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ORIGINAL ARTICLE

Posterior urethral valves: are neonatal imaging findings predictive of renal function during early childhood?

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Abstract
Background Obstructive renal dysplasia as observed on US is associated with posterior urethral valves and is regarded as predicting poor renal functional outcome.
Objective To investigate whether any characteristic of urinary tract imaging at birth is predictive of renal function in children with prenatally diagnosed posterior urethral valves.
Materials and methods We reviewed clinical data including renal function (at birth and up to 3 years of age) and clinical outcome (urinary infection, dialysis, renal transplantation). Imaging data included US (dilatation of the urinary tract, renal cortical echogenicity, signs of cystic dysplasia, urinoma) and cystourethrography findings (vesicoureteral reflux, bladder anomalies, presence of valves) from imaging performed directly after birth.
Results We retrospectively studied 30 children. Three of the 30 (10%) were in renal failure by the age of 3 years. Twelve of 14 (85%) children with parenchymal anomalies (cortical hyperechogenicity or cystic changes) and 8/9 (89%) children with bilateral high-grade reflux had normal renal function at age 3 years. One child without cystic dysplasia or reflux had abnormal renal function from birth. None of the six children with urinoma developed renal failure by the age of 3 years.
Conclusion Presence of cortical hyperechogenicity, cystic changes or bilateral reflux cannot be considered prognostic of renal failure by the age of 3 years.

Keywords Children · Chronic kidney disease · Micturating cystourethrography · Neonate · Posterior urethral valves · Prognosis · Renal failure · Renal function · Ultrasound

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Introduction

Posterior urethral valves are suspected during obstetrical US (usually during the 2nd or 3rd trimesters) whenever prenatal US shows an enlarged urinary bladder with thickened wall (>3 mm) associated with oligohydramnios [1, 2]. Associated upper urinary tract dilatation is frequent but variable, as is renal (cystic) dysplasia. The dilated posterior urethra can be demonstrated in some fetuses [3]. Posterior urethral valves can also be suspected in utero in case of bladder rupture with ascites or through the detection of a perirenal urinoma [4]. Still, the timing of diagnosis during pregnancy varies greatly and some cases are not detected until birth.

The outcome of posterior urethral valves is variable and depends on the severity of the bladder outlet obstruction and the degree of renal failure, and early treatment by endoscopic valve ablation in the neonatal period is intended to prevent worsening renal and bladder function [5, 6]. Postnatal mortality is estimated at 8%, and about 30% of affected children

progress to chronic renal insufficiency, the majority around puberty [7–9].

High morbidity of children with posterior urethral valves (from long-term renal failure) can be predicted on the basis of a high nadir creatinine value at birth [10], by renal cortical hyperechogenicity or (cystic) dysplastic changes [11], and by the presence of bilateral vesicoureteral reflux at diagnosis [12, 13]. On the contrary, urinomas are said to indicate a better prognosis [14]. Cystourethrography and a renovesical sonogram are recommended as early as possible, even the day of birth [15].

Therefore we investigated whether any imaging characteristics of the urinary tract at birth are predictive of the renal function during the first 3 years of life in children with prenatally diagnosed posterior urethral valves.

Materials and methods

We reviewed the clinical and imaging files of all neonates at our hospital with prenatal suspicion and endoscopic confirmation of posterior urethral valves during a period of more than 7 years (March 2007 to July 2014).

Prenatal suspicion of posterior urethral valves was based on an enlarged bladder with thickened wall (>3 mm) and was sometimes associated with oligohydramnios and upper urinary tract dilatation. Exclusion criteria included insufficient follow-up and prematurely born infants (before 37 weeks' gestational age) because of their potential physiological cortical hyperechogenicity that cannot be differentiated from hyperechogenicity associated with dysplasia [16].

Because this was a retrospective observational study, informed consent was waived by our institutional ethics committee.

We reviewed the clinical data for each child, including biological evaluation of renal function at birth, at 1 year, at 2 years and up to 3 years, as well as the clinical outcome (episodes of urinary infection, dialysis, renal transplantation).

