Arch Iranian Med 2004; 7 (3): 186 – 189

Original Article

POTTER'S SYNDROME: A STUDY OF 15 PATIENTS

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Background – **Potter's syndrome is a rare congenital disorder diagnosed at birth and characterized by bilateral renal agenesis, lack of amniotic fluid, pulmonary hypoplasia, limb deformities, and typical facies. It is found in 0.2% to 0.4% of the autopsies performed on stillborn infants or those who die soon after birth. Currently, there is no way to prevent or treat it and patients have a poor prognosis with the respiratory insufficiency being the leading cause of death. To the best of our knowledge, the current report seems to be the first report of Potter's syndrome in Iran.**

Methods – **In this prospective report, we studied 15 patients with clinical and pathological characteristics of Potter's syndrome.**

Results – **Male to female ratio was 2:1. Of the studied cases, 53% had history of oligohydramnios and 60% had intrauterine growth problems. All patients had congenital renal anomalies and two-third of them had lung hypoplasia. All of the cases died, with 70% of fatalities having occurred in the first few hours of life.**

Conclusion – **We recommend establishing the Iranian National Potter's Syndrome Supportive Group (INPSSG) and prenatal multicenter studies in high-risk populations.**

Archives of Iranian Medicine, Volume 7, Number 3, 2004: 186 – 189.

Keywords: Oligohydramnios due to renal disease • Potter disease • Potter facies • Potter's syndrome • renal agenesis

Introduction

Pulmonary hypoplasia in infants accompanied with bilateral renal agenesis was diagnosed in 1946 by Potter who worked as a pathologist in Chicago for three decades.[1] Potter found an incidence of 1 in 4,000 births with predominance in males.[2] Potter's syndrome is a rare fatal disorder that occurs in sporadic and autosomal recessive forms.[3, 4] It is accompanied by severe oligohydramnios, renal abnormalities (bilateral renal agenesis, severe hypoplasia, dysplasia, polycystic kidney, and obstructive uropathy), or chronic leakage of amniotic fluid (oligohydramnios sequence) during middle gestational weeks.[5 – 7] Renal failure is the main defect in Potter's syndrome. Other characteristic features include premature birth, breech presentation, a typical facial appearance (Potter's facies), and limb malformations. Severe respiratory insufficiency leads to a fatal outcome in most infants. Clinical and imaging findings and a positive family history are diagnostic.

To the best of our knowledge, the current report seems to be the first report of Potter's syndrome in Iran. According to literature, Potter's syndrome is rare but, it is believed to be more common because infants are either stillborn or die soon after birth.

Patients and Methods

This study was conducted over 10 years (1991 – 2001) in Ghaem Medical Center (Mashhad, Iran) which is a referral hospital for high-risk pregnancies with approximately 4,000 deliveries per year. All newborns who were born alive with clinical characteristics of Potter's syndrome and admitted to neonatal intensive care unit (NICU),

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were enrolled in the study. We reviewed the medical records of the 15 patients proved to be a case of Potter's syndrome. All the cases were examined by a neonatologist and received necessary primary care. In their medical records, they had the results of chest X-rays and blood tests. Autopsies were performed for all of the patients. Family history of the patients as well as the health records of the mothers and fetuses during pregnancy and labor were collected.

Results

Of the 15 patients, 10 (67%) were males and 5 (33%) were females. Five newborns (33%) were preterm and one (7%) of them was small for gestational age. Six cases (40%) were the product of the first pregnancy. Oligohydramnios was seen in 8 patients (53%). The birth weight was 1,500 to 1,999 g in 3 (20%), 2,000 to 2,499 g in 6 (40%), and 2,500 to 3,500 g in the rest 6 (40%). The route of delivery was normal vaginal in 11 (73%) and cesarean section in 4 (27%) i.e. one for abnormal presentation and 3 for fetal distress. Maternal age was below 20 years in one (7%), 20 to 30 years in 10 (67%), and 30 to 35 years in 4 (27%). The Apgar score of the first minute of life was less than 7 in all patients (less than 3 in one, 3 to 5 in 5, and 5 to 7 in 9). In 87% of patients, Apgar score was less than 7 in the 5th minute of life (less than 3 in one, 3 to 5 in 5, and 5 to 7 in 7 newborns).

