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Renal Malformations in Patients With Turner Syndrome: Imaging in 141 Patients

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ABSTRACT. Turner syndrome occurs in 1/2,000 to 1/5,000 live female births. The presence of renal malformations was evaluated in 141 patients with Turner syndrome and abnormalities were found in 47 (33%). Prior to 1980, IVP was the radiologic method used for initial screening, and subsequently, ultrasonography has been used as the initial imaging technique. With both methods, major malformations can be detected. Ten patients had a horseshoe kidney, 11 had double collecting systems, four had complete absence of one kidney, three had crossed ectopia, and one had a pelvic kidney. Three patients had ureteropelvic junction obstruction; two of these were asymptomatic and the obstructions were detected only because of the routine imaging. Two patients had ureterovesicular junction obstruction, with one studied as part of a routine evaluation for short stature. Four of these five patients required surgery. Ultrasonography should be used as the initial renal imaging study for all patients at the time the diagnosis of Turner syndrome is made. *Pediatrics* 1988;82:852–856; *Turner syndrome, renal malformation, ultrasonography.*

Turner syndrome is estimated to occur at a minimum frequency of 1/5,000 live female births[1] and a probable frequency of closer to 1/2,000. These girls have numerous major and minor congenital malformations, among which renal malformations are usually specifically cited[2–5] or separately reported.[6–8] However, the prevalence and spectrum of the renal malformations in patients with this syndrome and their contribution to morbidity have been less well investigated. We studied radiographically the kidneys of 141 patients with Turner syndrome and found renal abnormalities in 47 (33%). Herein, we report our findings and document the need for routine imaging of all patients with Turner syndrome.

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MATERIALS AND METHODS

The diagnosis of Turner syndrome was made or confirmed by peripheral blood leukocyte karyotype analysis in 154 girls seen at the UCLA Pediatric Endocrinology Clinic between July 1969 and June 1987. Of these, all were referred for a renal imaging study whether or not urinary tract symptoms were present. A total of 141 patients have had one or more studies performed, seven did not return for follow-up prior to evaluation, and six are still awaiting study. Thus, the findings reported herein do not represent ascertainment bias on our part based on clinical symptoms or prior history of urinary tract infection. Girls evaluated prior to 1980 had an IVP as their initial study. If there was a history of urinary tract infection or evidence of reflux or obstruction, then a voiding cystourethrogram was also performed. After 1980, the 45 patients studied had ultrasonography as their first procedure, with voiding cystourethrogram or IVP recommended only if there was a history of urinary tract infection or a significant abnormality was seen during the ultrasound examination.

IVP was performed using 2 mL/kg of iodinated contrast with routinely timed early and delayed films. Ultrasonography was performed with a Phillips 2500 real-time sector scanner using the highest frequency transducers that gave sufficient penetration (3.5 or 5.0 MHz). If pelvic anatomy was also to be demonstrated at the same time, a full bladder was required. Otherwise, no special preparation was necessary for the ultrasound examination. Magnetic resonance imaging was used in two patients, in one to confirm the unilateral absence of a kidney and, in the other, to better image the anatomy of a horseshoe kidney. A Fonar 0.3T permanent magnet

was used. Images were obtained in the coronal and axial planes using a T1 weighted sequence (spin echo technique, time of relaxation = 300 or 500, time of excitation = 18 or 28).

RESULTS

The method of imaging and the abnormalities demonstrated by each study are shown in Fig 1. Abnormal study results were obtained from 47 (33%) patients. IVP was used for 35 patients, ultrasonography for ten, and contrast during cardiac catheterization for two. Normal study results were obtained for 94 (67%) patients. IVP only was used for 57 patients, ultrasonography for 35, and catheterization for two.