A serum creatinine value (at birth and at follow-up) less than 1 mg/dl was considered normal. A nadir creatinine value <0.85 mg/dl — defined as the lowest serum creatinine value during the first year following diagnosis — was considered normal [17]. Renal function was determined by the Schwartz [18] formula, according to the level of creatinine clearance expressed in ml/min/1.73 m^2, and was classified as stage 1 (>90 ml/min/1.73 m^2), stage 2 (60–89 ml/min/1.73 m^2), stage 3 (30–59 ml/min/1.73 m^2), stage 4 (15–29 ml/min/1.73 m^2) or stage 5 (<15 ml/min/1.73 m^2, or substitutive treatment). Stage 1 corresponded to normal renal function, stage 2 to mild renal failure, stage 3 to moderate renal failure, stage 4 to severe renal failure and stage 5 to severe renal failure necessitating substitutive treatment.

We reviewed imaging data including US of the urinary tract and voiding cystourethrography, both performed within the first 2 days of age. Various US equipment was used during the years of the study. The highest-frequency linear transducers with optimized settings were used to assess the renal parenchyma. Voiding cystourethrography was always performed with a suprapubic bladder catheter.

The images were analyzed systematically by two pediatric radiologists (FA and VH, with 22 and 5 years of experience in fetal imaging, respectively) on the Picture Archiving and Communication System of the department (iSite Enterprise; Philips Healthcare, Eindhoven, the Netherlands) and the conclusions were drawn after consensus between them.

For each cystourethrography, the anomalies recorded included:

- presence of vesicoureteral reflux, including side and grade using the international grading system [19],
- evaluation of the urethra and any evidence of obstructive valves,
- presence of a patent urachus and
- bladder anomalies.

For each US examination, the data recorded included:

- kidney size measured on the longest sagittal diameter of each kidney and expressed as standard deviations away from the mean (age-dependent) [20];
- cortical echogenicity as compared to the liver or spleen (defined as increased, equal to or decreased);
- cortico-medullary differentiation expressed as present, absent or reversed, and dilatation of the urinary tract (uni- or bilateral, and defined as mild, which is anteroposterior diameter of the renal pelvis — as measured on a transverse scan of the kidney in the prone position — above 7 mm or ureteral diameter — as measured on a sagittal scan behind the bladder — above 3 mm; moderate, which is anteroposterior diameter of the renal pelvis above 10 mm or ureteral diameter above 6 mm; or severe, which is anteroposterior diameter of the renal pelvis above 15 mm or ureteral diameter above 10 mm);
- signs of (obstructive) renal dysplasia including hyperechoic cortex, absent cortico-medullary differentiation, and thinned cortex (signs of cystic dysplasia were the same but with visible cortical cysts [21]);
- presence of perirenal urinoma, and
- thickening of bladder wall (defined as >5 mm when full).

We compared the imaging findings of children with and without renal failure.

Because the series is relatively small, splitting the group according to the findings rendered a robust statistical analysis

difficult. Still, continuous variables were expressed as mean (standard deviation) and range, and the qualitative variables as frequencies and percentages.

Results

Between March 2007 and July 2014, 34 successive children were examined in the radiology department of Jeanne de Flandre Hospital, France, for prenatally suspected and endoscopically confirmed posterior urethral valves. Follow-up data were not available for 4 children, who were followed elsewhere. The evaluation was therefore based on the remaining 30 children.

The mean serum creatinine value at birth was 1.2 mg/dl (standard deviation [SD] 8.62, range 2–35) with a corresponding creatinine clearance of 16.9 ml/min/1.73 m^2. Fourteen of the 30 children (47%) had an abnormal creatinine value at birth (>1 mg/dl after 3 days of age), which normalized during the first month of life in 12 children.

Reno-vesical US data

In 2/30 children (7%), the entire urinary tract appeared normal at birth and during follow-up. The other 28 children (93%) had abnormal US at birth. All 28 children presented with renal dilatation: unilateral in 7/28 (25%), bilateral in 21/28 (75%). The width of the renal pelvis was 10 mm for the right pelvis (SD 5.69, range 0–20 mm) and 10 mm for the left pelvis (SD 5.54, range 0–20 mm). The mean size of the ureter was 5 mm for the right ureter (range 0–11 mm) and 6 mm for the left ureter (range 0–13 mm).

There were 49 dilated kidney-ureter units. Of these, dilatation was mild in 5/49 (10%), moderate in 30/49 (61%) and severe in 14/49 (29%). Fourteen of the 30 children (47%) had renal dilatation (uni- or bilateral) associated with a normal-appearing parenchyma, and 14/30 children (47%) had dilatation with parenchymal dysplasia, including 12/30 (40%) with parenchymal dysplasia with cysts (Fig. 1) and 2/30 (7%) with renal dysplasia without cysts. Six of 30 children (20%) had perirenal urinoma (Fig. 2).