All patients had the clinical features of Potter's syndrome and they needed cardiopulmonary resuscitation in delivery room. Eleven cases (73%) had severe respiratory distress in the first hour of life and needed assisted ventilation; pneumothorax was diagnosed in the chest X-rays of 10 newborns (67%). In spite of intensive care in NICU, all patients died. Eleven (73%) neonates died in the first few hours; 3, in 3 to 5 days and one, in 28 days. Autopsy results showed bilateral dysplastic kidney in 5 patients (33%), bilateral renal agenesis in 3 (20%), bilateral polycystic kidney (PCK) in 4 (27%), and unilateral polycystic kidney in 3 (20%) i.e. two on the left side and one on the right.

Other abnormalities were also found in the patients. Two had the clinical and pathological findings of prune-belly syndrome. Hepatic fibrosis was found in 7 cases with PCK; dilatation of biliary system and cholestasis, in 2; Meckel's diverticulum, in one; hypoplastic lung, in 12 (80%), and pancreatic cyst and intestinal duplication, in one preterm neonate (Table 1). No genetic or prenatal studies were conducted for parents and fetuses.

Discussion

Potter's syndrome is incompatible with life outside the uterus and is found in 0.2% to 0.4% of the autopsies performed on stillborn infants or those who die soon after birth.[8 – 10] The characteristic facial features include hypertelorism, redundant skin, Mongolian palpebral fissure, epicanthal fold, specific suborbital crease, depressed nasal bridge, parrot-beak nose, posteriorly rotated low-set ears, receding small chin, a crease below lower lip, bow legs, clubfoot, hip dislocation, wide and broad hands, and a short neck (Figures 1 and 2).[11 – 13] During nephrogenesis, the essential interaction between the ureteric bud and metanephric mesenchyme is controlled by genes, transcription factors, and growth factors.[3] The genetic disorder often occurs prior to day 31 of fetal development. The ureteric bud which forms the kidneys fails to develop and the absence of the kidneys causes a deficiency of amniotic fluid after the weeks 12 to 16.[4, 8, 11, 14 – 16] Renal agenesis when accompanied by these characteristic features is called "Potter's disease". In this study, we had 3 cases of Potter's disease.

Intrauterine growth retardation has been reported in many patients[13]; we found low birth weight in 60% of our patients. This genetic disorder occurs in males twice as often as in females and is more common in infants with a positive family history of kidney malformation.[8] The male to female ratio was 2:1 in this study too. Bilateral renal agenesis is two to three times more common in males than in females. Twenty percent of the cases with Potter's syndrome have bilateral kidney agenesis with an incidence of 1 to 2 per 10,000 and usually of sporadic occurrence. Twenty percent to 36% of bilateral renal ageneses arise in patients with a positive family history; the recurrence risk for sporadic cases is 3%.[3, 4, 11] The incidence of Potter's syndrome in this study was

Table 1. Frequency of the other abnormalities in patients.

Abnormality	Frequency
Prune-belly syndrome	2
Hepatic fibrosis	7
Cholestasis and biliary dysgenesis	2
Meckel's diverticulum	1
Intestinal duplication and pancreatic cyst	1
Lung hypoplasia	12
Pneumothorax	10

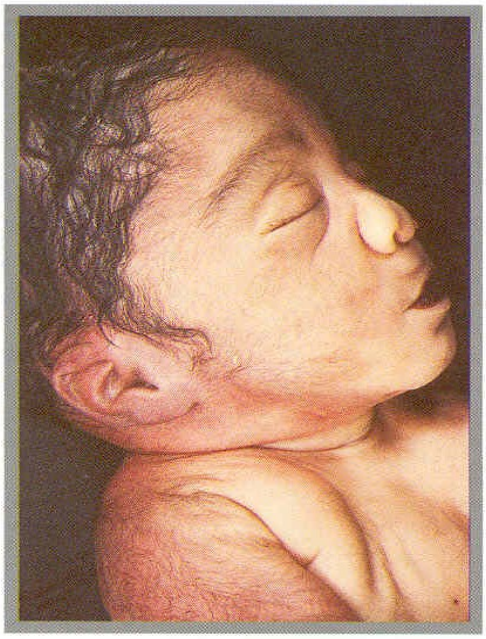

Figure 1. Lateral view of the facial features of Potter's syndrome.

approximately 1.5 per 4,000 births. Congenital renal malformations were present in 100% of the cases and all patients with renal agenesis (incidence 0.75 per 10,000 births) were males. There was no history of chronic amniotic fluid leakage. No racial predilection is known for Potter's syndrome.[3]

