The Turkish Journal of Pediatrics
Volume 25, No. 3, July - September 1983

POTTER'S SYNDROME: BILATERAL RENAL AGENESIS*
(A report of two cases emphasizing associated malformations)

*Keriman Tınaztepe MD**, *Sevim Balcı MD****, *Behçet Tınaztepe MD*****, *Elif Dağlı MD******

Key words: *bilateral renal agenesis, oligohydramnios, Potter's syndrome*

In 1946, Potter described the peculiar facial appearance of infants with bilateral renal agenesis, accompanied in general by external and internal organ and system malformations, which has since been known as Potter's syndrome[1]. The facial appearance of this syndrome, called "Potter facies", is of wide-set eyes, prominent epicanthal folds, an unusually flattened nose, receding chin, and large, low-set ears deficient in cartilage. However, the Potter facies, considered so typical in the recognition of renal agenesis on external examination, occur in other renal disorders which interfere with the formation of amniotic fluid, and in infants with normal kidneys but prolonged leakage of amniotic fluid[2-16]. Incidence figures vary, but Potter's syndrome is likely to occur in about one in 2900-4800 deliveries[4]. At the Hacettepe University Institute of Child Health only two cases of bilateral renal agenesis have been recorded among 2000 pediatric necropsies during a period of 15 years. The aim of this communication is to present those two cases of Potter's syndrome with emphasis on the associated extrarenal malformations, and to review briefly recent hypotheses about the development of Potter's syndrome and Potter facies.

Case Reports

Case 1

The mother was 26 years old, this was her second pregnancy, and she reported having received hormonal therapy in the first trimester of the pregnancy. No parental consaguinity was recorded. The one-year-old sibling was in good health. The amniotic membrane ruptured four hours prior to delivery, at the end of the 35th gestational week. Following spontaneous labor, the mother gave birth to a baby weighing 1740 grams with ambiguous genitalia.

---

* From the Hacettepe University Institute of Child Health, Ankara.
** Professor of Pediatrics and Pediatric Pathologist, Hacettepe University Institute of Child Health.
*** Professor of Pediatrics, Hacettepe University Institute of Child Health.
**** Professor of Pathology, Hacettepe University Faculty of Medicine.
***** Resident, Research Fellow in Pediatrics, Hacettepe University Institute of Child Health.

Physical examination revealed a body temperature of 36 °C, pulse rate of 120/min and respiratory rate of 26/min. Head circumference was 31.5 cm and chest circumference 26 cm. The nose was unusually flattened, the folds arising from the inner canthus swept downward and laterally below the eyes; the low-set, external ears showed deficient chondrification (Figures 1-3). The skin was dry and wrinkled. Both hands were spade-like with a unilateral simian line. Abduction of the flexed hip was limited. The knees showed flexion deformity and there was pes talo valgus bilaterally.

The anus was intact. The poorly developed ambiguous external genitalia showed scrotum-like swellings with a hairy skin, without phallus formation. There was a urethral groove in the place of the urethral orifice. The baby was cyanotic. The heart sounds were rhythmic and no murmur was heard. The ventilation of both lungs was diminished. The liver and spleen were not palpable. The hypotonic baby showed Moro's reflex, but no sucking or grasp reflexes.

Figure 1.

Deformities of extremities and face in Case 1.

