RENAL MALFORMATIONS IN CHILDREN WITH TURNER’S SYNDROME

Pin Chang, Yong-Kwei Tsau, Wen-Yu Tsai, Wen-Shiung Tsai, Jia-Woei Hou, Pei-Hung Hsiao, and Jing-Shang Lee

Abstract: Between 1988 and 1999, renal sonography and intravenous urography were performed to detect renal malformations in 54 patients with Turner’s syndrome (TS). The mean age of these patients at diagnosis of TS was 9.2 ± 4.6 years. Renal malformations were detected in 21 patients by intravenous urography and there was no significant difference in the frequency of renal malformations among different karyotype groups. Horseshoe kidney was the most common renal malformation, followed by duplex kidney. Fifteen of 21 renal malformations were not detected by renal sonography. We conclude that these TS patients had a high frequency of renal malformations, and that the detection rate of horseshoe kidney and duplex kidney by renal sonography was not satisfactory. Although renal sonography alone can be used to detect more severe renal malformations that may need further management, it may underestimate the frequency of renal malformation in children with TS.

An increased frequency of renal malformations has been reported in white patients with Turner’s syndrome (TS) [1–7], with horseshoe kidney being the most common type [1, 3, 5, 7]. However, whether ethnic differences in the patterns of renal malformations exist and whether renal sonography is a good tool to investigate these renal malformations remains unclear. The purpose of this study was to determine the frequency of renal malformations in Taiwanese children with TS and to compare the detection rates of renal sonography and intravenous urography (IVU) in these patients.

Subjects and Methods

Fifty-four Taiwanese children with TS who were followed up at the pediatric endocrine clinic of National Taiwan University Hospital from 1988 to 1999 were enrolled in the study. The diagnosis of TS was made using karyotyping peripheral lymphocyte culture. The mean age at diagnosis of TS in these patients was 9.2 ± 4.6 years. The age of the patients at the time data were collected for this study was 16.9 ± 5.3 years.

Renal structures were initially investigated by renal sonography, followed by IVU to confirm the diagnosis. Maximum renal length was measured in the prone position using renal sonography. All sonographic data were obtained using a model SAA 250 (Toshiba, Tokyo, Japan) with a 3.5-MHz probe. Data were analyzed using Fisher’s exact test or the chi-square test as appropriate. A p value of less than 0.05 was considered statistically significant.

Results

The 54 patients were classified into three groups on the basis of their karyotypes: complete monosomy, X-mosaic monosomies, and X structural abnormalities (Table 1). Renal malformations were detected in 21 of the 54 patients. This is a markedly higher prevalence of renal malformations than that in normal Taiwanese children (0.5%) [8]. There was no significant difference in the frequency of renal malformation among the three different karyotype groups (Fisher’s exact test, p = 0.27).

The distribution of various types of renal malformation in patients with TS and the detection rates of these malformations by renal sonography are shown in Table 2. Horseshoe kidney was the most common renal abnormality, followed by duplex kidney, malrotation, and obstructive hydronephrosis. Two patients with horseshoe kidney also had obstructive hydronephrosis. The other three cases of obstructive hydronephrosis in this series were related to ureteropelvic junction stenosis. A poor rate (29%) of detection of renal malformations by renal sonography was noted. The data indicate that renal sonography is not a good tool for the investigation of the
Renal Anomalies in Turner’s Syndrome

The frequency of renal malformation in patients with TS. However, all severe renal malformations, such as hydronephrosis and renal agenesis, were detected by renal sonography.

No patients with X structural abnormalities had horseshoe kidney, and only one such patient had renal malrotation. On the other hand, 10 of 13 patients with pure monosomy 45,X or X-mosaic monosomies had positional abnormalities involving migration of the kidney (Fisher’s exact test, \( p < 0.05 \)). No significant difference was found between renal size in this series of children with TS and previously reported renal size in normal Taiwanese children [9]. None of our patients with TS and renal malformation had a history of frequent urinary tract infection.

Discussion

TS is the most common sex chromosome abnormality in females. The prevalence of TS is estimated to be 1 in 1,500 to 1 in 5,000 live-born female infants [10, 11]. A recent study reported evidence for a TS locus or loci at Xp11.2–p22.1 [12]. The frequency of renal malformation in TS has been reported to be between 30% and 70% in white populations [1–7]. Our study also demonstrated a higher frequency of renal malformation in Taiwanese children with TS than that reported in normal children.

It has been reported that patients with pure monosomy 45,X have an increased risk of developing renal malformation [6, 7]. Similarly, 50% of our patients with pure monosomy 45,X had renal malformations, a higher rate than patients with other karyotypes. However, this difference was not statistically significant.

