imaging techniques, such as nuclear magnetic resonance, comput-

Figure 8-10. Fetus with severe oligohydramnios and bilateral renal agenesis. The shadow *(arrowheads)* in the renal fossa was confused with kidneys. It corresponded to an adrenal gland.

Figure 8-11. Autopsy specimen of an infant with bilateral renal agenesis. This photograph was shown in a pathologic conference. The adrenal gland *(black arrow)* was thought to be a kidney, and the structure indicated by the empty arrow was confused with a ureter but was an aberrant blood vessel.

erized tomography, intravenous pyelography,[40,50] and Doppler waveform analysis, of both maternal and fetal circulation has not been established.

Intravenous pyelography has been used to confirm the diagnosis. In this method, contrast medium is administered to the mother, and her abdomen is radiographed at 3 minutes and again 20 minutes later. This approach was originally proposed as a test for the detection of fetal life. Its overall accuracy was 47 percent.[70] Eighteen of 34 normal infants did not demonstrate kidneys in the pyelogram. The limitations of this approach are obvious.

Bilateral Absence of the Fetal Kidneys. The fetal kidneys can be visualized by the 10th menstrual week of gestations but it is only after the 12th week that they can be visualized in all fetuses. Since the adrenal glands are often enlarged during the second trimester, they can be confused with fetal kidneys (Figs. 8-9 through 8-12).[21,28,39,62,69] The differential diagnosis is based on visualization of a well-defined renal capsule and renal pelvis. In some cases, it is impossible to

differentiate between kidneys and adrenals. A method that could be used to improve visualization of the renal fossae is the instillation of warm saline (37C) into the amniotic cavity.

Oligohydramnios. The most severe examples of oligohydramnios are seen in BRA. This important finding may be present in BRA even early in the second trimester[68] .Less severe forms of oligohydramnios can be seen in cases associated with impaired dynamics of amniotic fluid exchange (e.g., esophageal atresia, pulmonary congenital cystic adenomatoid malformation).[43] The lack of amniotic fluid together with the fetal flexion often hampers clear visualization of the renal area.

The differential diagnosis should include the other renal malformations that can give rise to oligohydramnios and nonvisualization of the bladder (polycystic kidneys, multicystic kidneys, etc.).

An accurate diagnosis of BRA in all cases does not seem possible with ultrasound at this time. It is extremely difficult to establish the differential diagnosis between BRA and a functional cause of in utero renal failure.[35,64]

Some cases of BRA have come to the attention of the sonographer because of an elevated maternal serum AFP. The explanation for this observation is not known.[3,40]

Prognosis

BRA is invariably fatal. The infants are either stillborn or die in the first days of life due to pulmonary hypoplasia. Between 24 and 38 percent of infants with BRA are stillbirths.[57,60,74] The cause of intrauterine death is unknown. Neither pulmonary hypoplasia nor bilateral renal agenesis per se should cause fetal death, since the vital function of these organs in utero is executed by the placenta.

Figure 8-12. Discoid appearance of the adrenal glands of a fetus with bilateral renal agenesis.

Intrauterine growth retardation (IUGR) and associated congenital anomalies have been suggested as potential causes of death. As many as 47 percent of infants with BRA are growth retarded.[60] The incidence of IUGR seems to be higher after the 34th week of gestation.[2,57] Sixty percent of infants with BRA are born before the 37th week of gestation.[60]

Obstetrical Management

Identification of the sonographic signs associated with BRA conveys a poor prognosis to the pregnancy even if a specific diagnosis of BRA cannot be confidently made. Barss et al.[5] recently reported that all eight patients with severe oligohydramnios (largest amniotic fluid pocket <1 cm in any vertical plane) before 26 weeks of gestation died in utero or in the early neonatal period. Mercer et al.[48] reported 24 percent survivors in 33 patients with severe oligohydramnios before 26 weeks' gestation, with 18 percent having a good neonatal outcome. The option of pregnancy termination should be offered before viability. After 24 weeks of gestation, management depends on the certainty of the diagnosis. If a definitive diagnosis can be made, BRA would fulfill the criteria for offering pregnancy termination even in the third trimester (certain prenatal diagnosis and uniformly fatal disease). In the case of uncertainty secondary to difficulties in renal fossa visualization, expectant management is advised. A difficult problem involves the management of fetal distress in infants suspected of having BRA. This difficult clinical and ethical problem must await more data before firm guidelines can be offered. We advise our patients that severe oligohydramnios from early pregnancy seems to be associated with pulmonary hypoplasia and a poor outcome even if BRA is not present. Preliminary evidence suggests that the absence of fetal breathing in fetuses with oligohydramnios due to rupture of membranes in the second trimester is associated with poor prognosis. [8a]

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Infantile Polycystic Kidney Disease

Synonyms

Polycystic kidney disease type I, infantile polycystic disease of the liver and kidney, renal tubular ectasia, microcystic kidney disease, and autosomal recessive polycystic kidney disease.

Definition

Infantile polycystic kidney disease (IPKD) is an autosomal recessive disorder characterized by bilateral and symmetrical enlargement of the kidneys. Normal parenchyma is replaced by dilated collecting tubules. There is no increased amount of connective tissue.

Incidence

Potter reported 2 cases in 110,000 infants.[10]

Etiology

The disease is inherited with an autosomal recessive pattern. Therefore, there is a 25 percent recurrence risk. The possibility of the dominantly inherited adult form of polycystic kidneys must be ruled out by a thorough examination of the parents and of the family history before genetic counseling.

Pathogenesis and Pathology

A primary defect of the collecting ducts appears to be responsible for the disease. Since the renal pelvis, calyces, and papilla are normal, a defect in the ureteral buds is unlikely. The normal number of nephrons and their intact development, except for the collecting ducts, suggest that the insult does not occur early in gestation and that the lesion is not due to defective metanephric blastema. Cysts are not a result of obstructions

The disease is always bilateral. The kidneys are grossly enlarged but retain their reniform configuration (Fig. 8-13). Enlargement may be so massive as to cause soft tissue dystocia.[5,6] The bladder, renal pelvis, and ureters are normal. Cystic lesions measuring 1 to 2 mm can be visualized on the surface of the kidney. Histologically, the parenchyma is occupied by large cystic structures lined by cuboidal cells. An important feature is the absence of marked proliferation of connective tissue as seen with dysplastic kidneys.

The disease has been classified into four groups according to the patient's age at the time of clinical presentation [1]:

1. Perinatal. Onset of renal failure occurs in utero or at birth. The kidneys are massively dilated, with 90 percent involvement, and there is rapid neonatal death.

2. Neonatal. Onset occurs within the first month after birth. This group has smaller kidney size, with 60 percent involvement, and there is mild hepatic fibrosis. Death occurs within one year.

3. Infantile. The disease appears by 3 to 6 months of age, with 20 percent renal involvement, moderate hepatic fibrosis, and hepatosplenomegaly. It
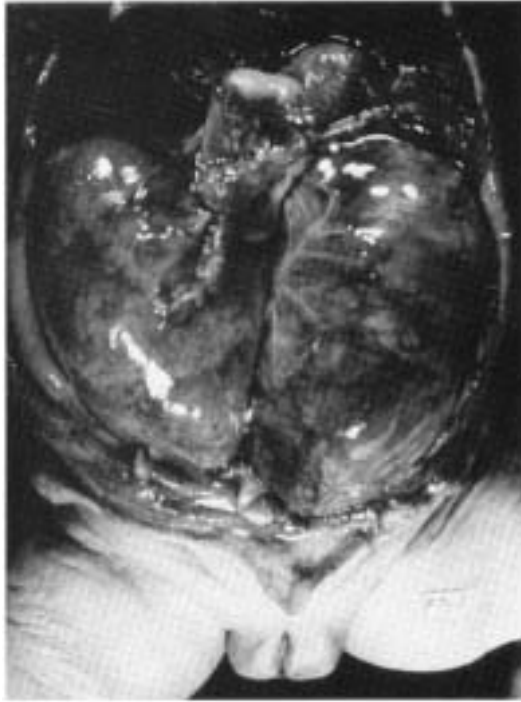
Figure 8-13. Bilaterally enlarged kidneys fill the abdomen of a fetus with infantile polycystic kidney disease.

progresses to chronic renal failure, hypertension, and portal hypertension.

15. Juvenile. The disease appears at 1 to 5 years of age. There is less renal involvement. The course of the disease is similar to that of the infantile group.

The most common clinical presentation is the perinatal variety[2] Multiple allelism has been proposed as an explanation for the variable age at onset of the disease.[18] Recurrences tend to be groupspecific,[1] although this observation has been challenged.[4,12]

Associated Anomalies

Infants with IPKD do not have an increased incidence of associated malformations when compared to the normal population.[12,15]

Cystic changes are also present in the liver. Portal and interlobular fibrosis accompanied by biliary duct hyperplasia and dilatation of the biliary tree may lead to portal hypertension. Hepatocytes are not affected.

Diagnosis

The criteria for diagnosis are (1) bilaterally enlarged kidneys, (2) oligohydramnios, and (3) absent fetal bladder. The typical hyperechogenic texture is attributed to

sound enhancement by the microscopic cystic structures present in the renal parenchyma (Fig. 8-14). Kidney enlargement can be assessed by using the kidney perimeter to abdominal perimeter ratio. An enlarged kidney should not be used as the sole diagnostic criterion, since nephromegaly has been reported without any demonstrable pathologic significance.[13,16]

Since there is a broad spectrum of renal compromise with IPKD, in utero diagnosis may be limited to the severe forms in which the signs can often be identified before the 24th week of gestation.[7,8,11] In some fetuses, prenatal diagnosis may not be possible until the third trimester [14] or not at all.[13] Our data, based on serial renal measurements, suggest that progressive enlargement of the kidneys occurs in utero and that kidney size may be normal in early stages of the disease.

Although some authors have claimed that a differential diagnosis with adult polycystic kidney disease cannot be made easily by ultrasound, [17] we believe that the massive enlargement of the kidneys (Figs. 8-13, 8-14) is rarely seen in adult polycystic kidney disease. Examination of the parents and other members of the family may be helpful as adult polycystic kidney disease is an autosomal dominant disorder.

Prognosis

The prognosis depends on the clinical variety of IPKD. The severe renal involvement typical of the perinatal type can lead to stillbirth [9,15] or neonatal death secondary to pulmonary hypoplasia. Death later in life is often the result of renal failure. In the juvenile form, renal involvement is less severe and may permit survival into later childhood or even into adult life.[3,11] It has been claimed that prognosis

Figure 8-14. Transverse scan of a fetus with infantile polycystic kidney disease. Multiple small cysts are visualized. The kidneys fill the entire abdominal cavity. The abdominal circumference is 40 cm. At the time of delivery, severe soft tissue dystocia occurred because the kidneys were nonreducible.

correlates better with the intravenous pyelogram pattern than with the age of presentations

Obstetrical Management

When the diagnosis is made before viability, the option of pregnancy termination should be offered to the parents. In a fetus at risk, a severe variant diagnosed after viability (with severe oligohydramnios and nonvisualization of fetal bladder) is a condition for which termination of pregnancy in the third trimester may also be offered, since this condition is uniformly fatal. Massively enlarged kidneys may cause a soft tissue dystocia at delivery.

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Adult Polycystic Kidney Disease

Synonyms

Autosomal dominant polycystic kidney disease and adult hepatorenal polycystic disease.

Definition

Adult polycystic kidney disease (APKD) is an autosomal dominant disease characterized by replacement of renal parenchyma with multiple cysts of variable size due to dilatation of the collecting tubules and other tubular segments of the nephrons.

Etiology

Unknown. The disorder is inherited as an autosomal dominant trait, and the recurrence risk is 50 percent. The genetic locus for this disorder is located on chromosome 16.

Incidence

One in 1000 people carries the mutant gene. APKD is one of the most common genetic disorders and the third most prevalent cause of chronic renal failure.[12] The penetrance of the gene is virtually 100 percent.[17] However, the expressivity of the gene may vary, ranging from severe forms that result in neonatal death to asymptomatic forms detected only at autopsy.[3] The disease is usually clinically manifested in the fourth decade of life, but infantile and neonatal cases have been reported. [1,4,5,7,9,11,16]

Pathogenesis and Pathology

APKD is one of the entities that can produce Potter's type III polycystic kidney. In Potter's type III kidneys, the defect seems to be at the level of the ampulla (distal end of the ureter bud), similar to that found in

type II. However, the involvement is not universal, and some ampullae are normal. The result is the presence of cysts coexisting with normal renal tissue. The cysts correspond to both dilated collecting ducts and other tubular portions of the nephron.

There is considerable variation in the degree of renal involvement in patients of the same age, suggesting variability in the expressivity of the gene. Cysts are visible in nephrons and in collecting tubules, and there is a mixture of normal and abnormal elements.[14] Macroscopically, the kidneys are almost always bilaterally affected and often enlarged. Unilateral involvement may be the first manifestation of the disease.[17] The size of the cysts may vary, and some cysts may reach several centimeters.[10] Involvement of the liver is less prominent than in IPKD. The lesions consist of periportal fibrosis;[13] they may be focal and detected only by chance.[1]

Associated Anomalies

Clinically overt APKD has been associated with cystic lesions in other organs, including liver, pancreas, spleen, lungs, testes, ovaries, and epididymis.[3] An association between APKD and liver cysts has been clearly demonstrated.[19] Whether cysts in other organs are due to random occurrence, an actual increased incidence, or the consequence of a detailed autopsy in patients with a known anomaly has not been established.