The mean length of the right kidneys was 52 mm (SD 2.66 mm, range 30–69 mm). The mean length of the left kidneys was 50 mm (SD 1.97, range 10–92 mm).

Cystourethrography data

Cystourethrography findings are detailed in Fig. 3. Twenty-nine of 30 children (97%) presented a characteristic dilatation of the posterior urethra. One child had normal urethra but with endoscopic confirmation of posterior urethral valves.

Bladder diverticula were present in 23/30 children (77%) (Fig. 4). Five of 30 (17%) had irregular appearance of the bladder wall, and the other 2 of 30 (7%) had a morphologically normal bladder.

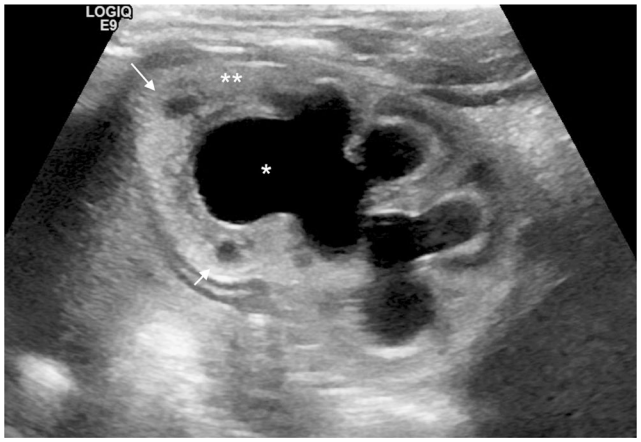

Fig. 1 Renal dilatation and cortical cysts in a boy with posterior urethral valves. Sagittal sonogram at 1 day old demonstrates pelvicalyceal dilatation (*asterisk*). The parenchyma (**) appears hyperechoic without cortico-medullary differentiation. Cysts (*arrows*) are visible

Four of 30 children (13%) had a patent urachus (Fig. 5).

Ten of 30 children (33%) had no vesicoureteral reflux; among these 10, 7 had bilateral dilatation and 3 had unilateral dilatation on US. The other 20 of 30 children (67%) had vesicoureteral reflux, including 11 unilateral and 9 bilateral, all scored as high-grade (grades IV or V). One child had bilateral vesicoureteral reflux (grade V) but neither dilatation nor parenchymal abnormality on US.

Follow-up imaging of the children with renal failure

Nine of the 30 children (30%) had a 1-year follow-up, 10/30 (33%) had a 2-year follow-up and 11/30 (37%) had at least a

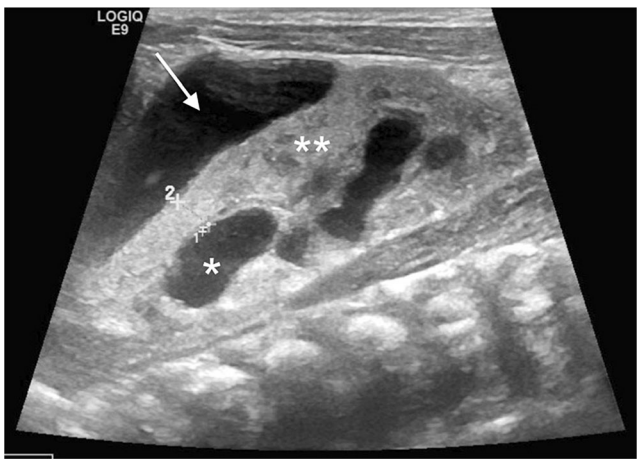

Fig. 2 Perirenal urinoma in a boy with posterior urethral valves. Sagittal sonogram at 1 day old (right kidney) demonstrates a dilated pelvicalyceal system (*asterisk*). The parenchyma (**) is hyperechoic with poor cortico-medullary differentiation. The urinoma is seen as a cystic collection (*arrow*) around the kidney