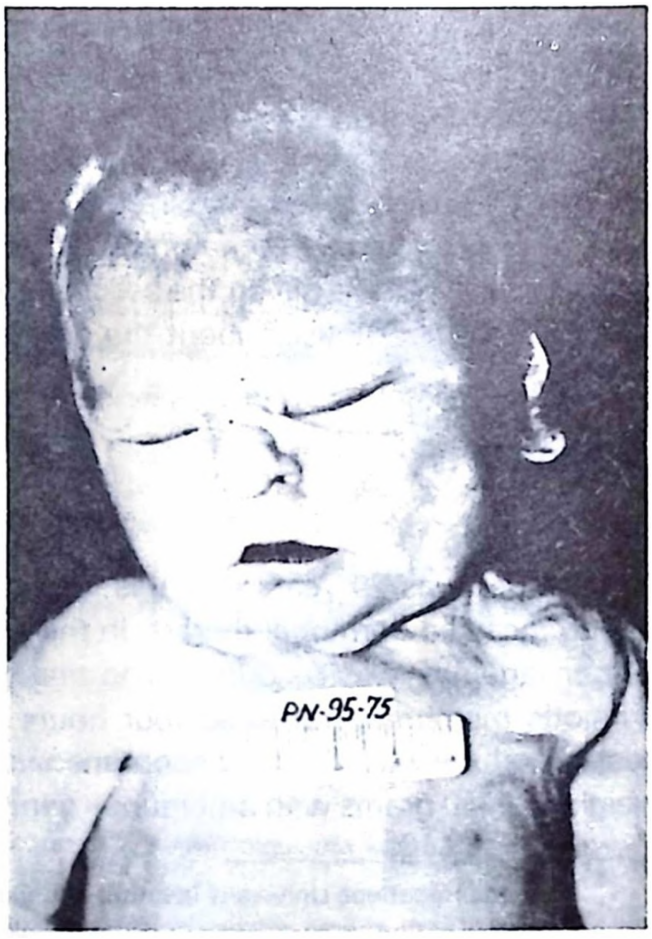

Figure 2.

Facial appearance.

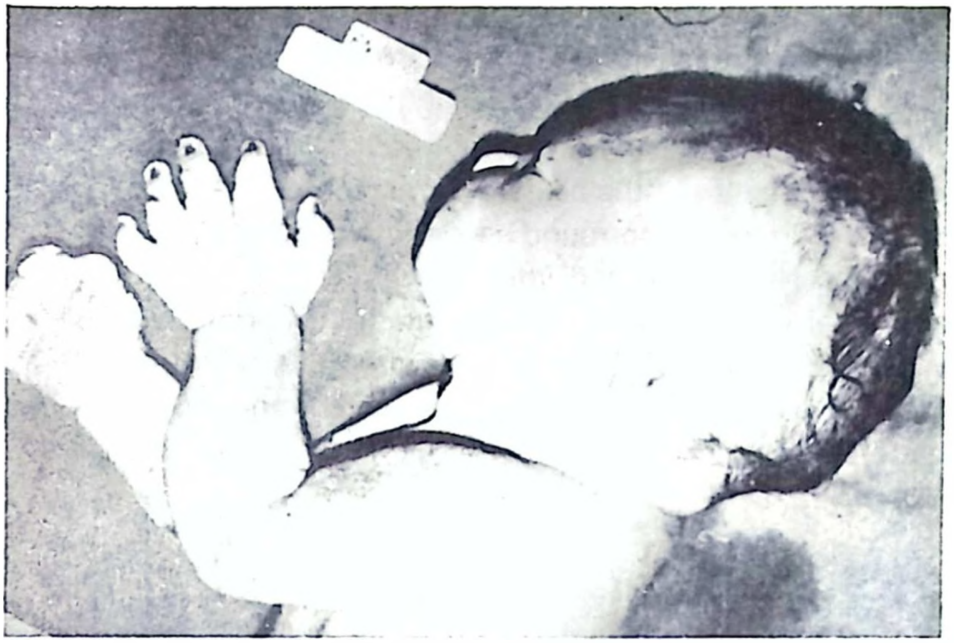

Figure 3.

Deformities of the ears.

On laboratory examination, the hemoglobin level was 17.25 g/dl; there were no remarkable peripheral blood smear findings. While taking intravenous fluid containing bicarbonate and 10% glucose, blood sugar was 240 mg/dl. The chest x-ray revealed bilateral atelectasis.

The baby had persistent respiratory distress and irregular respiration. Suitable intravenous fluid and oxygen therapy were administered. With increasing respiratory distress, the infant died eight hours after admission. A complete post mortem examination was carried out. Post mortem chromosome study revealed a normal XX karyotype.

Necropsy findings. The infant had the typical external features of Potter's syndrome as described above. Kidneys and ureters were absent bilaterally. There was no bladder. The adrenal glands were disk shaped. A lobulated greyish purple colored 0.4×0.5 cm sized soft tissue nodule was found distal to the adrenal gland, ventral to the vertebrae on one side.