It should be stressed that type III polycystic kidney disease is a common morphologic expression of a group of disorders other than APKD. Meckel syndrome (autosomal recessive), tuberous sclerosis (autosomal dominant), and Von-Hippel Lindau (autosomal dominant) are mendelian disorders associated with this type of renal disease.[19]

Diagnosis

There are several documented cases of prenatal diagnosis of this condition.[11,12a,18,20] The monographic appearance has been described as similar to that of IPKD: enlarged kidneys with increased parenchymal echogenicity or multiple cysts (Fig. 8-15). The amount of amniotic fluid has been normal or decreased. The earliest diagnosis has been made at 23 ½ weeks. In some fetuses where serial examinations were performed, the dimensions and appearance of the kidneys were normal in the midtrimester, and abnormalities were first detected at 30 and 36 weeks.[11] In some cases, the gross lesions may be more prominent in one kidney.[10,11] Therefore, unilateral involvement does not exclude diagnosis in the fetus. In one reported fetus, ascites was noted,[18] and in another, nonimmune hydrops was identified.[20]

APKD in the fetus should be suspected when cystic enlarged kidneys are detected in association with a normal amount of fluid. This condition is a late
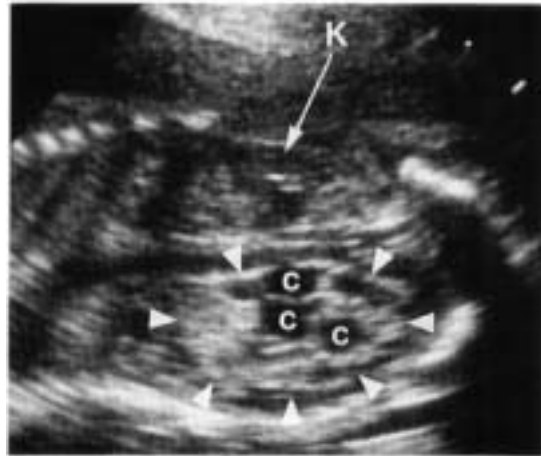

Figure 8-15. Unilateral adult polycystic kidney disease. This a coronal longitudinal section demonstrating both kidneys. The upper kidney (K) is normal. The lower kidney is polycystic and shows multiple cystic structures (C) and thickened renal parenchyma.

cause of renal failure, but the gross lesions may be present in fetuses and newborns.[1,4,6,7,9,15,19]

The diagnosis of APKD in a newborn or a fetus should prompt investigation of both parents. The prenatal diagnosis of APKD has been made by chronic villous sampling using a highly polymorphic DNA probe genetically linked to the locus of the mutant gene.[14]

Prognosis

Pretorius et al. have recently reviewed the follow-up of seven cases diagnosed in utero. One pregnancy was electively terminated at 23 ½ weeks. One infant died in the neonatal period. Of the five remaining infants, four had normal renal function, and all infants but one had normal blood pressure (follow-up 2 months to 4 years and 10 months).[13a] Since this information is based upon a limited experience, parents may be informed about the natural history of the disease with data on APKD from postnatal series. APKD is a chronic disease that may become symptomatic over a wide range of ages from the newborn period to adulthood. Sometimes, the disease can be completely asymptomatic and will be detected at autopsy. The mean age of onset of symptoms is 35 years, and the mean age of diagnosis is 43 years.[19] The symptoms are loin pain, renal enlargement, renal insufficiency, and uremia. Hypertension can be observed in 50 to 70 percent of patients. Berry aneurysms are demonstrated in 10 to 30 percent of patients, and their rupture is a cause of death in 10 percent of patients with APKD. There are not sufficient data to formulate adequate prognostic guidelines for patients diagnosed in utero or in the imme-

diate neonatal period. Stillbirth and early neonatal death have been reported by Potter.[13,16]

Obstetrical Management

Parents at risk should be counseled about the possibility of first trimester prenatal diagnosis. If the diagnosis is made before viability, the option of pregnancy termination should be offered to the parents. After viability, the diagnosis of APKD probably should not alter standard obstetrical management. Any time enlarged hyperechogenic kidneys are diagnosed in a fetus, members of the family should be screened with renal sonography. There are no data in which to base the management of fetuses with evidence of in utero renal failure.

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Multicystic Kidney Disease

Synonyms

Potter's type II cystic kidney disease, multicystic dysplastic kidneys, polycystic kidney disease type II, and dysplastic kidney disease.

Definition

Multicystic kidney disease is a congenital renal disorder characterized by cystic lesions that correspond primarily to dilated collecting tubules. The disorder can be bilateral, unilateral, or segmental.

Etiology

MKD is generally a sporadic conditions and familial occurrence is rare.[35] On occasion, MKD has been reported with maternal diabetes.

Potter's type II cystic kidney disease can occur within the spectrum of syndrome, usually as a secondary manifestations

Autosomal Recessive Syndromes. Meckel, Dandy Walker, short-rib polydactyly type I or Saldino-

Noonan and type II or Majewsky, Zellweger (cerebrohepatorenal syndrome), retina-renal dysplasia, Ivemark (dysplasia of kidney, liver, and pancreas), Roberts, Fryns, Smith-Lemli-Opitz.

Autosomal Dominant Syndromes. Apert syndrome.

Chromosomal Defects. Trisomy C, del (15) (q22) (q24).

Incidence

The incidence of bilateral MKD is estimated to be 1 in 10.000.[29] This figure may represent an underestimation of the real incidence of the disease, since not all perinatal deaths are followed by autopsy. The male to female ratio is 2:1 in unilateral MKD.[28]

Pathogenesis

The pathogenesis of multicystic kidney disease (MKD) is unknown. The current understanding of this disease suggests that it is a complex abnormality that may be the result of two types of insults: (1) developmental failure of the mesonephric blastema to form nephrons or (2) an early obstructive uropathy.

The normal development of nephrons requires differentiation of the mesonephric blastema. This process is induced by the ampulla, which is the distal growing end of the ureteral duct. Failure of induction because of an abnormal response of the metanephric blastema or because of a defective ampulla results in disorganized differentiation of the metanephric blastema, giving rise to renal dysplasia. This term refers to a histologic picture characterized by structures generally not represented in normal morphogenesis, including (1) focally dilated tubules that are frequently surrounded by muscle, (2) small ducts with hyperchromatic epithelium, and (3) heterotopic mesodermic structures, such as cartilage. The mechanism by which the collecting tubules are transformed into cysts is unknown. This pathogenetic hypothesis is supported by the frequent association of ureteral malformations and renal dysplasia.

Some cases of multicystic kidney disease occur in association with obstructive uropathy.[10] Some renal function can persist.[37] The obstructive process must take place early in embryogenesis. Otherwise, the renal lesion would correspond to cystic kidney disease type IV, in which the cystic dilatation is limited to the terminal portion of the collecting tubules and to nephrons developed in the latter part of gestation.

The defective metanephric blastema hypothesis can explain those cases of multicystic kidney associated with a hypoplastic or a malformed ureteral bud. However, some cases of unilateral absence of the ureter on the affected side would challenge this view. The explanation that regression of the ureter has
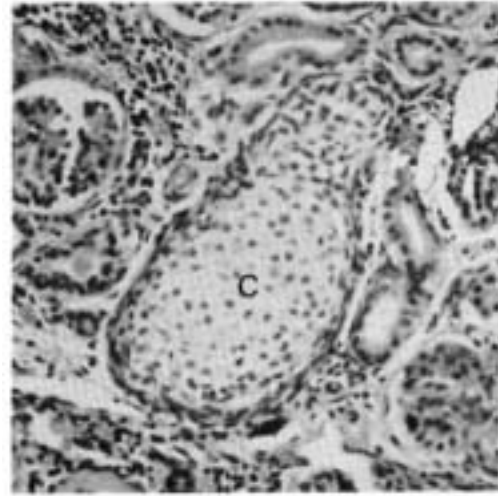

Figure 8-16. Histologic section of a multicystic kidney. C, cartilage.

occurred is not uniformly valid because, in some cases, there is agenesis of the hemitrigone. The pathogenesis in these cases cannot be attributed to a defective ampulla, and a plausible explanation is not available.

Pathology

MKD can be bilateral, unilateral, or limited to a localized portion of a kidney. The segmental variety of multicystic kidney disease is almost always unilateral and is frequently referred to as a "multilocular cyst." Potter[27] suggested that the disease be classified into IIA, characterized by normal or enlarged kidneys (multicystic-multilocular cyst group), and IIB, with small dysgenetic or aplastic kidneys. Recently, the cystic variety of MKD has been subdivided into two major categories: pelvicoinfundibular atresia[13] and the hydronephrotic variety,[10] according to the presence or absence of atresia of the ureter.

Macroscopically, multicystic kidneys may be enlarged (IIA), small (IIB), or of normal size. Enlarged kidneys may weigh several hundred grams and distend the abdomen. When the disease is type IIB, the kidneys may weigh as little as 1 g. Anytime there is involvement of an entire kidney, the ureter is virtually always affected with obstructive or developmental lesions. The renal artery is small or absent in most cases. Cartilage may be found in one third of affected kidneys (Fig. 8-16).

Cysts are usually terminal portions of collecting tubules, often located in the center of the kidney, and
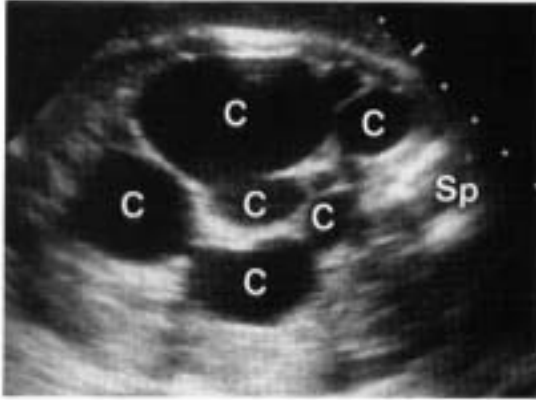
Figure 8-17. Transverse scan of a fetus with multicystic kidney disease. Note the multiple cystic structures (C). Sp, spine.
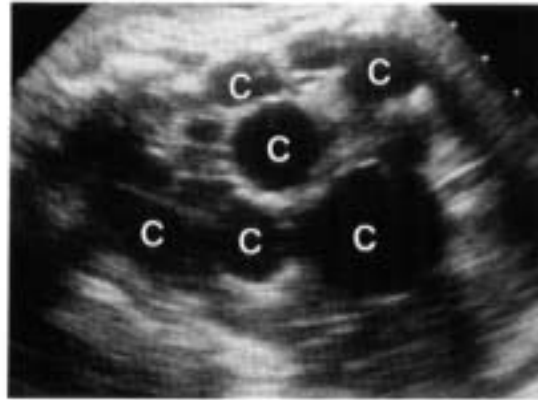

Figure 8-18. Coronal view of the same fetus shown in Figure 8-17. Cysts (C) do not communicate.

may be surrounded by zones of connective or myxomatous tissue.[38]

Unilateral MKD is often asymptomatic. In these patients, the contralateral urinary tract shows minor abnormalities in 30 to 50 percent of patients, including malrotation, ureteropelvic junction obstruction, horseshoe kidney, and other ureteral anomalies.[12,20,23,25,32] In some cases, the sonographic finding of contralateral hydronephrosis has been attributed to a compensatory overload on the functioning kidney.[4,29]

Associated Malformations

Besides the anomalies belonging to the Potter sequence or oligohydramnios sequence (p. 261), bilateral MKD may be associated with cardiovascular malformations, CNS abnormalities (anencephaly, hydrocephalus, iniencephaly, spina bifida, occipital meningocele), diaphragmatic hernia, cleft palate, microphthalmia, duodenal stenosis and imperforate anus,[27] tracheoesophageal fistula, and bilateral absence of radius and thumb.[8] In contradistinction to Potter type I or III, Potter 11 exhibits no cystic changes in the liver, pancreas, or other parenchymatous organs.[35]

An increased frequency of associated congenital anomalies is also found with unilateral multicystic kidneys.[3,12] They include hydrocephaly, anencephaly, spina bifida, myelomeningocele, esophageal atresia, imperforate anus, duodenal bands, tracheoesophageal fistula, ventricular septal defect, talipes equinovarus, hypospadias, vesical diverticulum, and patent urachus. Chromosomal anomalies can also occur.

Diagnosis

Multicystic kidneys have a typical appearance on ultrasound, and antenatal diagnosis of both the unilateral and the bilateral forms has been report-
ed on numerous occasions in the literature.[1,2,4,9,11,16,21,24,26,30] Ultrasound criteria for the diagnosis of bilateral multicystic kidney include:

1. Cystic kidneys. The cysts are multiple, peripheral, round, and of variable size. In most instances, the kidneys are enlarged (type IIA), but in some cases they are small and atrophic. The enlarged kidneys may fill a significant portion of the abdomen and may have a lobulated shape. In type IIa, the kidney may look like a cluster of grapes (Figs. 8-17, 8-18). The renal sinus cannot be identified (Fig. 8-17).
2. Failure to visualize the fetal bladder, even after furosemide administration. Limitations, interpretation, and technique of this test are discussed in the section on bilateral renal agenesis (p. 262).
3. Oligohydramnios. If amniotic fluid is present in association with a typical image of multicystic kidney, consideration should be given to the possibility of a unilateral MKD and incomplete or late obstruction of the contralateral kidney.

The differential diagnosis includes IPKD and ureteropelvic junction obstruction (UPJ). The differential diagnosis between UPJ obstruction and MKD is difficult,[28a] even in the neonatal period, using intravenous pyelography and scintillography.[5,29,33,36] Some criteria have been suggested for differential diagnosis in the newborn.[34] UPJ obstruction is suggested by:

1. Visible renal parenchyma
2. Cystic lesions nonspherical in shape and radiating from the renal pelvis
3. A dilated ureter or a single large cyst (multicystic kidney can occur as a single cyst as well) (Fig. 8-19).
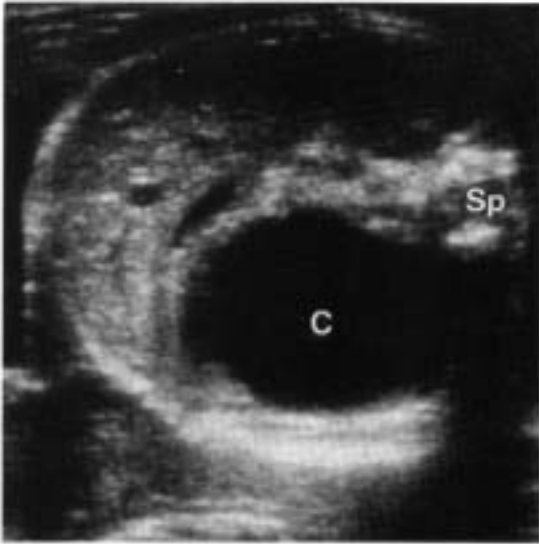4. Visualization of cysts that communicate with the renal pelvis

Figure 8-19. Fetus with unilateral multicystic kidney disease with a single cyst (C). This image stresses the difficult differential diagnosis between a UPJ obstruction and multicyctic kidney disease. The latter could occur as either multiple or single cystic structure. Sp, Spine.

