Familial ureteric bud anomalies

**Summary.** A family is described in which various renal anomalies occurred. The condition is considered to represent an autosomal dominantly inherited ‘instability’ of the ureteric bud.

There have been a number of reports on the occurrence of variable anomalies of ureteric bud development within a kindred (Atwell et al., 1974; Dietel, 1964; Nilsson, 1960; Rossle, 1942). We report here the rare finding of double kidney, unilateral renal agenesis, and horseshoe kidney in two generations of one family.

**Clinical findings**

The proband, II.1, was the first daughter of unrelated and healthy Caucasian parents aged 29 and 45 years, respectively. Pregnancy and parturition were uncomplicated and the birthweight was 2900 g. At routine neonatal physical examination (technique of Musseles et al., 1971) the left kidney was not palpable; no other defects were detected. Intravenous pyelography (Fig. 1) failed to detect functioning renal tissue on the same side. The presumptive diagnosis was left renal agenesis. At follow-up no additional anomalies were detected. The karyotype was that of a normal female. The second pregnancy resulted in the birth of an apparently healthy boy, II.2, following a normal pregnancy and parturition. Birthweight was 3410 g. Physical examination revealed a horseshoe kidney as the only abnormal finding, and both renal scan (Fig. 2) and intravenous pyelography confirmed the diagnosis.

As a result of the above findings the parents underwent radiological studies of the kidneys. The father was normal but in the mother, I.1, a right double kidney and collecting system were disclosed (Fig. 3).

There was no family history of renal disease or of hypertension. The mother’s parents and only sib refused to undergo pyelography.

**Discussion**

Malformations arising from the ureteric bud are common and, not infrequently, more than one instance of a single anomaly is found in a kindred (Atwell et al., 1974; Holmes, 1972; Lenz, 1964; Warkany, 1971). The occurrence of varying anomalies within a kindred is rare, and we have found only four reported instances in which two or more of the three above anomalies were found together. One of these examples was associated with Fanconi’s anaemia (Nilsson, 1960).

The present family is of interest from the aspects of both aetiology and pathogenesis. Discussion of the latter requires consideration of the embryology of the kidney and collecting system.

The human definitive kidney (metanephros) arises from two embryonic sources. The intermediate (metanephric) mesoderm which differentiates into the nephron and connective tissue of the kidney; and the ureteric (metanephric) bud which arises from the mesonephric (Wolffian) duct, and gives rise to the collecting system of the kidney (Potter, 1972; Warkany 1971).
Most of the congenital anomalies involving the kidney arise from a primary defect of the ureteric bud, either during its formation and growth (as in agenesis of the kidney), or as a result of disturbances of its inductive function in nephron formation (as in some types of polycystic kidney). Relatively few anomalies are attributed to a primary defect of the metanephric mesoderm (for example, solitary cysts of the renal parenchyma).

Unilateral agenesis can be explained by a unilateral failure of the normal growth of the ureteral bud. As a consequence the intermediate mesoderm on the same side fails to differentiate into kidney parenchyma. Boyden showed, as early as 1927, that interference with growth of the mesonephric duct can cause renal agenesis (Boyden, 1927).

Horseshoe kidneys are formed when the ureteric buds grow upwards nearer to the midline than normally (Warkany, 1971). In the early stages of renal development the lower poles are more closely approximated than the upper (Potter, 1972). This may explain why horseshoe kidneys are usually fused at their lower poles.

When a mesonephric duct gives rise to two ureteral buds on one or both sides, the result is
duplication of the ureters, and, frequently, separate renal pelves and kidney are formed in the metanephric blastema as well.

A number of teratogenic agents, such as chlorambucil, methyl salicylate, vitamin A deficiency, and irradiation (reviewed by Warkany, 1971), have been shown to give rise to ureteric bud anomalies. In addition, the incidence of the above anomalies is increased in some chromosomal aberrations. In trisomy 18 there is a high incidence of double kidney, unilateral renal agenesis, and horseshoe kidney (Warkany, 1971). Ureteric bud anomalies also occur in association with Fanconi's anaemia together with other malformations; the condition is inherited by an autosomal recessive gene (Nilsson, 1960).

The frequency of the described anomalies in the general population is approximately as follows: unilateral agenesis, 1 in 600; horseshoe kidney, 1 in 400; ureteral duplication including double kidney, 1 in 150 (Warkany, 1971).

There is increasing evidence that some instances of the renal anomalies encountered in this kindred are of genetic origin (Atwell et al., 1974; Holmes, 1972).

It is highly probable that the concentration of renal anomalies in the presently described family is a result of inheritance. Though data are available for only four individuals in this family, the renal anomaly predisposition appears to be inherited by an autosomal dominant gene. The gene appears to cause ‘instability’ of the ureteric bud, resulting in the production of variable anomalies of the kidneys and collecting system.

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REFERENCES


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