The uterus was bicornuate without a cervix. The part that mimicked a vagina constituted the above-mentioned urethral groove. Apparently normal ovaries and tubes were found. The combined weight of the small and unexpanded lungs was 14 grams as compared with an expected normal weight of 34 grams. The heart showed aneurysmal dilatation of the membrano ovalis, the right atrioventricular (bicuspid) valve and the mitral valve, with multiple myxomatous verrucous structures and blood cysts. Marked edema and congestion with areas of hemorrhage in the pia-

arachnoid membranes of the central nervous system were noted. Both lungs revealed diffuse atelectasis, focal areas of hemorrhage, scattered hyaline membrane formation with rather abundant eosin-staining homogeneous material in the alveoli and terminal bronchioli and early stage maturation of the parenchyma in places. Dilatation of the lymphatics of the heart, and marked extramedullary hematopoiesis in the liver and spleen were also found as were mild hyperplasia of the islets of the pancreas and acinar dilatation and interstitial eosinophilic infiltration of the pancreas. The adrenal glands showed prominent fetal cortices with poorly formed cortical layering. Examination of the nodular structure below the adrenal gland in the renal fossa revealed tubular and abortive glomeruloid structures and islets of cartilage scattered among the connective tissue (Figures 4 and 5).

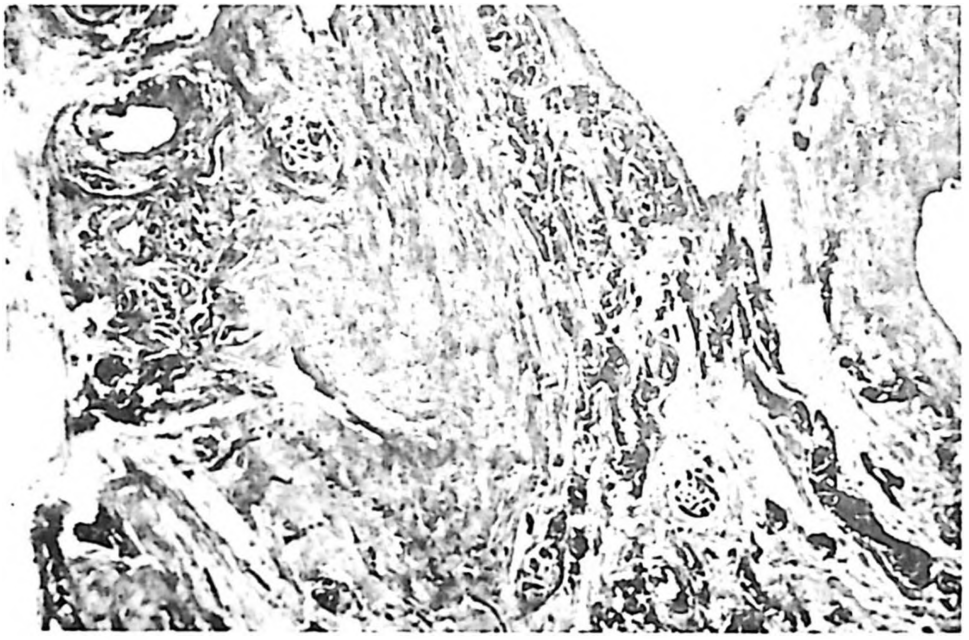

Figure 4.

Groups of tubular structures and abortive glomeruli in fibrocollagen connective tissue rich in vessels (HE×160).

Case 2

The second case concerns a six-hour-old baby who was delivered at term and referred to Hacettepe Children's Hospital. The family reported an apparently uneventful labor and delivery; however detailed information, including knowledge of oligohydramnios, could not be obtained. The gravida 1 mother and the father were both healthy with no consanguinity.

On admission a physical examination revealed a cyanotic baby weighing 1840 grams with a length of 45 cm. External genitalia revealed an absence of palpable gonads, and a sac and phallus with a single midline skin fold. There was also anal atresia.