Multilocular cysts should be differentiated from Wilms' tumor and hamartoma that has undergone necrosis.

In unilateral MKD, the only signs are renal in origin. The bladder and contralateral kidney may be completely normal. This type would be diagnosed only when focusing onto the size and morphology of kidneys in routine scans.

It must be stressed that the appearance of the kidney in MKD is related to the time of the insult. When this occurs early (between the 8th and IIth week of conception), the kidney adopts the classic morphology of MKD (there are 10 to 20 noncommunicating cysts, and the organ loses its reniform appearance). The renal pelvis and calyces are atretic or extremely small. If the insult occurs later, the morphology of the kidney depends on the duration of the obstruction. At an earlier stage, a typical hydronephrotic image is observed. Later, the typical image of the large multicystic kidney appears. Most characteristically, there are at least two cysts and a recognizable pelvis, which often communicates with the cysts. Some renal function can be demonstrated.[34]

Prognosis

Bilateral MKD is a fatal condition[12] Cole et al.[7] reported one infant who was doing well at 41 months of age, but since an IVP showed "prompt visualization of distorted calyces," we think the diagnosis of bilateral MKD is doubtful.

There is a paucity of data concerning the prog-

nosis of unilateral MKD. One risk is the development of hypertension.[6,18] Generally, urologists advocate follow-up of the patient rather than prophylactic nephrectomy.[29]

Obstetrical Management

When the diagnosis of bilateral MKD is made early in gestation, the option of termination of pregnancy should be offered to the patient. Fetal karyotype should be considered. If the diagnosis is made after viability, aggressive intervention for fetal distress would seem unwarranted, since the disease is uniformly fatal. Unilateral MKD with a normal contralateral kidney, normal karyotype, and no associated anomalies should not influence obstetrical management. If an obstructive uropathy is diagnosed on the opposite side, delivery should be accomplished when pulmonic maturity is documented. Evaluation in the neonatal period will be required. Delivery in a tertiary care center is recommended.

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Ureteropelvic Junction Obstruction

Definition
Obstruction of the urinary tract at the junction of the renal pelvis and the ureter.

Incidence
The incidence of ureteropelvic junction (UPJ) obstruction in utero is not known. In the cases diagnosed postnatally, it occurs more commonly in males than in females, with a sex ratio of 5:1.[1,16]

Etiology and Pathology
UPJ obstruction is essentially a sporadic phenomenon, although familial cases have been reported.[4,20]

In the family reported by Raffle, all affected patients were females, but males were not screened.[20] A dominant pattern of inheritance with incomplete penetrance and variable expression has been suggested for some cases of unflateral UPJ obstructions This could explain the occurrence of hydronephrosis in twins.[12]

The ureteropelvic junction is a frequent site of obstruction of the urinary tract. Anatomic causes responsible for UPJ obstruction include fibrous adhesions, bands, kinks, ureteral valves, aberrant lower pole vessels, abnormal ureteral insertion, and unusual shapes of the pyeloureteral outlet.[10] How-
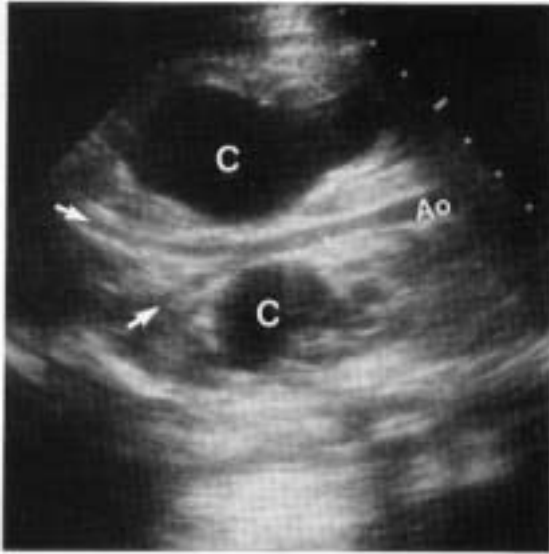
Figure 8-20. Coronal view of a fetus with bilateral ureteropelvic junction obstruction. Note the asymmetrical involvement of the kidneys. C, cystic dilatation of the renal pelvis; Ao; aorta; arrows point to bifurcation of the aorta.

ever, any of these anatomic causes for UPJ obstruction are seen in only a fraction of patients. Since in most instances of UPJ obstruction the junction is anatomically patent to the passage of a probe, the problem seems to be of functional nature.[2] The ureteropelvic junction is important in the formation and propulsion of the bolus of urine. The normal

interwoven pattern of the muscularis of the ureter is considered critical for this function. Abnormal development of the musculature would impair bolus formation and propulsion. In one study, 69 percent of patients with UPJ obstruction had an abnormal muscular arrangement in which the circular layer was present but the longitudinal layer was not.[2]

The condition occurs bilaterally in 30 percent of cases usually with an asymmetrical involvement of the kidneys. When the obstruction is unilateral, it occurs more frequently on the left side.[8,16,17,21] Infants with UPJ obstruction frequently have other associated anomalies of the urinary tract,[16] including vesicoureteric reflux, bilateral ureteral duplication, bilateral obstructed megaureter, contralateral nonfunctioning kidney, contralateral renal agenesis, meatal stenosis, and hypospadias.[1,8,16] In a recent series, the incidence of such anomalies was 27 percent.[8]

Associated Anomalies
Anomalies in extraurinary systems occurs in up to 19 percent of cases.[18] UPJ obstruction has been described in association with Hirschsprung's disease, cardiovascular abnormalities, neural tube defects, sagittal synostosis, mandibular hypoplasia, esophageal atresia and distal fistula, imperforate anus, syndactyly, congenital hip dislocation, and adrenogenital syndrome.[2,18]

Diagnosis
The diagnosis depends on the demonstration of a dilated renal pelvis (Figs. 8-20 through 8-24). The two problems with the diagnosis of UPJ obstruction are (1) the criteria used to classify a renal pelvis as
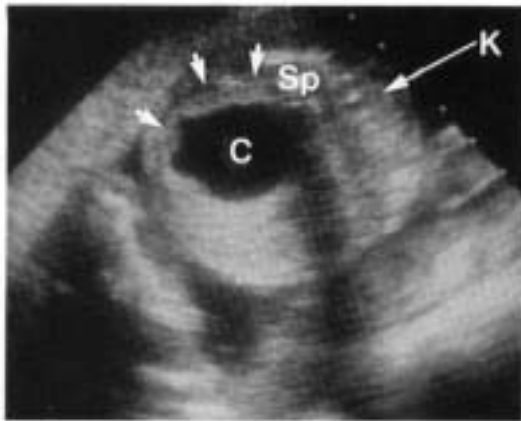

Figure 8-21. Transverse scan at the level of the renal fossa in a fetus with unilateral ureteropelvic junction obstruction. The cystic structure (C) corresponds to a dilated renal pelvis. The arrows point to the renal parenchyma. Sp, spine; K, contralateral normal kidney.
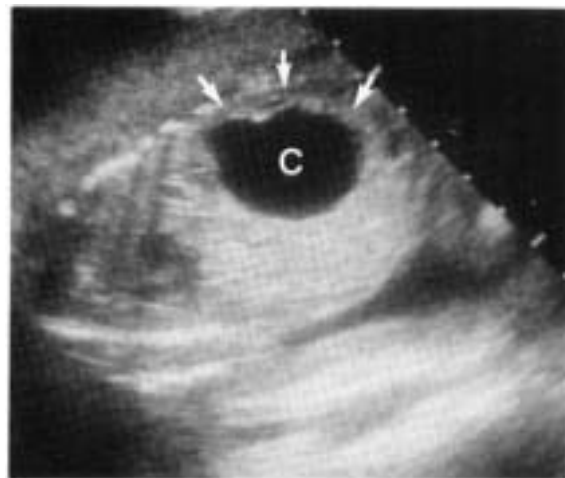

Figure 8-22. Longitudinal scan of the fetus shown in Figure 8-21. There is dilatation of the renal pelvis. Arrows point to the renal parenchyma. C, renal pelvis.
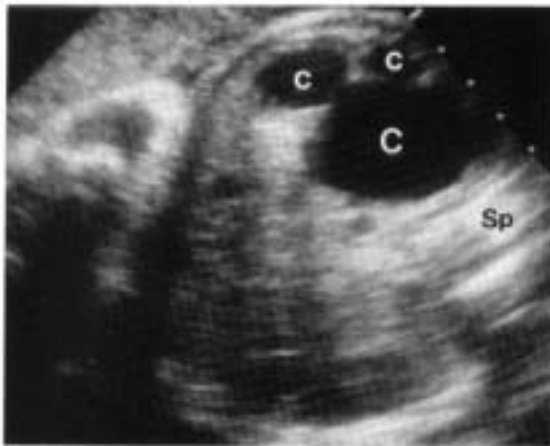
Figure 8-23. Transverse scan of a fetus with hydronephrosis. The largest cystic structures (C) correspond to the renal pelvis, and the other cystic structures (c) correspond to distended calyces. Sp, spine.
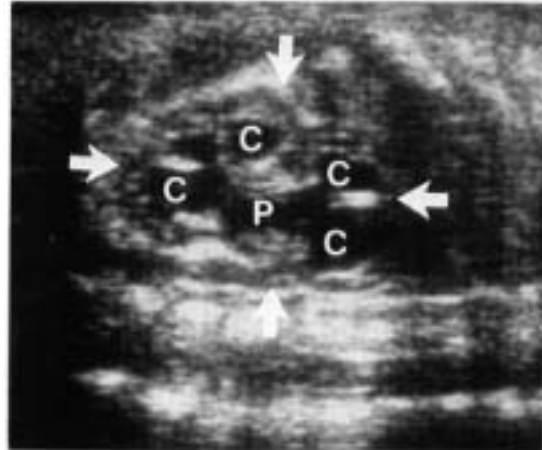

Figure 8-24. Longitudinal scan of the kidney of a fetus with unilateral hydronephrosis. An important clue in the differential diagnosis with multicystic kidney disease is that the cystic structures communicate with the renal pelvis. P, renal pelvis; C, dilated renal calyces.

dilated and (2) the natural history of the disease in utero.

At this time, there is no available nomogram of renal pelvis size and gestational age. Two criteria of renal pelvis measurements have been proposed[3]:

1. Anteroposterior diameter. Renal pelvises of less than 5 mm are normal, whereas those between 5 and 10 mm are normal in most instances but ma require follow-up. In a recent study of eight fetuses with a ≥10 mm renal pelvis diameter, seven had an anatomic abnormality at postnatal examination.[14]

2. The ratio between the maximum transverse pelvic diameter and the renal diameter at the same level. Ratios above 50 percent would suggest hydronephrosis. However, diagnostic indices with this criterion are not available.

Harrison et al. have suggested a semiquantitative estimate of hydronephrosis.[11] Mild dilatation would show enlarged renal pelvis, branching infundibula, and calices. Severe dilatation would be characterized by only a large, unilocular fluid collection.[11]Several patients have been reported in whom a diagnosis of hydronephrosis, either unilateral or bilateral, was initially made in utero, but follow-up scans in utero and postnatally failed to confirm the finding.[5,6,22] Interpreting these reports of transitory hydronephrosis is difficult because authors have not described the dimensions of the renal pelvis. However, this indicates that serial ultrasound scans are needed to predict trends in amniotic fluid volume and in hydronephrosis severity.

It has been suggested that the fetal renal pelvis may vary in size according to the volume state of the mother.[19] Some authors have recommended that patients be reexamined after 12 hours of water and fluid restriction. However, a study of the effect of this protocol on renal pelvis size failed to demonstrate a significant effect in 76.5 percent ot cases.[14] Therefore, the phenomenon of transient hydronephrosis cannot be explained by changes in the hydration of the mother.

Most UPJ obstructions are unilateral, and the amount of amniotic fluid as well as bladder dynamics should be normal. In cases of unilateral UPJ obstructions, the presence of severe oligohydramnios should raise the suspicion of contralateral renal agenesis or dysplasia.

In those patients with bilateral dilatation of the renal pelvis, the amount of amniotic fluid can provide information about the severity of the obstruction. If the amount of fluid is normal and the bladder is visible, the obstruction is either of recent onset or incomplete [5,15]. A normal to increased amount of amniotic fluid may coexist with a bilateral poor renal function in cases of associated anomalies that lead to polyhydramnios, such as diaphragmatic hernia, congestive heart failure, and gastrointestinal atresia.[11,22] The differential diagnosis includes multicystic dysplastic kidneys (Figs. 8-16 through 8-19, 8-24) and perinephric urinoma secondary to rupture of the severely dilated renal pelvis (see p. 272). A precise diagnosis is often impossible and would not change the dismal prognosis for that kidney.[6,11]

Prognosis

The overall prognosis for unilateral UPJ obstructions is good, and intervention is not urgent even after birth.

In one follow-up study of children who underwent surgery for unilateral or bilateral hydronephrosis secondary to UPJ obstruction within 6 months of age, there were no postoperative deaths. Although the calyceal dilatation did not improve and in some cases showed a deterioration on the excretory urogram, the clinical results in regard to symptomatology and renal function were good. Serum creatinine and urea were normal even in patients with bilateral disease. [1,21]

Obstetrical Management

Unilateral UPJ obstruction should not alter standard obstetrical management as long as the contralateral kidney looks normal. There are no data to support an early delivery for correction of the UPJ obstruction. Indeed, the only study available has shown no advantage to immediate surgical repair in cases of unilateral involvement diagnosed in utero versus those diagnosed postnatally after the onset of symptoms.[23] This report only presents data on short-term follow-up (mean follow-up 2 years) and, in our opinion, should not be used to unnecessarily delay the surgical correction of an obstructed kidney.