Renal sonography has been advocated as a potential replacement for IVU in initial screening for renal malformations in patients with TS. However, our data showed that renal sonography might miss horseshoe kidney, duplex kidney, or renal malrotation in a significant number of cases. Because overlying bowel may obscure the connecting isthmus, horseshoe kidney may be difficult to identify by renal sonography [13]. Abnormalities of the renal axis and rotation are also better shown by IVU [13]. It may also be difficult for renal sonography to detect nonobstructed duplex kidneys. Many patients with duplex kidney may not have the characteristic ultrasonographic signs, such as splitting of the renal sinus echo complex, two separate collecting systems at the renal hilum, and nephromegaly [14]. Our results indicate that renal sonography as a screening method may underestimate the frequency of renal malformations in children with TS. On the other hand, renal sonography can easily detect severe renal malformations and can, therefore, be performed as an initial screening method in patients with TS.

The pathogenesis of renal abnormalities ranges from structural malformations in budding of the metanephros (duplex kidney, extrarenal pelvis, and renal agenesis) to positional abnormalities in migration (horseshoe kidney, rotational abnormalities, and pelvic kidney) [6]. Both of these main categories of renal malformation were found in our patients, with horseshoe kidney being the most common. This result is consistent with previous reports [1, 3, 5, 7]. However, it is interesting that fewer patients with X structural abnormalities had positional

### Table 1. Distribution of karyotypes and frequency of renal malformation in 54 patients with Turner’s syndrome

<table>
<thead>
<tr>
<th>Classification</th>
<th>Karyotype</th>
<th>No. (%)</th>
<th>% with renal malformation†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete monosomy</td>
<td>45,X</td>
<td>24 (44)</td>
<td>50 (12)</td>
</tr>
<tr>
<td>X mosaic monosomies</td>
<td>45,X/46,XX</td>
<td>16 (30)</td>
<td>25 (4)</td>
</tr>
<tr>
<td></td>
<td>45,X/47,XX</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>X structural abnormalities</td>
<td>45,X/46,X,iXq</td>
<td>14 (26)</td>
<td>36 (5)</td>
</tr>
<tr>
<td></td>
<td>46,X,iXq</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>46,X,r(X)</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>46,X,Xp-</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>45,X/46,X,+M*</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>45,X/46,XX/46,X,+M*</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>54 (100)</td>
<td>39 (21)</td>
<td></td>
</tr>
</tbody>
</table>

* M = marker from X chromosome; † numbers in parentheses denote number of patients with renal malformation detected by intravenous urography.

### Table 2. The distribution of renal malformations and detection rate by renal sonography

<table>
<thead>
<tr>
<th>Malformation</th>
<th>No. detected by renal sonography</th>
<th>Detection rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Horseshoe kidney</td>
<td>6*</td>
<td>17</td>
</tr>
<tr>
<td>Duplex kidney</td>
<td>5</td>
<td>20</td>
</tr>
<tr>
<td>Malrotation</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>Hydronephrosis</td>
<td>3†</td>
<td>100</td>
</tr>
<tr>
<td>Renal agenesis</td>
<td>1</td>
<td>100</td>
</tr>
<tr>
<td>Extrarenal pelvis</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>21</td>
<td>29</td>
</tr>
</tbody>
</table>

* Two patients with horseshoe kidney also had hydronephrosis; † obstructive hydronephrosis due to ureteropelvic junction stenosis.
renal malformation in our study. It has also been reported that fewer cardiovascular abnormalities are detected in patients with X structural abnormalities than in those with other TS karyotypes [15–17].

Shepard and Fantel suggested that web neck, cardiovascular abnormalities, and horseshoe kidney are related to embryonic and fetal deformation from edema in TS patients [18]. The lower frequency of horseshoe kidney in our children with X structural abnormalities may indicate that they had less severe fetal edema than those with X monosomy or mosaic X monosomies. A recent study also showed that patients with less X-chromosome loss usually do not express the typical TS phenotype, such as web neck [7]. These data may explain our findings of less frequent positional renal malformations and cardiovascular abnormalities in patients with X structural abnormalities. Although none of our patients with X structural abnormalities had horseshoe kidney, they did have an increased frequency of other structural abnormalities of the kidney. Therefore, patients with any form of TS should have routine nephrologic screening [6, 7].

In conclusion, this study detected a high frequency of renal malformations (39%) in Taiwanese children with TS. These malformations have been reported to be associated with renal neoplasm in horseshoe kidney [19, 20] and secondary renal impairment due to obstruction and/or parenchymal infection [10]. Our data suggest that a renal imaging study should be performed when the diagnosis of TS is established, in order to detect renal malformations as early as possible. We also showed that the most common kinds of these malformations, such as horseshoe kidney and duplex kidney, were usually difficult to detect by renal sonography. Hence, renal sonography alone may underestimate the frequency of renal malformations in children with TS. On the other hand, because severe renal malformations, such as obstructive hydronephrosis and renal agenesis, would not be missed by renal sonography, it remains a useful tool for screening.

References