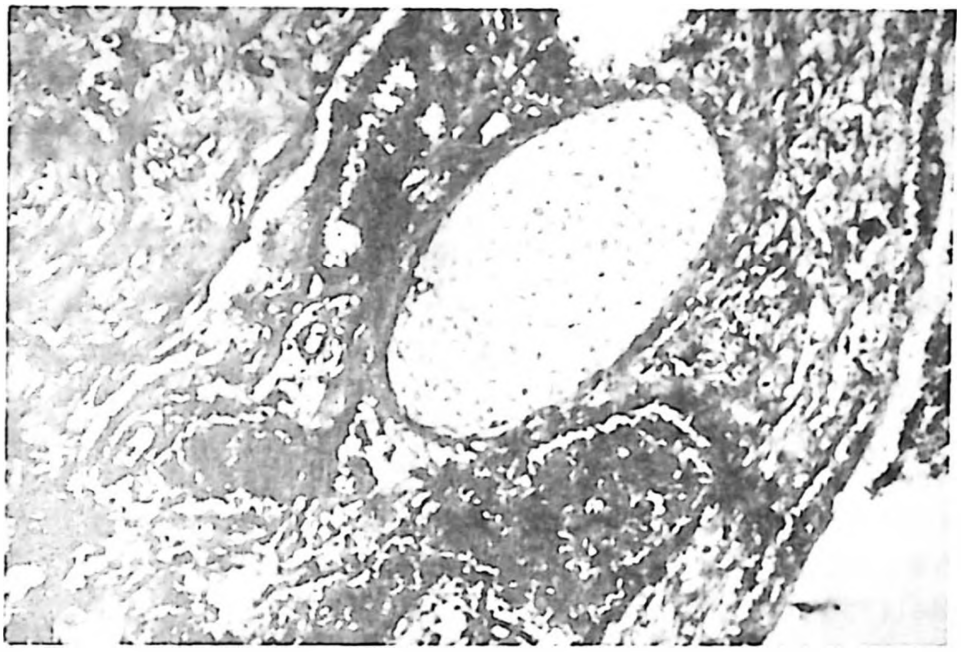

Figure 5.

Ovoid shaped cartilage islet in dense connective tissue (HE×400).

Respiration was difficult and superficial. Liver and spleen were not palpable. There was bilateral pes varus deformity. The neonatal reflexes were not brisk. There was a typical facial appearance with flattened nose, deep mentolabial sulci, hyperteloric eyes and low-set external ears with poor chondrification. In the lumbar region there was a sac 2×2 cm in size without a covering skin. The baby had bleeding through the mouth and nose. Oxygen was applied to the incubator he was kept in. The baby died ten hours after admission. A complete post mortem examination was performed.

Necropsy findings. In addition to the typical facial appearance mentioned above, macroscopically bilateral agenesis of the kidneys and ureters was found, together with unilateral absence of the tubes and ovaries, high type anal atresia, spina bifida in the lumbar region, meningomyelocele and small lungs. Both adrenals were disk-like in shape. In the renal fossa, a cyst-like structure was detected. Upon sectioning of the distal atretic bowel segment, a small sac with umbilical arteries on it was detected opening into the bowel.

Microscopic examination of this small cyst-like nodule revealed tubular and "S"-shaped structures suggestive of glomerulogenesis. The sac opening into the distal bowel was found to be the bladder. The lungs showed hyaline membranes, diffuse atelectasis and patchy hemorrhages. Prominent extramedullary hematopoiesis was noted in the liver and spleen, and marked congestion in the adrenal glands and all the visceral organs. There were two umbilical arteries and one umbilical vein.

Discussion

Potter's syndrome is a well-defined and easily recognizable clinical and pathological entity. The pregnancy, except in rare and unusual conditions, is associated with oligohydramnios, and at delivery the infant generally exhibits a typical facial appearance known as Potter's facies. There are deformities of the extremities such as spade-like hands and talipes equinovarus. The skin is usually wrinkled as if the child were suffering from severe dehydration. The infants are usually growth-deficient; those who are not stillborn exhibit severe respiratory distress. Even with assisted ventilation they do not survive more than a few hours. Hypoplastic lungs are the major cause of death, this being felt before uremia due to the renal agenesis has time to develop. Three fourths of the babies are male. The two cases presented in this paper both had typical facial and skin appearance and prominent genital malformations. In the second case there was anal atresia as well, as reported previously. In the first case cardiac anomalies were also involved. The aneurysmal dilatation of the membrano ovalis was thought to be secondary to the hydrodynamic changes due to pulmonary hypoplasia, while the other anomalies such as bicuspid right atrioventricular ostium and numerous myxomatous verrucae with blood cysts were developmental changes.

The majority of the patients show malformations of the external genitalia. One fifth of the affected infants have no ureters, bladder or external genitalia as in both of our cases. In addition the adrenal glands are generally of a disk-like shape as in our cases. In only 5% of cases are the adrenal glands absent[16].