The management of bilateral UPJ obstruction is based on gestational age, the amount of amniotic fluid, and functional renal reserve. The management issues are similar to those of posterior urethral valves (see p. 286). In cases of bilateral involvement, the amount of amniotic fluid may provide an index of renal functions and it usually correlates with the severity of neonatal pulmonary hypoplasia. A better estimate of residual renal function can be provided by chemical analysis of a fetal urine sample.[9] This is necessary whenever a surgical correction is planned because in some cases even early (20 weeks) fetal intervention may be too late to prevent gross renal damage.[11] A careful search for associated anomalies is always indicated, and a fetal karyotype should be performed whenever an intervention in utero is considered.

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Megaureter

Definition
Megaureter is a dilated ureter with or without dilatation of the renal pelvis and calyces.

Incidence
Ninety-two percent of in utero urinary tract obstructions are associated with megaureters. However, most of these obstructive uropathies are due to an obstacle to the passage of urine at the level of the bladder outlet associated with megaureters.[7] The disorder is more common in male than in female children.[5,25]

Etiology
Megaureter is a sporadic disease. For some specific causes of megaureter, such as primary vesicoureteral reflux, familial cases have been described.[11,12,17] Reflux has been found in 26 to 34 percent of asymptomatic siblings of patients with vesicoureteral reflux.[3,8]

Pathogenesis and Pathology
Ureteral enlargement may be caused by obstruction to the flow of urine, vesicoureteral reflux, or conditions in which neither obstruction nor reflux is present.[9,10,22] Distinction among these different conditions is important, since treatment varies. Obstructive or refluxing hydroureter requires sur-

gical correction, whereas nonrefluxing, nonobstructive megaureters can be managed expectantly. Figure 8-25 outlines the international classification of megaureter.[16]

The term "primary" refers to a ureteral defect, whereas "secondary" refers to a pathologic process in another organ leading to dilatation of the ureter. In primary obstructive megaureter, the obstruction is at or just above the ureterovesical junction. The obstacle may be caused by stenosis of the ureteral valves, but the most common cause is the presence of a narrow juxtavesical ureteral segment that does not dilate or transmit the peristaltic wave.[4,20,21] The pathologic basis for the obstruction may be segmental fibrosis or a localized absence of muscle. Developmental failure of the longitudinal muscle results in inability of the organ to propagate the peristaltic wave. In secondary obstructive megaureter, ureterectasis is due to an extrinsic pressure, such as by a vessel or tumor.

Primary refluxing megaureter is due to an abnormality of the ureterovesical junction, leading to failure of the antireflux mechanism at the level of the ureterovesical junction. Secondary refluxing megaureter is due to reflux associated with a coexistent abnormality (e.g., neurogenic bladder or posterior urethral valves). Primary nonrefluxing nonobstructive megaureter is an idiopathic dilatation of the ureter above the vesical junction, and secondary
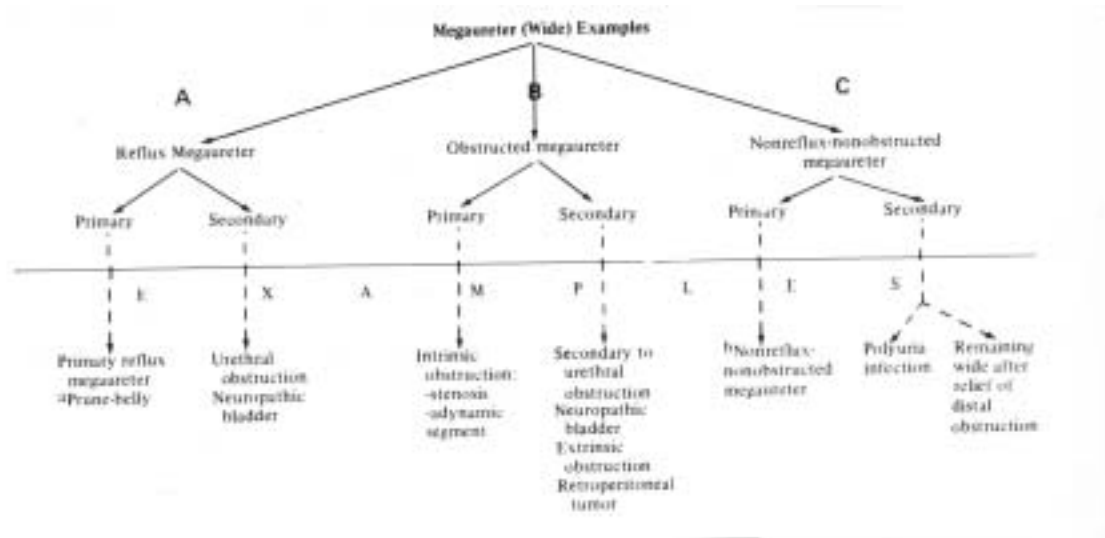

Figure 8-25. International classification of megaureter. *(Reprinted with permission from Smith et al.: Birth Defects 8(5):3, 1976.)*
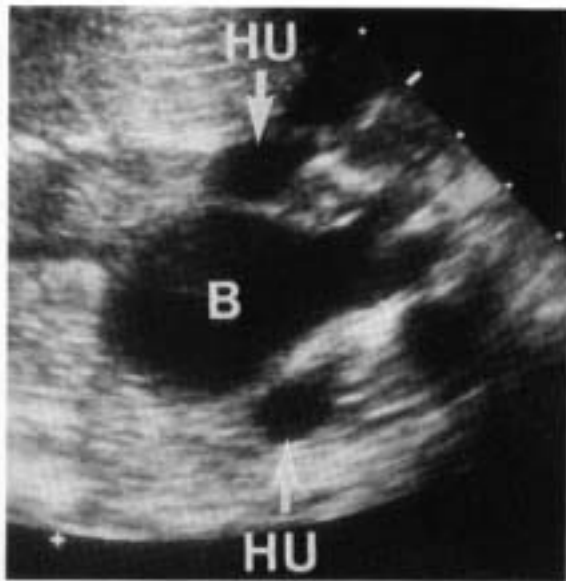
Figure 8-26. Coronal section of the fetal pelvis, showing bilateral dilatation of the ureters. This is a secondary obstructive megaureter. HU, hydroureter; B, bladder.

nonrefluxing nonobstructive megaureter is found with high rates of urine formation, such as in diabetes insipidus or infection, and in ureters that remain wide after spontaneous cessation of vesicoureteric reflux.

This chapter will only be concerned with primary megaureters, as secondary megaureters are discussed in other chapters.

Associated Anomalies

Megaureter may be associated with unilateral renal agenesis, complete or incomplete duplex system, ectopic kidney, contralateral cystic dysplastic kidney, horseshoe kidney, or Hirschsprung's disease.[15,19,25]

Diagnosis

Pathologic studies have shown that at 30 weeks the diameter of the middle portion of the fetal ureter is 1.5 mm, and, therefore, normal ureters are rarely visible with ultrasound in the human fetus. Megaureters are seen as hypoechogenic intraabdominal structures that can be traced back to the renal pelvis.

The diagnosis of a lower urinary tract obstruction is excluded by demonstrating a normal sized bladder. If an enlarged bladder is seen, the most likely diagnosis is a lower urinary tract obstruction (Fig. 8-26). However, exceptions to this have been reported. Megacystis and hydroureters associated with bilateral vesicoureteral reflux have been documented in the human fetus in the absence of any bladder outflow

obstructions The association of megaureter and megacystis has also been recognized in the absence of demonstrable obstruction or reflux (see p. 291).[18]

The renal pelvis may or may not be dilated (Fig. 8-27). In primary nonobstructive nonrefluxing megaureter, the renal pelvis is much smaller than one would expect from the ureteral dimensions, and the ureter has a straight course rather than the tortuous appearance seen in secondary refluxing hydroureter.[2] Ultrasound has been used to differentiate ureterovesical obstruction and megaureter in the neonatal period.[25]

The presence of a normal amount of amniotic fluid would suggest satisfactory renal function. However, megaureter may be associated with other malformations that lead to polyhydramnios (congestive heart failure, gastrointestinal tract abnormality). In these cases, therefore, the degree of renal deterioration is difficult to assess.[14]

Megaureter may be differentiated from mesenteric and adnexal masses because the shape of these cystic structures is not tubular but usually round. In bowel obstructions, there is usually polyhydramnios but no hydronephrosis. The dilated loops demonstrate peristalsis, and particulate matter may be seen in the lumen.

Prognosis

Whitaker and Witherow have shown that dilatations of the ureters are harmful to the kidney only if they are secondary to increased pressures within the urinary system.[23,24] At a 5-year follow-up, it was shown that when the pressure was elevated and operation was performed, improvement in the upper tract function was achieved. When the pressure was ele-
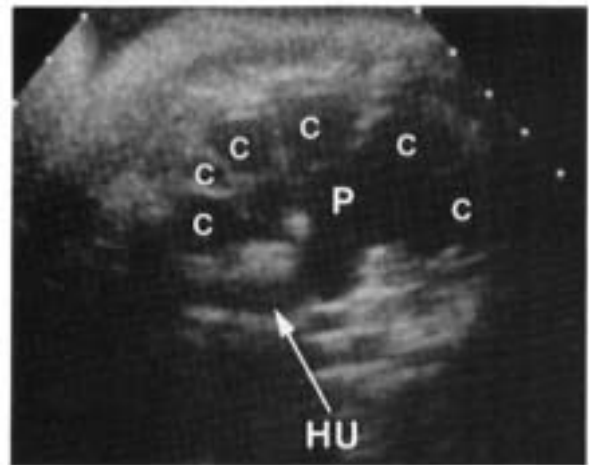

Figure 8-27. Coronal scan of a fetus with hydroureter (HU). Note the mild dilatation of the renal pelvis (P) and calices (C).

vated and operation was delayed, deterioration occurred. When the pressure was low, renal function did not worsen without operation, even though the intravenous urography appearance was unchanged. Attempts at surgical repair may worsen the prognosis by producing obstruction in at least 10 percent of patients.[1,23] Therefore, operation in these patients seems unnecessary.[24]

Obstetrical Management

Unilateral megaureter does not require a change in standard obstetrical management. Early delivery to preserve renal function may lead to respiratory distress and death of the infant.[13]

Bilateral involvement, with a normal amount of amniotic fluid, requires no intervention. There are no precedents for the management of bilateral megaureters (in the absence of lower urinary tract obstruction) associated with severe oligohydramnios.

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Posterior Urethral Valves

Definition

Lower urinary tract obstruction caused by a membranelike structure in the posterior urethra. It affects male fetuses almost exclusively.

Etiology

The disorder is usually sporadic. However, some cases of posterior urethral valves (PUV) have been reported in twins [7,20,31,32,38] and in siblings,[9,11,24,31] suggesting a genetic basis in some instances.

Embryology

Between 4 and 6 weeks of development, the primitive cloaca of a normal embryo is divided by the urorectal septum into the urinary and rectal compartments. The wolffian (mesonephric) ducts, which enter the
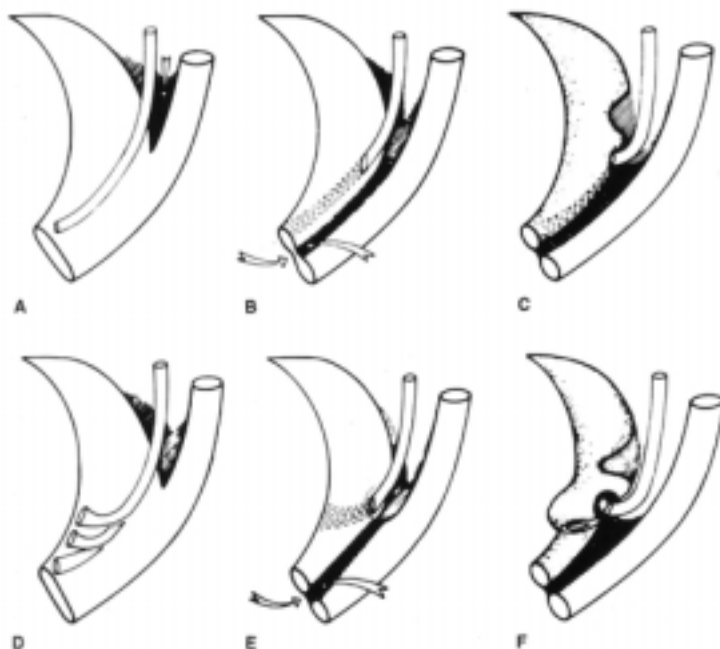
Figure B-28. Development of type I valves. **A, B, C.** Normally, the orifices of the wolffian ducts migrate from their anterolateral position to the level of verumontanum, on the posterior wall of the urorectal septum. Normal remnants of this migration are the longitudinally oriented plicae colliculi. **D, E, F.** Abnormal anterior insertion of the wolff ian duct orifices and consequent abnormal migration of the terminal ends of the ducts, resulting in circumferential obliquely oriented ridges. *(Reproduced with permission from King: In: Kelalis, King, Belman (eds): Clinical Pediatric Urology, 2d ed. Philadelphia, Saunders, 1985, Vol 1, pp 527-558.)*

anterior wall of the cloaca, recede to the level of the verumontanum (an elevation of the posterior wall of the prostatic urethra where the seminal ducts enter) in the posterior wall of the urinary compartment of the newly divided cloaca. Hence, the posterior wall of the urethra has two normal folds, called the "urethrovaginal folds" or "plicae colliculi." They are considered remnants of the cephalad migration of the wolffian ducts (Fig. 8-28). They extend longitudinally from Miiller's tubercule (a prominence located between the entrance of the two miillerian ducts in the

urogenital sinus) to the origin of the Cowper or Bartholin glands.

Urethral valves are of heterogeneous embryologic origin.[29] Some valves (Young type I) seem to result from an exaggerated development of the urethrovaginal folds with an abnormal insertion of the distal end of the wolffian ducts. Other valves (Young type III) develop because of abnormal canalization of the urogenital membrane. This explanation is consistent with the morphology of type III valves (Fig. 8-29).