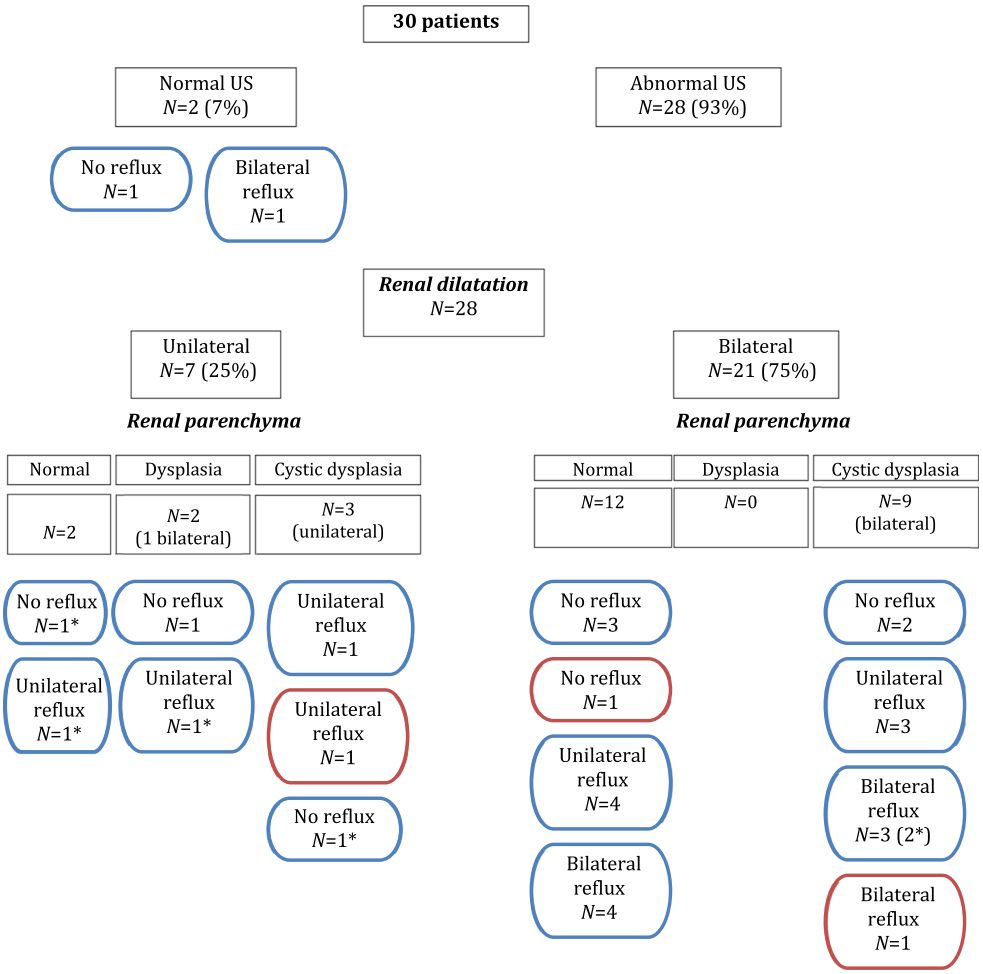

Fig. 3 Cystourethrography findings in 30 neonates with posterior urethral valves. *Rectangles* indicate US findings. *Blue rounded boxes* indicate cystourethrography findings in patients who did not develop renal failure. *Red rounded boxes* indicate cystourethrography findings in patients with renal failure. The number of patients with urinoma have been indicated by asteroids

3-year follow-up. The mean follow-up duration was 30 months (SD 18.30, range 12–72 months).

None of the 30 children died. The vast majority, 27/30 (90%) children, did not develop renal failure (including 7 children who had repeated bouts of pyelonephritis). Among these, 2/27 displayed at birth hyperechoic renal parenchyma (suggestive of dysplasia) and 9/27 had renal parenchymal changes suggestive of obstructive cystic dysplasia. Among the 6 patients with perirenal urinoma, none had renal failure; the mean follow-up duration for these patients was 25 months (SD 13.3, range 6–48 months).