It seems likely that, in some instances, genetic factors play a role in the etiology of this disorder. Occurrences of bilateral renal agenesis in siblings are suggestive of an autosomal mode of inheritance[2,6,14]; but the fact that in a pair of identical twins one twin was seen to be affected suggests that nongenetic factors can also be involved[8]. The chromosome analyses are normal. In one of our cases chromosomal study was performed and found to be normal. Even so, in some cases, apparently male infants have an XX sex chromosome complement[3].

The development of the major features of Potter's syndrome is mainly considered to be a consequence of multiple mesodermal defects. On the other hand, extrarenal features of Potter's syndrome are thought to be secondary to oligohydramnios and compression of the uterus[4] (Figure 5). Experimentally, similar facial appearances have been shown in rats[7]. Further, it seems reasonable to suppose that in the case of both monoamniotic and monochorionic twins where one has bilateral renal agenesis, except for low-set ears the characteristics of Potter's facies may be absent as was reported in one instance in the literature[8]. Bain and Scott[9] reported a case with anencephaly and normal amount of amniotic fluid showing bilateral renal agenesis without any external appearance of this syndrome. In a similar mechanism, pulmo-

nary cystic adenomatous malformation associated with bilateral renal agenesis could prevent most of the external features of Potter's syndrome[15].

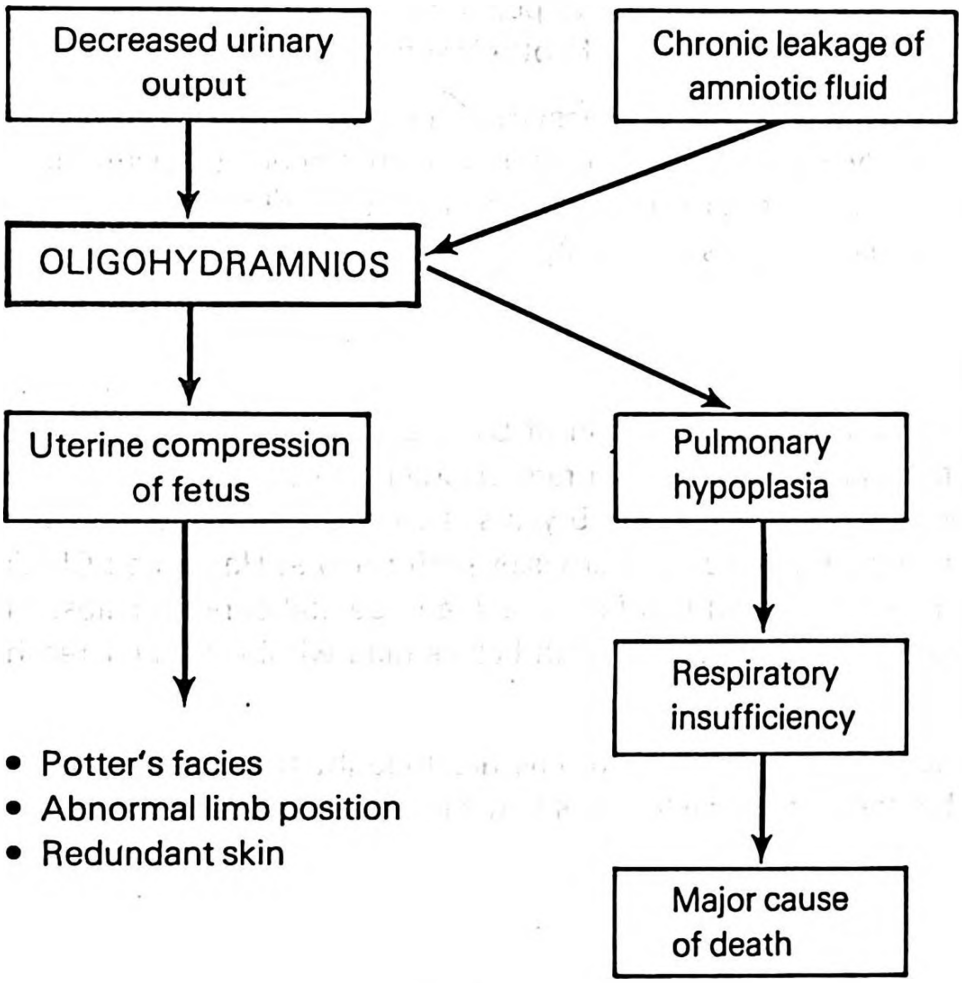

Figure 6.

Hypothetical genesis of some features of Potter's syndrome.