The full spectrum of renal abnormalities reported to occur in patients with Turner syndrome, except retrocaval ureter,[9,10] was seen in this patient population. Horseshoe kidney was present in ten patients (7%) and was demonstrable by IVP, ultrasonography, and magnetic resonance imaging (Fig 2). Double collecting systems occurred in 11 patients and were seen also by both IVP and ultrasonography (Fig 3). Four patients had an absent kidney (three missing the left, one the right); two were detected by IVP and two by ultrasonography. Of the three patients with ureteropelvic junction obstruction, two were asymptomatic. The obstructed kidney of one patient was not visualized by IVP, but with subsequent ultrasonography massive dilation was seen and a nephrectomy was done. The other patient had a functional hydronephrotic kidney and has subsequently required continuous antibiotic therapy. The symptomatic patient had recurrent urinary tract infections and has subsequently required surgery. Two patients had ureterovesical junction obstruction. One was detected with IVP after several urinary tract infections and the other with IVP during an evaluation for short stature and possible Turner syndrome. Both have required surgery. Only mild rotational abnormalities, without dilation of the calyceal system, and without clinical significance, were clearly detected more frequently with IVP. This difference likely represents a difference in technical resolution and, fortunately for this patient population, does not lessen the clinical usefulness of ultrasonography. Four patients were investigated for hypertension with angiography. Two had normal study results, one had multiple renal arteries and veins without evidence of stenosis, and one had an aberrant vessel which resulted in a dilated calyx but was thought not to be responsible for the hypertension. However, this study was not designed to provide a basis for the systematic evaluation of hypertension, because many of these patients did not maintain follow-up for a time sufficient to determine the natural history of hypertension.

The relationship of the renal abnormalities (independent of detection method) to chromosomal karyotype is shown in the Table. Although no single karyotype is preferentially associated with renal anomalies, it appears that they occur more frequently in X monosomy or mosaic X monosomy than in patients with lesser losses of X chromosome material. Presence or absence of the webbed-neck phenotype (present in 34 of the 141 patients) could not be correlated with presence or absence of any of the renal anomalies (data not shown).

DISCUSSION

The current study suggests that renal abnormalities occur in about one third of all girls with Turner

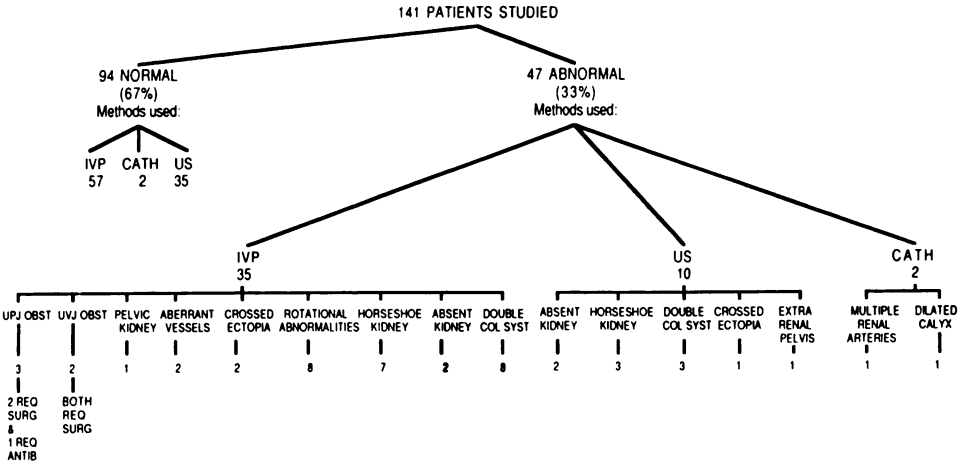

Fig 1. Renal abnormalities detected in patients with Turner syndrome. Abbreviations: CATH, catheterization; US, ultrasonography; UPJ OBST, ureteropelvic junction obstruction; UVJ OBST, ureterovesical junction obstruction; REQ, required; SURG, surgery; ANTIB, antibiotics.