Three of the 30 children in the study (10%) developed renal failure, and all 3 of these children had abnormal renal function from birth (stage 5), and 2 had an abnormal nadir value (>0.85 mg/dl). One child underwent kidney transplant at age 24 months. His creatinine value at birth was 2.7 mg/dl (creatinine clearance = 7 ml/min/1.73 m^2; stage 5). On US at birth, he displayed small kidneys (4.9 and 5.6 standard deviations below the mean for the right and left kidneys, respectively) and moderate bilateral dilatation, but no sign of dysplasia. There was no vesicoureteral reflux. At age 4 months, his nadir was 1.4 mg/dl and his creatinine clearance 17 ml/min/1.73 m^2 (stage 4), and at age 1 year, his serum creatinine was 2.5 mg/dl (creatinine clearance 11 ml/min/1.73 m^2; stage 5). He started dialysis at age 18 months. The second child underwent kidney transplant at age 5 years. His serum creatinine at birth was 3 mg/dl (creatinine clearance 6.8 ml/min/1.73 m^2; stage 5). On imaging at birth, findings included mild unilateral ureteral dilatation, unilateral cystic dysplasia with ipsilateral reflux grade IV and a normal contralateral kidney. His nadir was 2.4 mg/dl at age 2 months (creatinine clearance 9.5 ml/min/1.73 m^2; stage 5). His serum creatinine value was 2.1 mg/dl at age 1 year (creatinine clearance 14 ml/min/1.73 m^2; stage 5). He underwent dialysis between the ages of 1 month and 10 months. The third child, presently 7 years old, had renal failure since age 4 years and began dialysis at age 5 years. He was waiting for a kidney transplant at the time of writing. His imaging findings at birth included severe bilateral dilatation, bilateral cystic dysplasia and bilateral reflux grade V. His

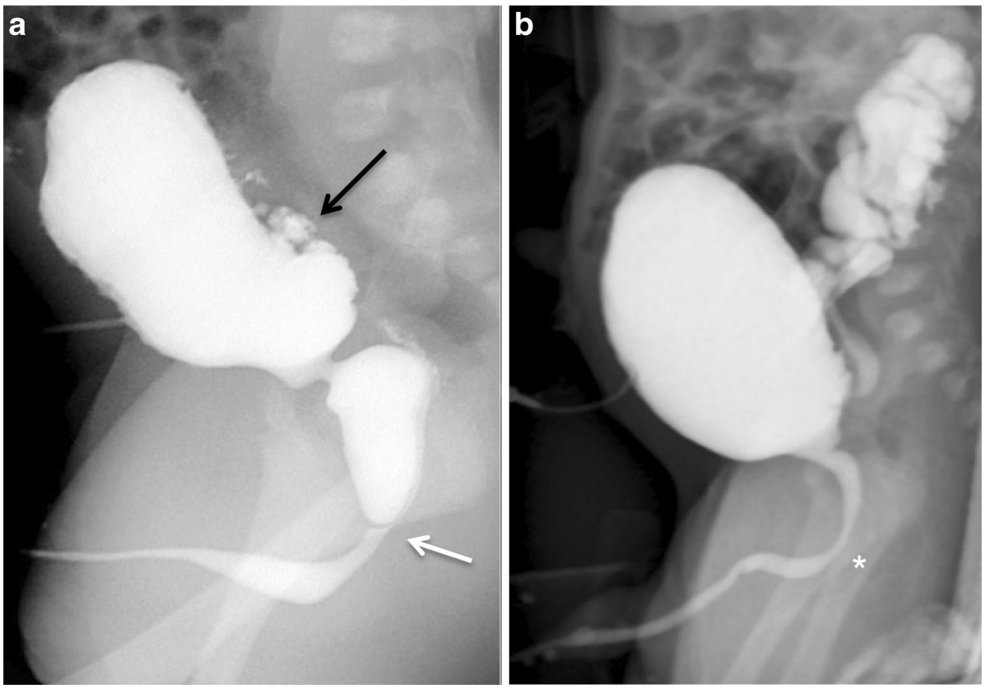

Fig. 4 Cystourethrography in two newborn boys with posterior urethral valves. **a** In one boy there is dilatation of the posterior urethra above the valves (*white arrow*) and bladder diverticula (*black arrow*). **b** In the other boy, also with surgically confirmed valves, the posterior urethra (*asterisk*) appears normal

serum creatinine value at birth was 1.5 mg/dl (creatinine clearance 13 ml/min/1.73 m^2; stage 5). His nadir was 0.7 mg/dl at age 2 months (creatinine clearance 32 ml/min/1.73 m^2; stage 3). His serum creatinine value was 0.7 mg/dl at age 1 year (creatinine clearance 41 ml/min/1.73 m^2; stage 3).