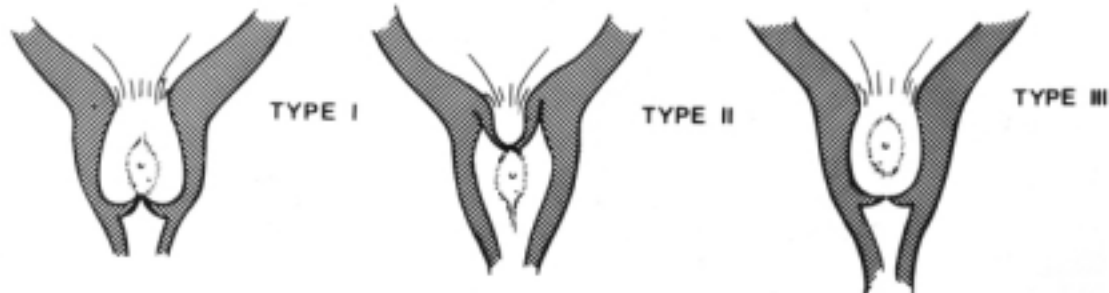

Figure 8-29. Young's classification of posterior urethral valves into three types. *(Reproduced with permission from King: In: Kelalis, King, Belman (eds): Clinical Pediatric Urology, 2d ed. Philadelphia, Saunders, 1985, Vol 1, pp 527-558.)*

Pathology

The classification of urethral valves is that proposed by Young et al. in 1919 and is simply based on the gross anatomic characteristic of the valves.[47] Type I valves are folds distal to the verumontanum that insert into the lateral wall of the urethra (Fig. 8-29). Type II valves are folds arising in the verumontanum, passing proximally to the bladder neck where they divide into fingerlike membranes. Type III valves consist of a diaphragmlike structure with a small perforation and are located distal to the verumontanum but not attached to it. In practice, type II valves do not cause obstruction, and only types I and III have clinical relevance.[14,36] Type I valves are much more common than are type III. The valves may be extremely thin and covered purely by their transitional epithelium or may contain variable amounts of connective tissue, which in extreme cases gives them a fleshy appearance.

Obstruction of the urinary flow due to the urethral valves results in compensatory hypertrophy of the detrusor. The portion of the detrusor within the

Figure 8-30. Anatomic specimen of a fetus born with posterior urethral valves. Note the distended bladder (B), tortuous ureters (U), and atrophic kidneys.

bladder neck also undergoes hypertrophy and may give the appearance of a bladder neck contracture in voiding cystourethrograms. The bladder neck may, in itself, obstruct the urine outflow.

Distention of the bladder (megacyst) eventually leads to vesicoureteral reflux and hydronephrosis (Fig. 8-30). The vesicoureteral reflux is thought to be produced by the shortening of the intravesical portion of the ureters when there is bladder distention. The portion of the ureter contained in the bladder wall is crucial for the prevention of reflux, since it acts as a valve preventing retrograde flow of urine into the ureter when intravesical pressure increases. Bilateral reflux, though not necessarily symmetrical, has a higher mortality rate and is usually present in PUV cases detected in utero. In neonatal series, reflux is generally unilateral.[28,37,46] In these patients, reflux is mainly on the left side,[21,28] the corresponding kidney is severely affected, and the contralateral kidney is usually spared, leading to a favorable prognosis.

Experimental and clinical evidence suggests that urinary obstruction severe enough to lead to hydronephrosis can cause renal dysplasia. This phenomenon is critically dependent on the time at which the obstruction occurs.[15] Observations in human and animal fetuses indicate that early obstruction leads to renal dysplasia, whereas late obstruction does not. Beck[3] demonstrated that ureteral obstruction in the fetal lamb before 70 days of gestation (term, 147 to 150 days) resulted in a renal picture similar to that of renal dysplasia (large amounts of undifferentiated mesenchymal stroma, parenchymal disorganization, cystic dilatation of the Bowman spaces, and marked fibrosis). Ligature of the ureters after 80 days of gestation resulted in hydronephrosis, but renal dysplasia did not occur. More recently, Harrison's group reported similar findings[18] and demonstrated that early in utero decompression may prevent the development of renal dysplasia.[17]

According to Potter's classification, the type of cystic kidney associated with obstructive uropathy varies depending on the timing of the obstruction. Type II dysplastic kidneys result from early obstruction. (See section on multicystic kidney disease for further details about the pathology of this condition.) If the obstruction occurs late in intrauterine life, a type IV cystic kidney results. With this variety of cystic disease, all structures are normal except for the terminal portion of the collecting tubes and the nephrons derived from them, which are dilated. There is no proliferation of connective tissue, and renal dysplasia does not occur.[25,43]

Associated Anomalies

PUV are associated in sequence with other abnormalities of the urinary tract, depending on the severity of
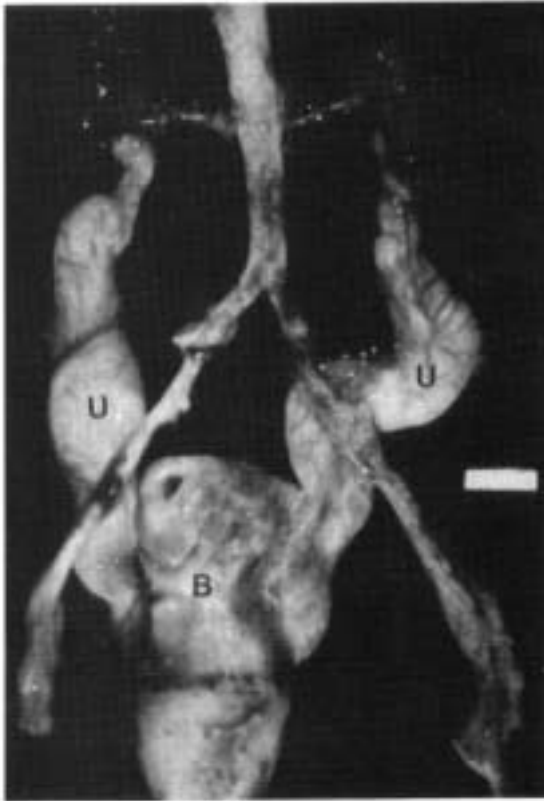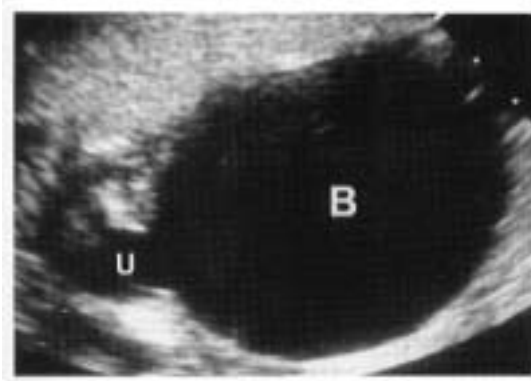
Figure 8-31. A markedly dilated bladder (B) suggests an outlet obstruction. The proximal portion of the urethra (U) is dilated.

Figure 8-32. A dilated bladder (B) and proximal urethra in a fetus with posterior urethral valves. Sp; spine.

the obstruction: megacystis, megaureter, hydronephrosis, paraureteral diverticula, and dilatation of proximal urethra. The pathogenesis of these abnormalities is obviously related to the increased upstream pressure.[36]

Other anomalies of the genitourinary tract that are associated with PUV include duplication of the urethra,[12,39] megalourethra,[33] cryptorchidism,[34] and hypospadias.[37]

Reported extraurinary anomalies include tracheal hypoplasia, patent ductus arteriosus, total anomalous pulmonary vein drainage, mitral stenosis, scoliosis, skeletal anomalies in lower extremities, imperforate anus.[16,37] Chromosomal abnormalities, including trisomies 18 and 13, del 2q, and 69 XXY have been reported in 9 of 38 cases with documented obstructive uropathy.[41]

Diagnosis

Visualization of the urethral valves is not possible with ultrasound because of their small size. A diagnosis of PUV should be suspected in the presence of sonographic signs of lower urinary tract obstruction (dilated bladder, hydroureter, and hydronephrosis) in a male infant (Figs. 8-31, 8-32, 8-33). Sex determination is important, since PUV do not occur in female infants. Causes of lower urinary tract obstruction in females include agenesis of the urethra, megacystismicrocolon-intestinal hypoperistalsis syndrome, and variants of the caudal regression syndrome. Sometimes it is possible to demonstrate the dilated posterior urethra proximal to the valves (Figs. 8-31, 8-32).

Another sign of PUV is bladder wall hypertrophy, which is visible after relief of the obstruction (Fig. 8-34). The ureters are characteristically dilated and tortuous, and in severe cases their entrance into the bladder can be observed.
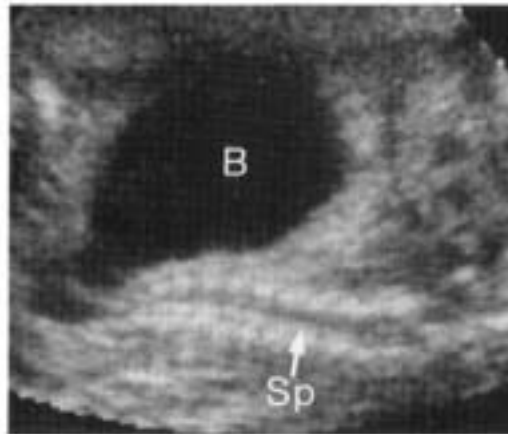
The degree of dilatation of the renal pelvis is variable. In some patients, there may be severe obstruction and renal dysplasia in the absence of marked distention of the renal pelvis. This can be explained by one of the following reasons: (1) renal dysplasia has decreased urinary production, (2) rupture at the level of the bladder or any other point along the urinary tract has resulted in decompression of the renal pelvis, or (3) there is pelviureteric atresia.

The most important consideration in regard to the kidney involves the prenatal detection of renal dysplasia.[40] Renal dysplasia can occur with both small and enlarged kidneys. The most important sonographic signs of renal dysplasia are multiple
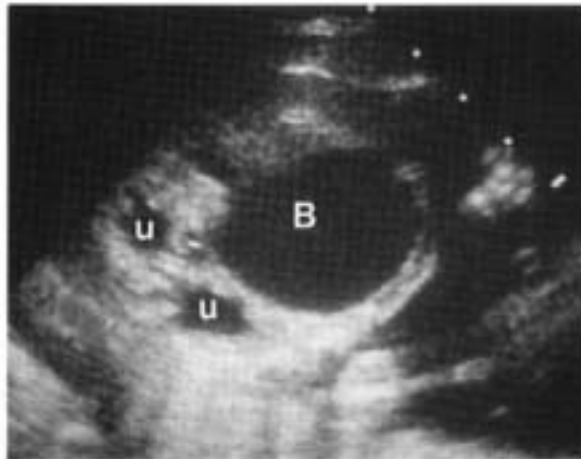

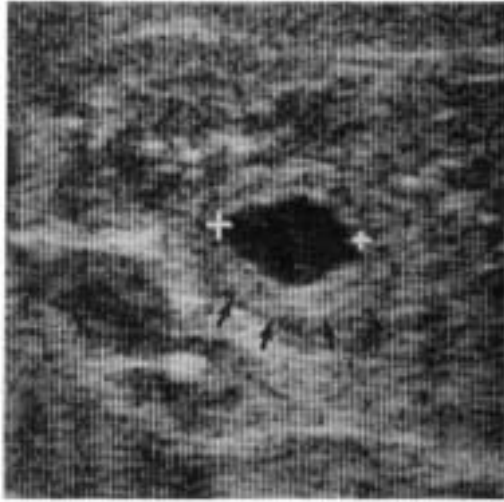**Figure 8-33.** Dilated bladder (B) and bilateral hydroureters (u).

Figure 8-34. A fetus who had posterior urethral valves and experienced resolution of the obstructive process in utero after shunting. A thickened bladder wall is visible. Arrows point to the outer bladder wall.

cysts and the hyperechogenicity of the renal parenchyma. Table 8-3 shows the diagnostic indices of renal dysplasia. The detection of renal cysts is relatively insensitive, but their presence indicates dysplastic kidneys (Fig. 8-35). Renal echogenicity is more sensitive but also less specific (Fig. 8-36). Hydronephrosis is the weakest of the renal signs in the prediction of renal dysplasia.

Urine can extravasate into the peritoneal cavity (ascites) or the perirenal space.[1,15,22] The mechanisms responsible for urine extravasation are often unknown. Rupture of the bladder can account for some cases, but the rest are attributed to transudation of urine into the peritoneal cavity. The degree of ascites is variable and can reach extreme proportions, leading to atrophy of the abdominal wall muscles (the prune-belly sequence). On occasion, there is no freefloating ascites, but an isolated perirenal urinoma persists.

Oligohydramnios is not an invariable finding and is related to the severity and duration of the obstruction. The presence of severe oligohydramnios is considered a poor prognostic sign; conversely, a normal amount of amniotic fluid is a good prognostic sign.[8,13]

In utero intravenous pyelograms have been used to confirm the diagnosis.[19] After the placement of a needle in the urinary tract, dye (2.5 ml of renographin 69)was injected to procure better visualization. The

indications for this diagnostic maneuver decrease as experience with ultrasound increases.

Some fetuses with PUV have come to the attention of the sonographer because of an elevated amniotic fluid and maternal serum AFP.[8]

The differential diagnosis includes other obstructive uropathies, such as ureteropelvic junction (UPJ) obstruction, ureterovesical junction (UVJ) obstruction, primary megaureter, and massive vesicoureteral reflux.[42] In both UPJ and UVJ obstructions, the bladder should not be dilated. The differential diagnosis between PUV and other causes of low urinary tract obstruction, such as absence of the urethra or detrusor hypertrophy, may not be possible in all cases.[27] Megacystic-microcolon-intestinal hypoperistalsis syndrome (MMIHS) is a rapidly fatal triad that affects females in 91 percent of cases and is characterized by a massively dilated, thick-walled bladder, normal to increased amniotic fluid, dilatation of the stomach with little peristaltic activity, bilateral hydronephrosis with no signs of renal damage, and no hydroureters (see p. 291).

A critical aspect of evaluation of the fetus with obstructive uropathy is the assessment of renal reserve. Infants with bilateral dysplastic kidneys have a uniformly poor prognosis. Although monographic detection of cortical cystic changes has excellent specificity in the prenatal diagnosis of renal dysplasia, its sensitivity is relatively poor. Therefore, infants with normal kidneys on ultrasound can still be born with nonfunctioning kidneys. Management decisions, such as pregnancy termination and in utero surgery, rely on assessment of renal reserve. For example, a diagnosis of renal dysfunction even in the absence of sonographic findings would render in utero shunting useless.