Kidneys normally produce the amniotic fluid (as urine) which is necessary for normal lung development.[17] Oligohydramnios causing a continuous pressure of uterine wall on the fetal chest wall and the pressure of fetal intraabdominal organs on the diaphragm are the main causes of lung hypoplasia and insufficiency in Potter's syndrome.[12, 13] The degree of hypoplasia depends on the degree and duration of oligohydramnios as well as the stage of lung development at which oligohydramnios occurs. Though there was no history of chronic amniotic fluid leakage in our patients, oligohydramnios was found in 53% of them and 73% of the cases had lung hypoplasia. Because of severe respiratory distress and lung hypoplasia, the patients with dysplastic kidneys were either stillborn (40%) or died shortly after birth (60%). The cause of death in the first few days of birth was renal failure. All of our patients died; 73% of fatalities occurred in the first few hours after birth.

There have been reports of genital abnormalities in 20% to 70% of cases of renal agenesis. Associated extragenital abnormalities include congenital heart disease (30%), digestive system abnormalities (20%) (i.e. esophageal atresia, colonic agenesis, anal and duodenal abnormalities, Meckel's diverticulum, and pancreatic and splenic cysts),[18] skeletal disorders (15%), brain abnormalities, and many other associations (Vacterl, Meckel, chromosome 22 malformations) have been described.[11]

Congenital hepatic fibrosis and biliary duct abnormalities have been reported in all patients with autosomal recessive PCK.[13] Our study showed a similar result. Hallermann et al reported two brothers with PCK, hepatic fibrosis, dysmorphic features, abnormalities in bone radiography, and different haplotypes in their family.[19] In this study, one patient had PCK with Meckel's diverticulum, cleft palate, and microcephaly. In another report, 6 siblings in one family had PCK, telecanthus, heart defect, abnormal ears, microcephaly, and Potter type 1 (infantile PCK).[20]

Despite the primary abnormalities, diagnosis is first suggested by the absence of amniotic fluid and absence of urinary bladder.[11, 14] The couples who have had an affected pregnancy should rely on ultrasound screening of the subsequent pregnancies between 16th and 18th weeks of gestation.[21] The postnatal diagnosis can be confirmed by ultrasonography, chest X-ray,[17] high-dose

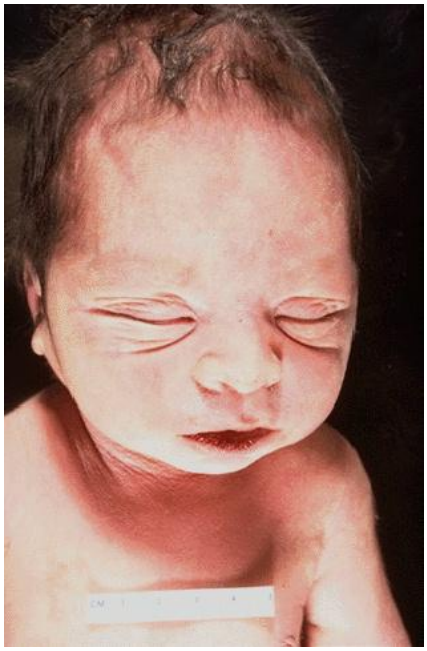

Figure 2. Plane facial features of Potter's syndrome.

urography, scan tomography, radioisotope scans with DTPA Tc^{99}, endoscopic findings, family history, and genetic studies.[19] Bilateral renal medullary cystic dysplasia and bilateral renal hypoplasia may appear as bilateral renal agenesis.

According to other studies, about 10% of the first-degree relatives of the neonates delivered with Potter's syndrome had asymptomatic renal malformation.[14] Consequently, ultrasound evaluation of parents and sibling is important. [7, 22] Potter's syndrome has a fatal outcome and is incompatible with life. Treatments aim at any urinary outlet obstruction. There is no known prevention and the mortality rate is high. Children with Potter sequence due to other conditions (i.e. not due to bilateral renal agenesis) have a higher survival rate.[3] Many authors have suggested the use of amnioinfusion or intraabdominal saline infusion for better visualization of the anatomy. Although there might be indications for such aggressive approaches in nonviable fetuses, these are quite uncommon and not justified in the majority of cases. Termination of pregnancy may be offered before viability. When continuation of pregnancy is opted for, the standard prenatal care is not altered. Confirmation of diagnosis after birth is important for genetic counseling.[11] Autopsy is also recommended.[3]

National Potter's Syndrome Supportive Group (NPSSG) has been formed in many countries. We recommend establishing the Iranian National Potter's Syndrome Supportive Group (INPSSG) and meticulous genetic and prenatal multicenter studies in high-risk populations.

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