Apart from these a baby with bilateral normal kidneys who had Potter's facies was reported. His mother had had a premature rupture of the amniotic membranes in the 26th gestational week and subsequent leakage of amniotic fluid up to the time of delivery in the 33rd week of gestation[10]. Contrarily, a case of Potter's facies with a normal amount of amniotic fluid has also been reported[11]. The normal amount of amniotic fluid in this exceptional case was assumed to have accumulated after the intrauterine formation of the defects.

Usually, internal organ and system malformations are present in patients with bilateral renal agenesis, and in only one fourth of the reported cases has renal agenesis been an isolated anomaly.

Hypoplasia of the lungs is a significant finding in renal agenesis. Oligohydramnios is thought to destroy the hydrodynamics of the lungs and cause hypoplasia, although this is contrary to the theory of an accessory lung which does not have any communication with the bronchi. Both of our cases died in the first day of life following increasing respiratory distress due to pulmonary hypoplasia which, except in rare cases, is a mandatory component of Potter's syndrome.

The cases presented here show almost every feature of the syndrome including the rarer ones. Finally, it is worthwhile to reemphasize that newborn infants with severe respiratory distress who have Potter's facies are subject to evaluation for bilateral renal agenesis and other associated organ and system malformations.

Summary

Potter's syndrome is a combination of bilateral renal agenesis and acompanying facial and nonrenal features. It is a rare disorder and occurs in one in every 2900-4800 deliveries. Over a period of 15 years, two cases of Potter's syndrome were recorded among 2000 pediatric necropsies performed at Hacettepe Children's Hospital. Both cases presented had facial, skin and genital abnormalities. The second one showed anal atresia as well. Both babies died within the first ten hours after admission.

The nonrenal features of the syndrome are thought to be secondary to oligohydramnios, but there are some features that cannot be explained by uterine compression.

REFERENCES

1. Potter EL. Bilateral renal agenesis. *J Pediatr* 29:68, 1946.
2. Warkany J. *Congenital Malformations: Notes and Comments.* Chicago: Year Book Medical Pub, 1971, p 1037.
3. Woolf RB, Allen WM. Cancomitant malformations; frequent, simultaneous occurrence of congenital malformations of reproductive and urinary tracts. *Obstet Gynecol* 2:236, 1953.
4. Potter EL. *Normal and Abnormal Development of the Kidney.* Chicago: Year Book Medical Pub, 1972, p 83.
5. Potter EL. *Pathology of the Fetus and Infant* (2nd ed). Chicago: Year Book Medical Publishers Inc, 1961, p 431.
6. Schmidt ECH, Hartley AA, Bower R. Renal aplasia in sisters. *Arch Path* 54:403, 1952.
7. DeMyer W, Baird I. Mortality and skeletal malformations from amniocentesis and oligohydramnios in rats: cleft palate, clubfoot, microstomia and adactyly. *Teratology* 2:33, 1969.
8. Mauer SM, Dobrin RS, Vernier RL. Unilateral and bilateral renal agenesis in monoamniotic twins. *J Pediatr* 84:236, 1974.

9. Bain AD, Scott JS. Renal agenesis and severe urinary tract dysplasia: a review of 50 cases, with particular reference to the associated anomalies. *Br Med J* 5176:841, 1960.
10. Fantel AG, Shepard TH. Potter syndrome. Nonrenal features induced by oligoamnios. *Am J Dis Child* 129: 1346, 1975.
11. Sylvester PE, Hughes DR. Congenital absence of both kidneys; report of 4 cases. *Br Med* 1:77, 1954.
12. Potter EL. Oligohydramnios: further comment. *J Pediatr* 84:931, 1974.
13. Thomas IT, Smith DW. Oligohydramnios, cause of the nonrenal features of Potter's syndrome, including pulmonary hypoplasia. *J Pediatr* 84:811, 1974.
14. Rizza JM, Downing SE. Bilateral renal agenesis in two female siblings. *Am J Dis Child* 121:60, 1971.
15. Krous HF, Harper PE, Perlman M. Congenital cystic adenomatoid malformation in bilateral renal agenesis. Its mitigation of Potter's syndrome. *Arch Pathol Lab Med* 104:368, 1980.
16. Kissane JM, Smith MG. *Pathology of Infancy and Childhood* (2nd ed). St. Louis: CV Mosby, 1975, p 578.