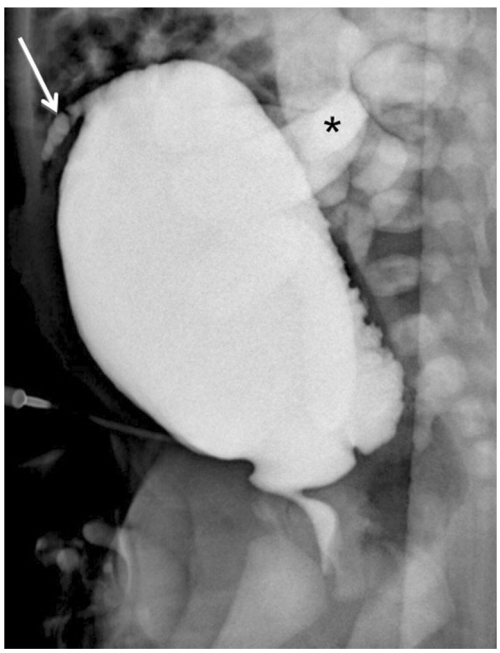

Fig. 5 Patent urachus. Cystourethrography in a newborn boy with posterior urethral valves demonstrates a patent urachus (*arrow*) and bilateral vesicoureteral reflux (*asterisk*)

Discussion

Posterior urethral valves are the most frequent cause of congenital lower urinary tract obstruction affecting boys [22]. The antenatal suspicion of posterior urethral valves leads to a tailored postnatal workup that includes a detailed US evaluation of the urinary tract and voiding cystourethrography. If the diagnosis is confirmed, the valves undergo endoscopic ablation [14]. This early treatment by endoscopic ablation of the valves significantly reduces perinatal mortality to 8%. The morbidity — related in the long term to renal damage, bladder dysfunction and urinary infections — remains high because nearly 30% of these children experience renal failure before adolescence [4]. Therefore these children have to be continually monitored and followed by means of clinical, biological and imaging techniques to prevent complications. For this reason it would be interesting to specifically monitor children with a poorer prognosis and at higher risk of complications.

In our study only 10% (3/30) of the children progressed to chronic renal failure (by the age of 3 years), which is lower than noted in the literature [4]. One might speculate that prenatal diagnosis and early postnatal management improve prognosis. Interestingly, all these children were in renal failure at birth, but no child in our series died.

US findings of renal cortical hyperechogenicity and cystic parenchymal changes, and cystourethrography findings of bilateral vesicoureteral reflux have been associated with higher morbidity and are indicative of poorer renal outcome [11].

Two children in our study had completely normal US at birth, while the most common US anomaly was urinary tract dilatation (in 93% of the children). The mean pelvic dilatation was about 10 mm (moderately dilated). The renal parenchyma never appeared abnormal in the absence of dilatation. Conversely, considering the 49 renal units with dilatation, the renal parenchyma was abnormal in 49% (24/49) and cystic dysplasia was demonstrated in 21/24.

Noteworthy, 85% (12/14) of the children with parenchymal anomalies had normal renal function at the time of the study (including 10/12 [83%] with cystic dysplasia).

High-grade vesicoureteral reflux was found in 20/30 children (67%); in 9 the reflux was bilateral. Reflux was found in children with and without parenchymal anomalies on US. Similarly, 89% (8/9) of the children with bilateral high-grade reflux had normal renal function at the time of the study. Conversely, one of our patients with chronic renal failure had neither parenchymal anomaly nor vesicoureteral reflux despite abnormal creatinine levels from birth.

There is no clear pattern of association between neonatal imaging findings and renal functional outcome in our study. Specifically, abnormal renal tract and renal parenchymal US or abnormal voiding cystourethrography findings in the neonate were not systematically associated with abnormal renal function during the period from birth to 3 years of age. Our findings therefore contradict previous research. It follows that neonatal imaging findings (renal cortical hyperechogenicity, cystic changes and bilateral vesicoureteral reflux) should be interpreted cautiously in predicting normal or abnormal functional outcome. On the other hand, none of the children with perirenal urinoma had renal failure, which is in agreement with prior research [14].

There are several limitations to our study. First, it was a retrospective study (yet all the images and reports were carefully reviewed). The number of cases is relatively small and therefore statistical confirmation could not be ascertained for each sign reported. A prospective larger case study would be important to confirm our findings. Finally, the follow-up duration of some patients (1 year) might be insufficient to detect developing renal failure.

Conclusion

Standard neonatal imaging is not sufficient to predict the renal function by age 3 years in boys with a prenatal diagnosis of posterior urethral valves. Renal cortical hyperechogenicity, cystic changes or bilateral reflux at diagnosis cannot be considered poor prognostic factors.

Compliance with ethical standards

Conflicts of interest None

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