Attempts at evaluating renal reserve have been undertaken with (1) single drainage of the fetal bladder and documentation of reaccumulation of urine,(2)furosemide stimulation of urine production, and (3)electrolyte determination in fetal urine. The first two methods have proven to be unreliable and, therefore, have been abandoned in favor of the third option.

TABLE 8–3. DIAGNOSTIC INDICES OF DIFFERENT SONOGRAPHIC CRITERIA FOR THE IDENTIFICATION OF RENAL DYSPLASIA IN OBSTRUCTIVE UROPATHY

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Renal cysts	44	100	100	44
Hyperechogenic renal parenchyma	73	80	89	57
Hydronephrosis	41	73	78	35

Reproduced with permission from Mahony, Filly, Callen, et al.: Radiology 152:143, 1984.
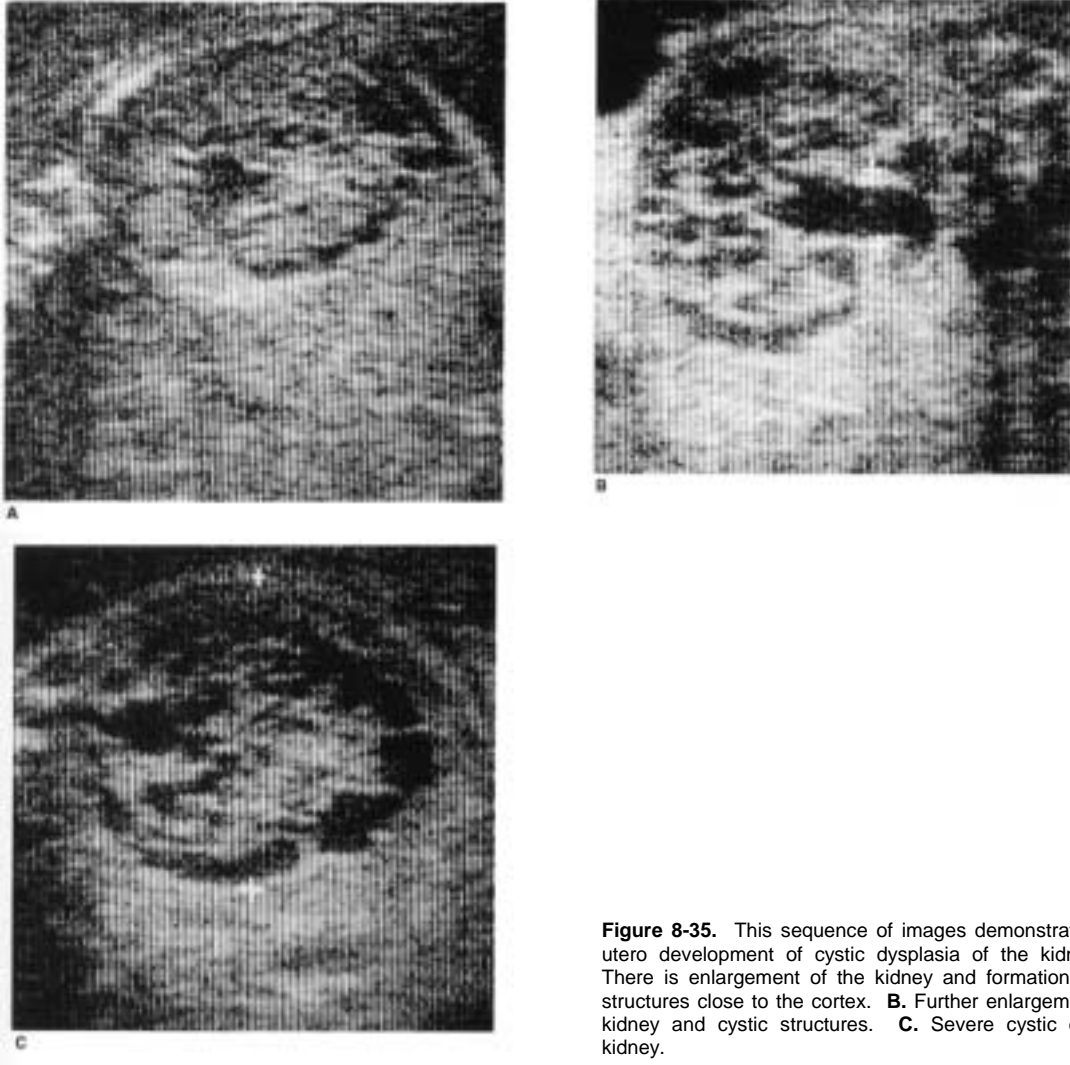
Figure 8-35. This sequence of images demonstrates the in utero development of cystic dysplasia of the kidneys. **A.** There is enlargement of the kidney and formation of cystic structures close to the cortex. **B.** Further enlargement of the kidney and cystic structures. **C.** Severe cystic dysplastic kidney.

Studies have been accomplished by puncturing the bladder and assaying electrolytes and osmolarity in the first urine sample obtained.[16] In addition, fetal urinary output has been measured by placing a balloon-tipped catheter (4F Model JC-211, Critikon Inc, Tampa, FL) into the dilated fetal bladder. The concentrations of sodium, chloride, and osmolarity correlated with renal function at birth. Poor function was defined as the presence of severe renal dysplasia and pulmonary hypoplasia at autopsy or biopsy, or renal and pulmonary insufficiency at birth. Good

function was based on nondysplastic kidneys at autopsy or biopsy or normal renal and pulmonary function at birth. Table 8-4 illustrates the prognostic criteria for fetuses with bilateral obstructive uropathy. The fetus with renal damage acts as a salt loser, and, therefore, the concentration of electrolytes and osmolarity in the urine are elevated. With the exception of urinary output per hour, information about these prognostic criteria can be obtained by a single puncture of the fetal bladder and a sonographic examination. It is unclear if quantitation of fetal
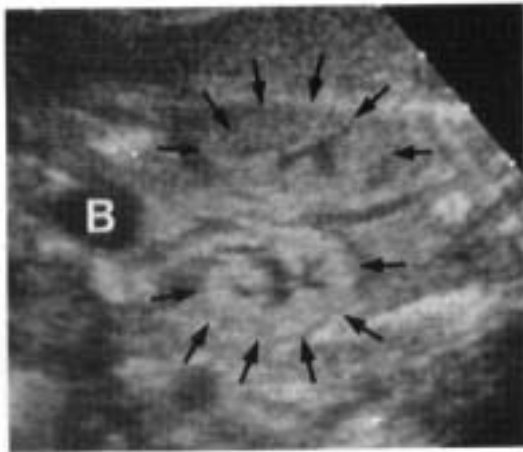
Figure 8-36. Coronal scan showing increased echogenicity of the renal parenchyma of a fetus with posterior urethral valves. There is oligohydramnios, and a normal-sized bladder (B). The infant was born with cystic dysplastic kidneys. Arrows point to the renal parenchyma.

diuresis provides valuable information. Furthermore, infectious complications have occurred during exteriorization of the fetal bladder, leading to death in 3 of 9 fetuses. Therefore, this invasive procedure does not seem justified.

Prognosis

The only data on long-term prognosis have been gathered from cases diagnosed after birth. Caution is advised in extrapolating these figures to infants diagnosed in utero, since the natural history of the disease may be different. The timing of the occurrence of urinary obstruction is a critical factor in determining the extent and severity of renal damage. When the condition is diagnosed in utero, the prog-nosis seems much worse. Affected neonates are at high risk (32 to 50 percent) for death,[10,44] as a result of pneumomediastinum and pneumothorax related to pulmonary hypoplasia, associated congenital anom-alies, renal failure, and surgical complications after decompressive surgery.[37] Survivors have a higher incidence of growth retardation, expressed as a lower percentile of height and weight for a given age. Catch-up growth occurs after corrective surgery.[35] Improvement in renal function is demonstrated in most patients after surgery. However, chronic parenchymal deterioration can continue despite treatment. Renal hypoplasia and dysplasia and chronic pyelonephritis are thought to play a role, but the precise mechanisms for progressive renal failure despite correction of the obstruction are unknown. The development of end- stage renal disease may be delayed for 9 to 10 years.[45]

The incidence of chronic renal failure in infants diagnosed in the first 3 months of life is 39 percent.[1] The most important prognostic factor for the prediction of good renal function seems to be the postoperative nadir of serum creatinine during the first year. Levels of 0.8 mg/ml or less are associated with good prognosis, and levels of 1 mg/ml or less are associated with long-term normal growth.[46]

The outcome of infants who have undergone vesicoamniotic shunt is available from the International Fetal Surgery Registry. Of a total of 73 treated patients, 11 elected to terminate the pregnancy after shunt placement. The reasons for termination were an abnormal karyotype (n = 6) or the development of monographic signs of renal dysplasia. The survival for the remaining 62 patients was 48 percent. Survival could not be related to fetal age at the time of diagnosis or treatment but was related to fetal sex and to the etiology of the obstruction. Male infants did better (survival = 51 percent) than female infants (survival = 20 percent). There were 3 stillbirths and 29 postnatal deaths. Pulmonary hypoplasia was the most common cause of neonatal death.

Obstetrical Management

Once the diagnosis of the lower urinary tract obstruction is made, management depends on the detection of other life-threatening anomalies, gestational age at diagnosis, and status of renal function.

A search for associated anomalies is important, but sonographic evaluation is frequently hampered by the associated oligohydramnios. The instillation of fluid into the amniotic cavity may be required to improve visualization. This can be accomplished by the injection of a solution warmed to 37C. Chromosomal analysis should be undertaken when feasible by either amniocentesis or fetal blood sampling. A recent study indicated that 23 percent of infants with obstructive uropathy had chromosomal abnormalities.[41] If a chromosomal or anatomic anomaly incompatible with life is detected (e.g., trisomy 18 or holoprosencephaly), the option of preg-

TABLE 8–4. PROGNOSTIC CRITERIA FOR FETUSES WITH BILATERAL OBSTRUCTIVE UROPATHY

Poor Prognostic Signs	Good Prognostic Signs
Severe oligohydramnios	Normal amniotic fluid
Cystic kidneys	Normal kidneys
Na > 100 mEq/ml	Na < 100 mEq/ml
Cl > 90 mEq/ml	Cl < 90 mEq/ml
Osmolarity > 210 mOsm	Osmolarity < 210 mOsm
Urinary output of < 2 ml/hr*	Urinary output > 2 ml/hr

* Urinary output was measured by exteriorizing the fetal bladder with an indwelling catheter for several hours.
Reproduced with permission from Glick, Harrison, Golbus, et al.: J Pediatr Surg 20:376, 1985.

nancy termination at any stage of gestation can be considered.

The next step in the evaluation process is assessing the renal reserve by referring to the criteria outlined in Table 8-4. Of particular importance is the amniotic fluid volume, since infants with normal amniotic fluid seem to have an excellent prognosis.

With good prognostic criteria, there are little data to advise parents about the long-term risks to the infant. Theoretical risks would include worsening of the condition in utero, requirement of in utero surgery or premature delivery, development of pulmonary hypoplasia, or some long-term impairment of renal function.

If prognosis is poor based on the criteria outlined in Table 8-4, alternatives include pregnancy termination or nonintervention. If the prognosis is good, further management decisions are based on the gestational age. If the diagnosis is made at a gestational age when pulmonic maturity is likely, an L:S ratio determination is indicated. In the presence of lung maturity, the patient should be delivered in a tertiary care center where urologic evaluation can be performed after birth. The mode of delivery should not be affected by the diagnosis.

When the diagnosis has been made after viability but before lung maturity, weekly serial examinations are required. The options are (1) preventive utero decompression or (2) expectant management and intervention only when the amniotic fluid volume decreases. The optimal management between these options has not been established. Harrison's group[23] at the University of California, San Francisco, favors the second option.

Choice of Intrauterine Surgery. Two different procedures can be performed for decompression of obstructive uropathy in utero: placement of a shunt and suprapubic vesicostomy. Indwelling catheters frequently become dislodged or occluded, and, therefore, they are most effective when used in circumstances that require short-term decompression (urinary obstructions detected in late pregnancy while awaiting fetal lung maturity). Harrison's group[23] has performed two suprapubic vesicostomies in early pregnancy. This procedure seems more efficient in the treatment of an obstruction, since the likelihood of reobstruction is small. However, it requires a hysterotomy, and the risks of this operation are yet to be established.

Technique for Catheter Placement. The procedure requires sedation of both fetus and mother. This can be accomplished by the parenteral administration of diazepam or morphine. In the presence of severe oligohydramnios, the instillation of fluid into the amniotic cavity is necessary to create a space in which the amniotic coil can be placed.

Several catheters have been employed to create a vesicoamniotic shunt. We have used a 6.5 Fr polyethylene instrument constructed from an angiographic catheter.[5] Harrison's group uses a kit that contains a Harrison fetal bladder stent, 8 Fr (Model 03408-1, VPI, Inc., Spencer, IN).[23] The catheters have a double pigtail. One end is destined to coil into the bladder and the other into the amniotic cavity. The catheters are constructed from material that maintains the curved shape and will not disappear even when the catheter is mounted onto a straight needle for insertion. This property is referred to as the "memory" of the shunt. Several lateral sideholes are made along both coils. The straight portion of the catheter should not contain any holes; otherwise, leakage of urine into the fetal peritoneal cavity will occur.

The needle is 19 gauge and 29 cm long. A pusher made of the same material as the catheter is required and should be long enough to permit advancement of the catheter. The other instrument required is a sterile ruler to intraoperatively assess the amount of catheter that has been advanced. The catheter is specifically designed for each patient, taking measurements of the fetal bladder and of the fetal abdominal wall into account.

The procedure can be conducted in three major steps:

1. Introduction of the catheter into the fetal bladder. A small incision in the maternal abdominal wall and rectus sheath is performed with a scalpel. Local anesthesia is required. Once the needle is in the fetal bladder, the catheter is advanced the length of the distal pigtail. The last orifice of the pigtail should be inside the fetal bladder. Ultrasound can demonstrate the coiled catheter within this organ.
2. Withdrawal of a segment of the needle until its tip is in the amniotic cavity. The length of needle to be removed corresponds to the straight portion of the catheter. During this maneuver, the pusher must not be moved. It is important that a pocket of fluid be created at the beginning of the procedure if one was not already present. Otherwise, the creation of the second coil becomes extremely difficult.
3. Advancement of the pusher until the second coil is created inside the amniotic cavity. This is the most difficult part of the procedure. If calculations have not been correct, the distal end of the catheter may end up in the uterine or maternal abdominal wall. Another technique of inserting the catheter through an introducer needle is now being evaluated. Initial results are encouraging.