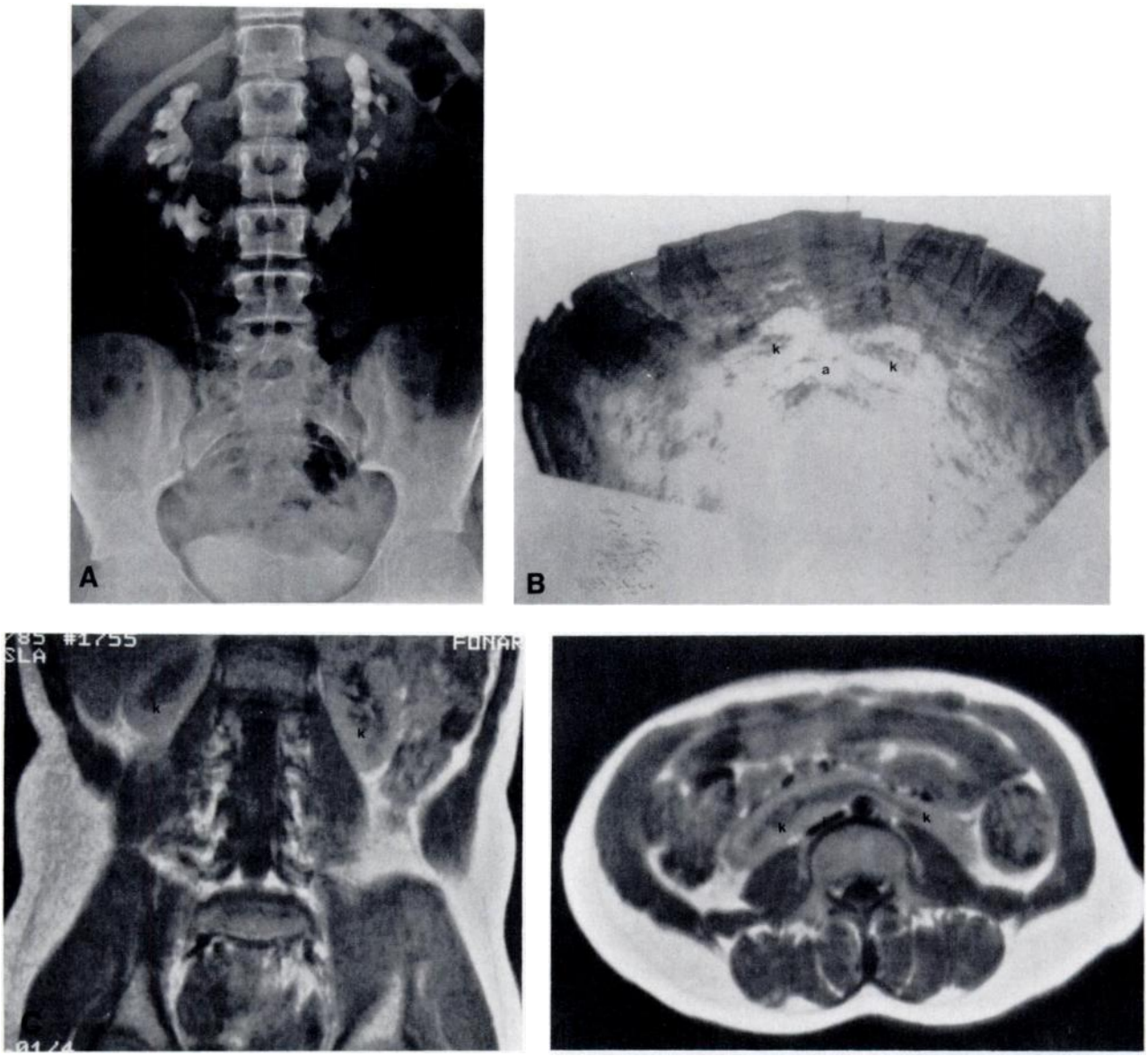

Fig 2. Horseshoe kidney. A, IVP shows reversal of normal axes of kidneys, with closer proximity of lower poles than upper poles. B, Ultrasonography, axial plane, shows proximity of lower poles of kidneys (k) anterior to aorta (a). C, Magnetic resonance image, coronal plane (SE 300/18) shows axes of kidneys (k) to appear relatively normal on this posterior cut. D, Magnetic resonance image, axial plane (SE, 300/18), however, shows fusion of lower poles of kidneys (k) anterior to aorta (a) and inferior vena cava (i).

