Acta Paediatrica Hungarica 31 (1), pp 13-21 (1991)

FAMILIAL OCCURRENCE OF BILATERAL RENAL AGENESIS

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Received 13 Oct 1989

The 58 cases of bilateral renal agenesis (Potter syndrome) registered in the Genetic Counselling unit of our institute in the last 12 years are reviewed. The only familial recurrent case which has been prenatally diagnosed is described in detail. A urinary bladder anomaly like that of the subsequent third child has not been previously reported.
The authors analyze the possible inheritance patterns. They suggest the malformation is a genetically heterogeneous entity. They emphasize that nowadays the birth of a newborn with bilateral renal agenesis can be prevented in all cases.

INTRODUCTION

The 135 cases of Potter - the first author who described the bilateral renal agenesis (BRA) and the consequent deformities - do not include any familial recurrences /14/. Although such cases have already been published, they can be considered even nowadays as rarities /1,2,4,6,7,9,10,12,13,15-21/. The incidence rate of BRA is estimated between 0.1 - 0.3/1000 births, and the recurrence rate is referred as 1 - 5 % after the first affected newborn or fetus /4,16,21/. Unilateral renal agenesis can be detected by ultrasound in 5 % of parents and siblings of the affected infants /16/.

Since the establishment of our Genetic Counselling unit twelve years ago, we have come across only one familial case of BRA. After the birth of a newborn with BRA and the induced abortion of a similar mid-trimester fetus, a child suffering from lower urinary tract malformation was born.

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MATERIALS AND METHODS

After the delivery of a newborn or fetus with BRA or an induced abortion because of prenatally diagnosed Potter syndrome we registered 58 women (i.e. couples) at our Genetic Counselling between 1st January, 1977 and 31st December, 1988. Autopsy records of newborns or stillbirths were collected from other institutes as well. During their next pregnancy they were regularly in contact with our Genetic Counselling unit. The state of health of infants born in other institutes are documented in all cases.

After the definite diagnosis of the malformation we informed the couple of its fatal outcome. They asked for the interruption of the mid-trimester pregnancies in all cases. We performed the induction by extraovular injection of Rivanol (0.1 %) and continuous infusion of oxytocin /8/. Autopsy of the fetuses was performed in our fetal pathology laboratory.

Our cases are presented in Table I. We give a detailed report on the cases observed in the same family.

TABLE I

BRA cases registered in the Genetic Counselling of the University of Medicine, Debrecen, between 1977 and 1988

	Cause of the first attendance	
	A previous child/fetus with BRA	Prenatally diagnosed BRA in the current pregnancy
Outcome of the following pregnancies	35	23
No more pregnancy undertaken or registered	7	18
Healthy newborn	26	4
Aborted in the 1st trimester	-	1
Infant suffering from congenital heart anomaly	1	-
Recurrent BRA	1	-

CASE REPORT

The parents are healthy. The mother was 23, the father 34 years of age at the time of the first delivery. They are not known to be related and have negative history concerning the usage of unusual medicines or drugs. It is noteworthy that the mother of the gravida had been operated on because of renal stones, but she was not aware of any urinary tract malformation.

The first pregnancy of the mother resulted in the birth of a premature male infant by breech delivery at 32 weeks' gestation, following an attempt of tocolysis. His Apgar score at one minute was 4. Gasping, bradycardia, deep cyanosis could be observed, and in spite of resuscitation death occurred at 15 minutes of age. During her pregnancy the mother visited neither an ultrasound laboratory, nor a genetic counselling unit. The 45 cm male newborn with a mild degree of Potter's face weighed 1980 gms. Besides hypognathia, the narrow skull was elongated mento-occipitally, the ears were low-set. The left fingers and nails were hypoplastic.

The autopsy findings revealed the total absence of both kidneys and ureters. The urinary bladder was 1 cm in diameter without any urine in it. Other remarkable findings are the hypoplastic lungs, absence of the left umbilical artery and a small additional spleen near to the hilus lienis.

Before deciding about the next pregnancy the parents visited our Genetic Counselling. After studying the autopsy record we estimated the recurrence risk under 5 % based on the data of the literature, and suggested to undertake the pregnancy with prenatal diagnostic measurements.

A few months later the woman reported again, pregnant and in the 15th week of gestation. The ultrasonography showed oligohydramnios, and compressed position of the limbs. Subsequent examinations performed at the 17th and the 19th weeks showed similar conditions, urinary bladder and kidneys could not be observed. The maternal serum AFP level was normal.

Because of the fatal outcome the parents were advised the pregnancy be interrupted, which they accepted. The male fetus was not alive, weighed 255 gms, had Potter's face and limbs strictly pressed to the body. The autopsy findings were: total absence of both kidneys and ureters, as well as the urinary bladder. The renal arteries also could not be found. The size of adrenal glands was normal, but they were discoid in shape. The testes were undescended. The lungs were mildly hypoplastic. The number and the running of the umbilical vessels were normal.

A year later - being aware of the higher risk of conceiving an unhealthy infant - the pregnant mother reported for prenatal diagnostic measurements. This time we could not detect any kidney malformations throughout the ultrasonographic series (at the 9th, 18th, 28th weeks).