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Prune-Belly Syndrome

Synonyms

Triad syndrome (abdominal wall distention, urinary tract obstruction, and cryptorchidism) and Eagle-Barret syndrome.

Definition

Prune-belly syndrome describes the association of hypotonic abdominal wall, large hypotonic bladder with dilated ureters, and cryptorchidism. Prune-belly syndrome may be considered a malformation sequence due to intrauterine abdominal wall distention. Such distention is most frequently due to an obstructive uropathy, but other causes could lead to the morphologic features of the syndrome in the absence of urinary involvement.

Epidemiology

The incidence varies from 1 in 35,000 to 1 in 50,000 live births.[9] The overwhelming majority of affected infants are males. Fewer than 20 of more than 300 reported cases have been females.

Etiology

Genetic basis for prune-belly syndrome has not been established, although it has been documented in siblings.[2,8] The risk of recurrence of this condition is unknown, but parents should probably be told that this is a possibility. Cases associated with chromosomal anomalies (trisomy 13, 18, and 45XO) have been reported.[3,7,13]

There is an association between prune-belly syndrome and twinning. The incidence of twinning in the general population is 1:80, and in prune-belly syndrome, it is 1:23.[11] All reported cases in twins are discordant for the syndrome.

Pathogenesis

There are two theories to explain this syndrome. The mesodermal defect theory proposes that abdominal wall laxity is the result of an early embryologic insult affecting the mesoderm of the anterior abdominal wall and the urinary tract.[4,5] However, increasing evidence suggests that the pathogenesis of prune-belly syndrome can be explained by the urethral obstruction malformation complex.[15,17] According to this view, urethral obstruction leads to massive distention of the bladder and ureters, which in turn causes pressure atrophy of the abdominal wall muscles. Bladder distention also interferes with the descent of the testes and is responsible for cryptorchidism. The obstructive nature of the bladder distention explains the presence of muscular hypertrophy in the bladder wall, tortuous hydroureters, renal dysplasia, and a persistently open urachus. A distended bladder could also exert compression on the iliac vessels and lead to limb deficiencies. The urethral obstruction causes severe oligohydramnios and features of the oligohydramnios sequence, such as pulmonary hypoplasia, skeletal deformities, and Potter facies.

The major objection to this theory has been that not all newborns with prune-belly syndrome have a urethral obstruction at birth. However, it is possible for transient in utero urinary obstruction to cause the sequence responsible for the syndrome.[6] Prune-belly syndrome could be the result of an intraabdominal distention unrelated to obstruction of the urinary tract. For example, transient ascites,[12,19] intestinal duplication cysts,[16] and megacystis-microcolon syndrome also cause the malformation sequence.

Pathology

The deficiency in abdominal wall muscles ranges from a virtual agenesis to hypoplasia.[10] Poor abdominal wall musculature does not increase significantly the risk for postoperative hernias. The impaired support of the lower chest contributes to ineffective coughing, hence, the susceptibility of these infants to respiratory infections. Cryptorchidism is associated

with impaired fertility probably due to abnormal spermatogenesis.[21] Hormonal production by the undescended testes is normal. Intraabdominal testes are at risk for malignant transformation.[23] The limb deformities have a wide spectrum, from those associated with oligohydramnios (equinovarus and dimple in the elbow and knee joint) to amputations. Most patients also have some intestinal malrotation, which has been attributed to a universal mesentery with unattached cecum.[22] Congenital heart disease has been reported in 10 percent of patients.[1]

Diagnosis

Prune-belly syndrome can be diagnosed in utero if spontaneous resolution of the intraabdominal distention responsible for the sequence occurs. Then, an abnormal tendency of the abdominal wall to depress when in contact with solid parts of the fetus (limbs) or to move by external percussion applied to the maternal abdomen can be documented.[14,19,20]

Prognosis

Prune-belly syndrome has a wide spectrum of severity. Some infants with severe oligohydramnios die in the neonatal period because of pulmonary hypoplasia or pneumothorax (type I prune-belly syndrome). Others survive the neonatal period and may develop renal insufficiency if urinary obstruction was the cause of the sequence (type II). The mild cases may have incomplete extrarenal features of the syndrome; the uropathy is less severe, and renal function is stable (type III).[22]

The abdomen offers a serious cosmetic problem. Several operations are available to assist in the correction of the abdominal wall reconstructions The other aspect of the rehabilitation of patients with prune-belly syndrome is the surgical treatment of the obstructive uropathy (see Posterior Urethral Valves, p. 280). Urologic evaluation is mandatory. Surgical correction of the large bladder, vesicoureteral reflux, and megaurethra may be required. Undescended testes are generally treated surgically.[23]

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Megacystis-Microcolon-Intestinal Hypoperistalsis Syndrome

Synonym
Neonatal hollow visceral myopathy.[6]

Definition
Megacystis-microcolon-intestinal hypoperistalsis (MMIH) syndrome consists of the association of a distended unobstructed bladder, a dilated small bowel, and distal microcolon.

Incidence
This syndrome was first described in 1976,[2] and since then, 26 cases have been reported in the literature. The condition affects predominantly female infants. Of the 26 reported cases, only 3 have occurred in males.[4,9]

Etiology
Most cases are sporadic, although some familial cases have been reported.[2]

Pathology
There is a distended unobstructed bladder. Hydronephrosis is present in virtually all patients. Gastric and intestinal motility is impaired and leads to malnutrition. The small bowel is short, dilated, and malfixed, but no anatomic obstruction can be found in most patients. Microcolon (narrow rectum and sigmoid colon) is a transient feature of the syndrome, possibly related to the hypoperistalsis. Should the baby survive, all the segments of the colon become normal in size or dilated.[9] Histologically, there are normal ganglia.[1,3] Puri et al.[6] called attention to the similarity between MMIH syndrome and a smooth muscle disorder seen in adults, chronic idiopathic intestinal pseudoobstruction (CIIP). This syndrome is a familial condition characterized by bladder, intestinal, ureteral, and esophageal dysfunction. Electromicroscopic studies have shown vacuolar degeneration of smooth muscle similar to that reported by Puri et al. in MMIH. Therefore, it is possible that MMIH syndrome and CIIP represent expressions of the same disorder.

Diagnosis
In eight cases, antenatal visualization of this syndrome has been reported.[4-8] MMIH syndrome should be suspected in the presence of a distended bladder with a normal or increased amount of amniotic fluid in a female fetus. There may be hydronephrosis. The main differential diagnosis is obstructive uropathy due to posterior urethral valves. In a female fetus, a low urinary tract obstruction can be due to absence of the urethra, to variants of the caudal regression syndrome, or to the rare detrusor hypertrophy. In these conditions oligohydramnios is severe.

Prognosis
MMIH syndrome is a lethal condition in most cases. Of the 23 reported patients, 21 died in the immediate postoperative period or shortly thereafter. The cause of death is bowel renal dysfunction. Infants have died despite hyperalimentation. Sepsis is frequently noted in published reports as a final complication.

Obstetrical Management
In the absence of a positive family history, it is unclear if this diagnosis can be made with certainty. A massively dilated bladder has been a cause of soft tissue dystocia in one patient.[6] Therefore, consideration should be given to prenatal drainage of this organ. There does not seem to be any reason to induce preterm delivery of these infants.

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Congenital Mesoblastic Nephroma

Synonyms

Leiomyomatous hamartoma, fetal mesenchymal hamartoma, and fetal renal hamartoma.

Incidence

Congenital mesoblastic nephroma (CMN) is a rare renal tumor occurring in the neonatal period.[10] It affects males more frequently than females.[13]

Pathology

CMN is generally a solid tumor that is identified as a unilateral mass varying in weight from 35 to 450 g.[5] On several occasions, it has been confused with Wilms tumor,[7,16,17,19] from which it is indistinguishable by radiography and sonography.[7,11,15] However, prognosis and treatment of the two tumors are very different.

Macroscopically, CMN occurs most often as a solid, circumscribed mass resembling leiomyoma of the uterus, but the tumor may exhibit pseudocystic areas resulting from cavitation necrosis or hemorrhage.[4,10-12,18,20]

Histologically, it is composed of mesenchymal cells, regarded as smooth muscle cells, immature fibroblasts, or both,[2,5,7,22] with islands of glomeruli, tubules, vascular structures, and hematopoietic elements. The tumor is not encapsulated and may infiltrate the tissues located nearby. In rare instances, it may show a malignant pattern ("malignant mesenchymal nephroma of infancy") with irregularly shaped cells, a high nucleus:cytoplasm ratio, areas of necrosis, and more than 10 mitoses per 10 HPF (high power fields).[2,10,16]

Associated Anomalies

Of 51 children with CMN, 7 had congenital anomalies (14 percent), including polydactyly, gastrointestinal malformations, hydrocephalus, and genitourinary anomalies.[13]

Diagnosis

The antenatal visualization of mesoblastic nephroma has been reported on several occasions,[1,6,11,14,21,23] with the earliest diagnosis made at 26 weeks.[1] A specific diagnosis is not feasible with ultrasound. The condition can be detected by identification of a unilateral solid mass in one of the upper abdominal quadrants (Fig. 8-37). The mass usually arises from the renal fossa and compresses the involved kidney. The interface between the tumor and the normal parenchyma may give the monographic appearance of a capsule surrounding the tumor. Polyhydramnios is always present although the reason for this association is unknown.[3]

Differential diagnosis should include Wilms tumor, other renal tumors, such as teratomas, and neuroblastomas of adrenal glands. IPKD can be excluded by the association of oligohydramnios and nonvisualization of the fetal bladder, with bilaterally enlarged kidneys.

Prognosis

All babies in whom the tumor was diagnosed in utero were operated on in the neonatal period and did well. Preterm labor or premature rupture of membranes complicated four of the pregnancies in which there was prenatal visualization of the tumor.[1,9,14,21] The mean weight of the patients diagnosed prenatally was 2140 g. In one report, 7 of 30 infants with CMN weighed less than 2275 g.[3] To date, the tumor has been reported in two stillborn infants.[19] The prognosis for this condition is generally good since it is unilateral and nearly always benign. However, reports in the literature have documented recurrences after incomplete surgical excision[7,13,16,20] in one infant[20] and metastases to the lung in another.[10] It would seem that infants diagnosed in the first 3 months of life usually have a benign variety of this tumor, with more aggressive behaviors appearing after 3 months of age.[10]

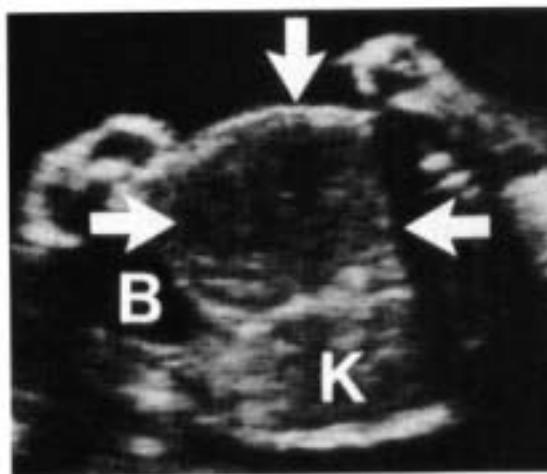The treatment of choice is surgical removal (ne-

Figure 8-37. Transverse section of the fetal abdomen demonstrating a unilateral solid mass in the renal fossa adjacent to the fetal bladder (B). The contralateral kidney (K) is normal. *(Reproduced with permission from Giulian: Radiology 152:69, 1984.)*

phrectomy).[5,8,13] If the histologic status is worrisome or

10. Gonzalez-Crussi F, Sotelo-Avila C, Kidd JM:

there is some residual tumor left behind following surgery, follow-up is indicated and postoperative chemotherapy or radiotherapy may be necessary.[2,10]

Obstetrical Management
The diagnosis of a renal tumor is an indication for serial sonography to monitor tumor growth and to check for associated anomalies.

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Wilms' Tumor

Synonym
Nephroblastoma.

Incidence
The random risk of developing Wilms' tumor has been estimated to be 1 in 10,000 live births.[17] The annual incidence has been estimated to be 7.8 per 1,000,000 children under the age of 15 years.[10,14] The precise incidence of this tumor in the neonatal period is unknown. The male to female ratio is nearly 1:1.[2,14]

Etiology
The tumor can occur sporadically or with a familial tendency. The pattern of inheritance has been suggested to be autosomal dominant with variable penetrance (the likelihood that an individual who inherits the gene will develop the disease) and expressivity (the clinical variability of the inherited disease). The

overall penetrance for inherited tumors is 63 percent.

Diagnosis

Bilateral tumors are more likely to be familial than unilateral tumors. The likelihood that a sibling will have the tumor after one affected sibling is less than I percent if the tumor is unilateral and 1 to 2 percent with bilateral tumors. The offspring of a patient with Wilms' tumor has a 5 percent risk of having the neoplasm if the tumor was unilateral and a 32 percent risk if the tumor was bilateral.[3]

Wilms' tumor can be part of Perlman syndrome, a condition inherited with an autosomal recessive trait, characterized by renal dysplasia, fetal gigantism, and hyperplasia of the endocrine pancreas. [12,13]

Pathology

The tumor possibly results from abnormal differentiation of metanephric blastema. Most cases are unilateral (95 percent). Spread occurs by local invasion and also by vascular and lymphatic dissemination. However, it can develop simultaneously and multifocally in both kidneys,[11] suggesting a coexisting malformation.[15] The tumor is solid, and growth can be exophytic or endophytic. The renal parenchyma is frequently replaced by the tumor.

Associated Anomalies

Similarly to mesoblastic nephroma, Wilms' tumor is associated with an increased incidence of congenital anomalies, with a reported incidence of 13.7 percent.[2] Genitourinary abnormalities account for 28 percent of all anomalies seen in Wilms' tumor, and they are found in 3.9 percent of all patients.[2] External genital abnormalities seem to be 12 times more common in bilateral than in unilateral tumors.[1] Most of these anomalies cannot be detected antenatally. They include cryptorchidism, hypospadias, double collecting system, fused kidneys, and ambiguous genitalia.