syndrome with monosomic patients at greatest risk. This may explain what appears to be a decreased number of significant anomalies detected since the introduction of ultrasonography (10/45 [22%]) as compared with those detected earlier with IVP (35/92 [38%]) because more of the patients studied with IVP had a 45,X karyotype, whereas more patients with recently diagnosed Turner syndrome had less characteristic karyotypes. This may suggest also that, recently, the more classical 45,X patients are not referred as frequently to a tertiary center. If this is the case, then we may be somewhat underestimating the incidence of renal abnormalities.

The serious anomalies previously described in patients with Turner syndrome, including absent kidney (four [2.8%]), ureteropelvic junction obstruction, and ureterovesical junction obstruction (five [2.5%]) were all detected in this series by both IVP and ultrasonography. These prevalence rates far exceed the estimates of 1/450 to 1/1,800 for agenesis[11] and less than 1% for nonfamilial obstruction. Double collecting systems can be considered a premorbid abnormality if obstruction to drainage occurs or if there is secondary infection or stone formation. This anomaly was also detected by both methods. Although we have yet to have a patient

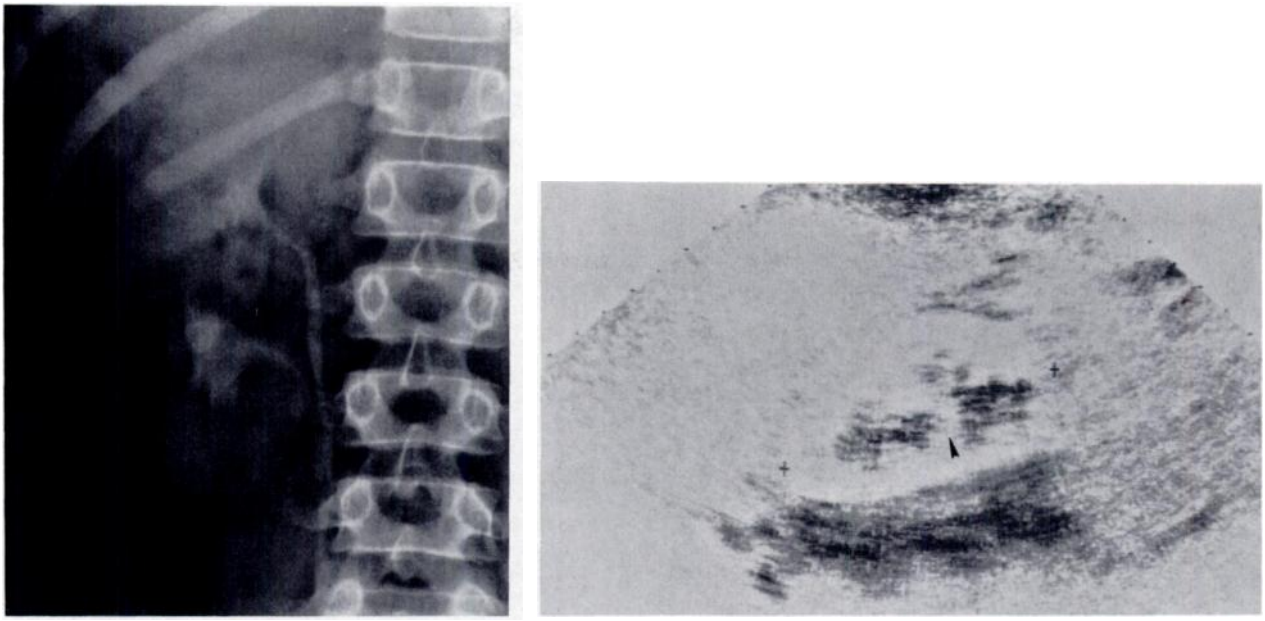

Fig 3. Duplex collecting system. Left, Excretory urography shows two right ureters arising from separate upper and lower pole collecting systems. Right, Ultrasonography demonstrates anatomy of duplex collecting system by showing separation of two echogenic renal sinuses by a less echogenic cortical bar (arrow).