At the 39th week of gestation a boy, weighing 4000 gms was delivered. After having recurrent pyelonephritis, cystography and intravenous pyelography were performed at the age 1 year, and several diverticuli of the urinary bladder and a consequent hydroureter - caused by the dislocation because of the largest diverticulu - were detected. Using continuous

catheter application, the congestion of the upper urinary tract was eliminated. After this, diverticulectomy and ureterneoimplantation was carried out. (It was performed at the Department of Pediatric Surgery of Borsod-Abauj-Zemplén County Hospital).

At the age of two and a half years in 1989 the child is normal, but sometimes needs urodesinficients because of pyuria. No abnormality was detected during the control pyelography, except a mild congestion on one side. The urinary bladder was of normal size, but irregular shape because of surgical manipulations.

Following strict genetic care the woman gave birth to another male newborn some months ago, who is - according to the first examinations - healthy.

DISCUSSION

Our Eastern Hungary Regional Genetic Counselling Unit is visited by couples from distant counties too, so an exact incidence rate cannot be calculated. Based on the data of the prenatal screening program going on in three Eastern-Hungarian counties (Hajdú-Bihar, Szabolcs-Szatmár, Szolnok) we found the incidence rate of BRA to be 0.32/1000 births.

Table II lists the 22 cases found in a review of the literature, where two or more members of the family were noted to have BRA. Familial occurrence means mostly siblings, except two cases. Another four relatives suffer from other kinds of upper urinary tract malformation. In the family No. 16 two unilateral and two bilateral renal agenesis occurred. Until now, none has reported on the birth of a child with lower urinary tract malformation following two siblings with BRA.

These reports show a considerable variability of the effect of genetic factors on the phenotype in the familial cases. The case observed by Mauer et al. has a crucial importance: one of two monoamniotic co-twins had bilateral, and the other unilateral renal agenesis. A sibling with soliter dysplastic kidney of a newborn with BRA has also been observed /3/.

Concerning the inheritance pattern several possibilities therefore present themselves. The autosomal recessive trait seems to be likely, but the predominance of affected males suggests that some sex limiting factors may be involved /6/.

The cases observed in cousins /9,13/ do not support this explanation: the low probability of a marriage of heterozygous persons is decreased by the necessity of a third heterozygous person without consanguinity. However, in the case of consanguineous parents it is the most probable possibility /18/.

Several family cases suggest an X-linked recessive inheritance /13/. The great number of siblings of different sex, however, makes it unlikely that this possibility could play an important role, except if we suppose that BRA is a genetically heterogeneous entity.

Taking into account all the cases presented in Table II, in particular the case of those families which have members with a urinary tract malformation of less severe degree, the autosomal dominant trait with variable expressivity presents itself, too. Roodhoft et al. found unilateral renal agenesis in three cases, double ureter in two, and multicystic kidney in one case among the 71 parents of 41 infants with BRA, who were evaluated by ultrasonography for renal malformations. It is difficult to fit our case to these findings because of the lack of reports on similar cases. However, presuming a gene defect influencing the formation of the ureteric buds one can give the explanation.

The multifactorial etiology with sex limiting factors seems to be the most probable one. After the birth of one affected child we estimate the recurrence risk under 3-5 %.

The increased risk of pregnants with an affected child or fetus makes it necessary to submit them to careful ultrasound examination that can assure the detection of fetuses suffering from a life-incompatible urinary tract malformation with oligohydramnios, and the interruption of the mid-trimester pregnancy. Given the routine screening of all pregnants the oligohydramnios sequence can be detected in almost every case (i.e. in 100 %).

Diagnostic value of the increased level of maternal serum AFP, which was reported in some cases with BRA /5/, is questionable. Therefore, BRA can be detected only by a screening program including ultrasonography, too.

TABLE II

No.	Authors	BRA male	BRA female	Siblings with other urinary tract anomaly	Healthy siblings	Other relatives with urinary tract anomaly
1.	Madisson	2	-		2	
2.	Carter et al.	2	-		1	
3.	"	1	1		1	
4.	"	1	1		2	
5.	"	1	1		2	
6.	"	-	2			
7.	Roodhoft et al.	1	1			mother (multi-cystic kidney)
8.	Schmidt et al.	-	2		2	
9.	Baron	2	-		1	
10.	Rizza and Downing	-	2		1	
11.	Whitehouse and Mountrose	1	1		1	
12.	Hack et al	2	-		1	

13. Buchta et al	1	1			mother (unilateral agenesis)
14. "	2	-			
15. "	4	-			
16. Kohn and Borns	-	1	1 male (unilateral agenesis)	3	father (unilateral agenesis) father's cousin (BRA)
17. Kaffe et al.	1	1			
18. Pashayan et al.	2	-			mother's cousin (BRA)
19. Schinzel et al.	2	-			
20. Sangal et al.	2	-			mother (horseshoe kidney)
21. Morse et al.	1	2		1	
22. Wilson and Baird	2	-			
23. present report	2	-	1 male (diverticulum of the urinary bladder)	1	
Total	32	16	2	17	BRA 2 other 4

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