Hemihypertrophy consists of total, segmental, or crossed hypertrophy of the body. This complication may not be present at the time of birth, and, therefore, it may not be diagnosable in utero. It is more common in association with bilateral Wilms' tumor, and the overall incidence of this complication is 2.47 percent. If the Beckwith-Wiedemann syndrome (exophthalmos. macroglosia, gigantism, and visceromegaly) is associated with hemihypertrophy, the likelihood of a neoplasm is 25 percent. This tumor could be an adrenocortical neoplasia, Wilms' tumor, Hepatoblastoma, or gonadoblastoma.

An association of Wilms' tumor with deletion of 1l p3 and aniridia has been reported. Other occasional chromosomal abnormalities reported with Wilms' tumor include trisomy 18, Turner syndrome, and a B-C chromosomal translocation.[7]

The prenatal diagnosis of this tumor has not been reported as yet, but is seems feasible, since Wilms' tumor is known to occur in newborns[5,6,8,9,13,16] and in fetuses.[15] The condition should be considered in the presence of a solid mass in the fetal renal fossa, even though the most common tumor in the neonatal period is mesoblastic nephroma, which is not distinguishable sonographically from Wilms' tumor.[10] Careful examination of the opposite side is indicated.

Prognosis

The prognosis depends on the histologic type, lymph node invasion, and stage and size of the tumor at the time of the diagnosis. The treatment approach includes surgery (nephrectomy), with adjuvant therapy according to the stage and histologic type. Adjuvant therapy consists of chemotherapy or radiotherapy. The results of the second national Wilms' tumor study revealed over a 90 percent 2-year survival rate for patients with a favorable histology in stages I, II, and III, 60 percent in stage IV with a favorable histology, and 35 percent in stage IV with an unfavorable histology.[4]

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Normal Anatomy of the Adrenal Glands

The adrenal glands are relatively large organs in the fetus and the newborn (Fig. 8-38). Relative to body weight, their size is 10 to 20 times greater in the fetus than in the adult.[1]

The adrenal glands consist of two different endocrine organs: the medulla and the cortex. The medulla is of ectodermic origin, and the cortex is a mesodermal derivative. The large size of the fetal adrenal glands is due to the cortex, which decreases in size after birth.

The normal adrenal glands can be imaged with ultrasound as early as 9½ weeks of gestation. They appear as bilateral midecho structures located immediately above the fetal kidneys (Figs. 8-39, 8-40).

During early gestation, they may appear as a hypoechogenic ring with a central hyperechogenic line. The thickness of the central hyperechogenic line gradually increases from one third to one half after 35 weeks. The large vessels can be used as two landmarks to define adrenal gland position; the inferior vena cava is close to the anterior part of the right adrenal gland, and the aorta is close to the left adrenal gland.[2,3]

Normal dimensions of the adrenal gland are given in Table 8-5. The thickness and width are measured in a transverse scan obtained by moving the transducer slowly cephalically to a transverse scan of the kidney. The longitudinal section is of

Figure 8-38. Pathologic specimen from a stillbirth. Note the relative large size of the adrenal glands (A) compared to the kidney (K).
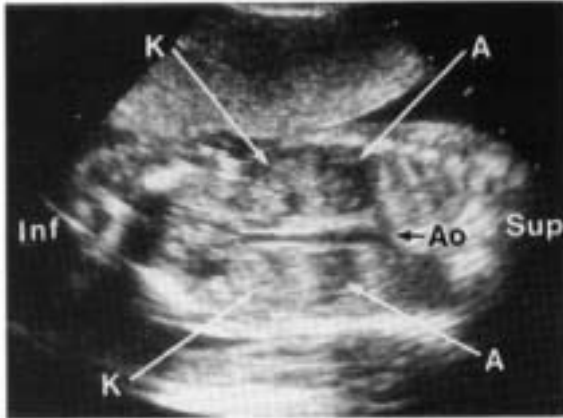
Figure 8-39. Longitudinal scan of a 21 -week-old fetus showing the adrenal gland **(A).** The kidneys **(K)** can be demonstrated inferior to the adrenals. Ao, aorta; Sup, superior; Inf, inferior.
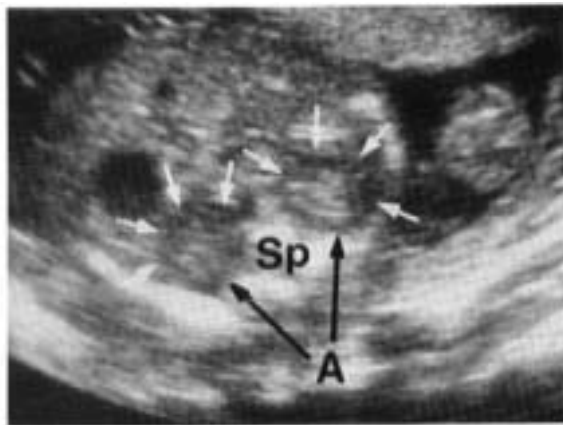

Figure 8-40. Transverse scan in a 22-week-old fetus. White arrows point to both adrenal glands (A). The hypoechogenic image anterior to the adrenal corresponds to the fetal stomach. Sp, Spine.

TABLE 8-5. SIZE OF THE FETAL ADRENALS

Gestational Age (weeks)	Mean Thickness (range) (mm)	Mean Width (range) (mm)
20–25	3 (2–5)	10 (7–12)
26–30	5 (2–8)	13 (12–17)
31–35	5 (3–7)	16 (14–18)
36–40	6 (4–9)	19 (16–24)

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limited value because acoustic shadowing from the ribs often conceals the interface between the kidney and the adrenal gland.

The sonographer should be familiar with the image of the fetal adrenals to avoid confusing them with fetal kidneys. Furthermore, some pathologic conditions, such as adrenoblastomas, could be diagnosed with ultrasound. The value of fetal adrenal biometry in the prenatal diagnosis of congenital adrenal disorders is speculative at this time.

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Congenital Adrenal Neuroblastoma

Synonym
Adrenoblastoma.

Incidence
Congenital adrenal neuroblastoma is the most common abdominal tumor found in newborns, and it accounts for 12.3 percent of all perinatal neoplasms.[23] Its incidence has been estimated to vary from 1 in 10,000 to 1 in 7100 live births.[13,52] The neuroblastoma in situ is a histologic variant of malignant neuroblastoma characterized by its microscopic size and absence of metastases. Autopsy series show that incidental neuroblastomas in situ occur in 1 in 200 to 250 stillbirths and infants who have died under 3 months of age. This is 40 times greater than the incidence of clinically manifested neuroblastoma.[6,20,43] Therefore,

neuroblastoma in situ is either not a true tumor or has an extremely high rate of spontaneous regression.[22,27]

Embryology

The cortex and the medulla of the adrenal glands have different origins. The cortex develops during the 6th week of conceptional age by an aggregation of mesenchymal cells from the coelomic epithelium that lines the posterior abdominal wall between the dorsal mensentery and the developing gonad. The medulla originates from neuroectoderm. Neuroblasts migrate from the neural crest into the developing adrenal cortex to form the adrenal medulla.

Etiology

Adrenal neuroblastomas are considered a defect in neuroblast maturation. The presence of tumorspecific chromosome abnormalities in some neuroblastomas suggests a hereditary form.[32] Indeed, there are reports of neuroblastomas in monozygotic twins[30] and in families.[11,17,19,29,39] This, together with the tumor bilaterality and its occurrence in early life, suggests a familial tendency. It has been estimated that about 20 percent of neuroblastomas have a hereditary component.[28] Neuroblastoma has been associated with fetal hydantoin syndrome.[1,13]

Pathology

Neuroblastomas are almost always unilateral tumors. Fifty percent have metastases at birth.[42] They can invade the surrounding tissues (e.g., kidneys) or produce distant metastases. In the fetus, the most common sites for metastasis are liver (two thirds), and subcutaneous tissue (one third).[5,42] Placental involvement, both as tumor embolism and metastatic spread, has been described.[2,25,37,45,46,48]

Macroscopically, these tumors are soft, often with areas of hemorrhage, calcification, or necrosis. The histology may vary, ranging from the very malignant and poorly differentiated neuroblastoma through the ganglioneuroblastoma to the relatively benign and mature ganglioneuroma. Different patterns of malignancy can be found in the same tumor, and histologic type has not been found to be a reliable indicator of prognosis. Staging of the tumor is based on surgical findings. Stage I is a tumor limited to the adrenal gland, stage II consists of regional spreading that does not cross the midline, stage III refers to tumors extending over the midline, and stage IV includes patients with metastasis to distant lymph nodes, bone, brain, or lung. A special category is stage IV-S which includes patients with a small primary tumor and distant metastases limited to liver, skin, and bone marrow without radiologic

evidence of bony metastases.[15] In 75 to 90 percent of cases, neuroblastomas have hormonal activity with production of cathecolamines.[15,41] However, endocrine symptoms are rare, probably because the catecholamines are quickly converted into the inactive vanillylmandelic and homovanillic acids, which are excreted in the urine.[14]

Associated Anomalies

Neuroblastoma may be associated with other lesions resulting from maldevelopment of the neural crest, such as Hirschsprung's disease.[8,11] The possible association of neuroblastomas with other anomalies has been a matter of discussion. Most associated anomalies have been reported with neuroblastoma in situ. Since this entity is a relatively common finding in autopsy series and is thought to represent a normal variation of the morphogenesis of the adrenal glands,[6] such associations are not relevent to clinical neuroblastomas.[47] This view is supported by the report of Miller, who reviewed the records of 502 children with clinically apparent neuroblastoma and could not find an increased incidence of associated anomalies.[31] Furthermore, a case-controlled study of 157 children who died from neuroblastoma did not show an increased incidence of associated anomalies.[26]

Diagnosis

Prenatal visualization of neuroblastomas has been made in the third trimester.[4,18,24] The tumor appears as a mixed cystic and solid mass in the upper part of the kidney (Fig. 8-41), but its sonographic aspect varies considerably.[51] Calcifications may be present. A precise identification of the adrenal origin of the mass is difficult. The visualization of the kidneys separate from the mass would be helpful. These organs may be deformed by the tumor. In one patient, the primary tumor was not visualized, but cervical metastasis resulted in the visualization of solid masses in the region of the neck.[16] In some patients, congenital neuroblastoma is associated with hydrops fetalis.[2,16,25,33,34,38,46,48] No clear explanation has been proposed for this association.

About 75 to 90 percent of neuroblastomas release catecholamines. Transplacental passage of these hormones can lead to maternal symptoms and signs of catecholamine excess (nausea, vomiting, nervousness, sweating, headaches, hypertension).[34,49] The combination of maternal symptoms of cathecolamine excess and a suspected fetal mass is highly suggestive of fetal adrenoblastoma. Objective evidence of a cathecolamine excess can be gathered by demonstrating elevated vanillylmandelic and homovanillic acid in a 24-hour maternal urine specimen.

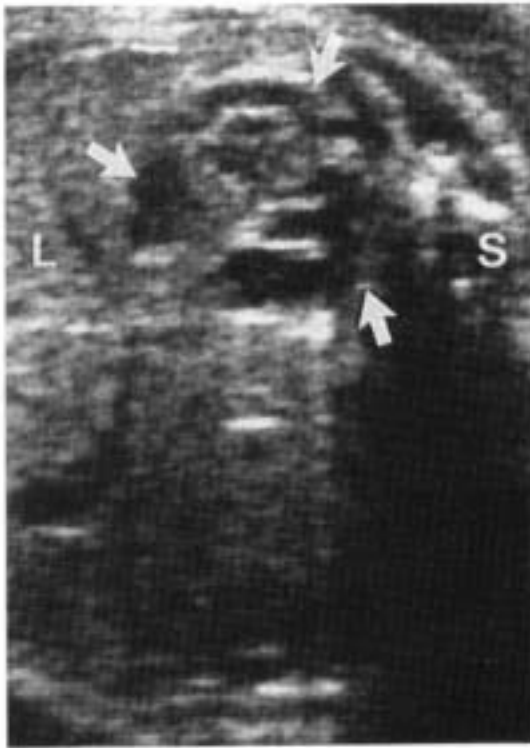The differential diagnosis should include Wilms'

Figure 8-41. Oblique scan of the fetal abdomen shows a complex mass with mixed solid and cystic elements interposed between liver (L) and spine **(S).** *(Reproduced with permission from Giulian et al.: **J** Clin Ultrasound 14.-225, 1986.)*

tumor, renal mesoblastic nephroma, multicystic kidney, liver diseases (hepatic hamartoma or hemangioma), and retroperitoneal teratoma. Sonographic differentiation is difficult also in children.[21,51] A definitive diagnosis is often possible only at laparotomy and after histologic examination. Nonetheless, a rapidly enlarging mass suggests a tumor.

Prognosis
Rare cases of stillborn infants with diffuse neuroblastoma have been reported in the literature.[2,3,7,40,46,48] After birth, the prognosis depends on age at diagnosis and stage. [12,36,41,44] The younger the infant at the time of diagnosis, the better the prognosis. The demonstration of catecholamine excretion does not seem to alter the prognosis.[41] Patients with a favorable prognosis are younger (under 2 years), have the tumor in an extraabdominal or midline location, and are in stages I, II, or IV-S.[35] The clinical course of neuroblastomas is unpredictable. Spontaneous regressions have been reported even in patients with metastasis.[10] The primary therapy is surgery, but this tumor is both radiosensitive and

susceptible to chemotherapeutic agents.

Obstetrical Management
The detection of an enlarging adrenal mass should prompt repeated ultrasonic examinations to evaluate the speed of growth of the tumor. In one report, the tumor diameter doubled in 2 weeks.[24] The timing and method of delivery depend in part on the behavior of the tumor; explosive tumoral growth may require preterm delivery. Hemoperitoneum from rupture of the neuroblastoma has been reported following both nontraumatic and traumatic delivery.[9] Fetal hydrops or metastatic liver enlargement may cause dystocia.[46,48,50] A cesarean section may need to be considered.

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