TABLE. Relationship of Chromosomal Karotype to Occurrence of Renal Abnormalities in Patients With Turner Syndrome

Chromosomal Karyotype	No. of Patients Studied	No. (%) of Abnormalities
45,X	80	36 (45)
45,X/46,XX	12	3 (25)
45,X/46,Xi(Xq)	13	4 (30)
45,X/46,XY	7	2 (29)
45,X/46,Xr(X)	8	1 (12.5)
45,X/46,XXq−	2	1 (50)
46,Xi(Xq)	10	0 (0)
45,X/47,XXX	2	0 (0)
46,XXq−	2	0 (0)
46,XXp−	2	0 (0)
45,X/46,XXp−	1	0 (0)
45,X/46,Xmar/46,XXp−	1	0 (0)
45,X/46,Xi(Xq)/46,XXp−	1	0 (0)

with infection and reflux since the introduction of ultrasonography as our first imaging technique, there is a growing body of literature in which it is reported that ultrasonography can successfully replace IVP as a screening procedure even for these patients.[12-15] Thus, we now recommend that ultrasonography be the renal imaging method of choice to screen all patients with Turner syndrome and that all of these patients have an initial renal ultrasound as part of their primary evaluation.

This series, and others,[7] clearly demonstrate the spectrum of renal abnormalities that occurs in patients with Turner syndrome. The abnormalities range from embryologic malformations in budding of the metanephros (double collecting systems, extrarenal pelvis, and absent kidneys) to abnormalities in migration (ectopia, rotational abnormalities, and pelvic kidney). That the proposed mechanisms of ureteropelvic junction obstruction (also found in Turner syndrome and documented in this series) range from embryologic failure of normal ureteral recanalization to extrinsic compression on a vascular basis[16] further supports the heterogeneity of etiology of the renal malformations.

The high percentage (7%) of horseshoe kidneys seen in this series merits comment. This percentage far exceeds the reported prevalence of 1/600 to 1/1,800[16] in the "normal" population and could be clinically significant because there may be an increased incidence of Wilms tumor in the horseshoe kidney.[17] The mechanism of horseshoe formation is thought by some to represent a primary defect of embryogenesis resulting in the union of the two metanephric blastemas, whereas others believe that it is secondary to malposition of the umbilical arteries causing a mechanical malposition and union. If the increased incidence of Wilms tumor reported to occur in horseshoe kidney resulted from an abnormal proliferation of the metanephric blastema and if that occurred in patients with Turner syndrome, then these patients would be at the same risk as others with a horseshoe kidney and the incidence of Wilms tumors in patients with Turner syndrome should be high. Alternatively, if the high incidence of horseshoe kidney in patients with Turner syndrome is secondary to a vascular mal-

position, then these patients should be at no greater risk for Wilms tumor than is the general population. At present, only one patient with both Wilms tumor and Turner syndrome has been reported,[16] suggesting the latter hypothesis. Therefore, at this time we do not recommend repeat ultrasonography or magnetic resonance imaging examination of the horseshoe kidney of a patient with Turner syndrome if the first study results are adequate and not suggestive of a tumor.

In summary, we have demonstrated that at least one third of patients with Turner syndrome have a renal malformation that is demonstrable by current imaging techniques. At this time, we recommend that renal ultrasonography be used as a screening technique for all patients with Turner syndrome during their initial evaluation.

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