Unusual association of diseases/symptoms

Pelvi-ureteric junction obstruction in autosomal-dominant polycystic kidney disease: an association yet to be reported

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Summary

Autosomal-dominant polycystic kidney disease (ADPKD) is the most common inherited renal cystic disease. It is characterised by the development of renal parenchymal cysts and a variety of other extrarenal manifestations. Pelvi-ureteric junction (PUJ) obstruction has not been described in association with ADPKD in the literature. We present a case of a 23-year-old man presenting with bilateral flank pain. On evaluation he was diagnosed to have ADPKD with bilateral renal calculi and left-sided PUJ obstruction. He underwent successful right percutaneous nephrolithotomy and left laparoscopic dismembered pyeloplasty with simultaneous stone removal.

BACKGROUND

Autosomal-dominant polycystic kidney disease (ADPKD) is the most common and well-studied Mendelian disorder of the kidney that affects all racial groups worldwide with a prevalence of 1 in 500 to 1000.¹ It is characterised by focal and sporadic development of renal cysts that increase in number and size with age. Nearly one-third of the patients are found to have renal calculi, usually associated with the metabolic abnormalities.² We report an unusual case of autosomal-dominant polycystic kidney disease (ADPKD) with bilateral renal stone having left pelvi-ureteric junction (PUJ) obstruction. Although the association of PUJ obstruction with ADPKD has been reported once in a nephrectomy specimen, to the best of our knowledge, this is the first case of PUJ obstruction associated with ADPKD and bilateral renal calculi, appropriately diagnosed and managed using minimally invasive surgery.

CASE PRESENTATION

A 23-year-old man presented with complains of intermittent bilateral flank pain and few episodes of haematuria for last 6 months. His physical examination was unremarkable. His two elder brothers also complained of intermittent bilateral flank pain for 4 years. His father had died of renal failure at the age of 52 years.

INVESTIGATIONS

Initial evaluation with ultrasonography revealed bilateral multiple renal cysts with bilateral renal calculi. All routine blood investigations including renal function were within normal limits. Urinalysis revealed microscopic haematuria. Contrast-enhanced CT scan of abdomen with CT urogram (figures 1–3) confirmed the presence of numerous bilateral renal cysts with right renal pelvic and left inferior caliceal calculi and left hugely dilated extrarenal pelvis, suggestive of PUJ obstruction. Isotope renal scan confirmed significantly obstructed drainage. The family history was conclusive of ADPKD, as his father

had died of renal failure and both of his elder brothers were found to have bilateral multiple renal cysts on screening ultrasonography.

TREATMENT

After complete evaluation he underwent successful right percutaneous nephro-lithotomy followed by left laparoscopic Anderson Hynes dismembered pyeloplasty with simultaneous stone removal. The postoperative period was uneventful. Bilateral double-J stents were removed after 4 weeks. He is on regular follow-up and doing well.

DISCUSSION

In ADPKD, kidney is usually the first and most seriously affected organ. Annual incidence rates for end-stage renal disease caused by ADPKD are 6–8 per million in

Figure 1 Axial cut of the CT scan of the abdomen showing bilateral multiple renal cysts, bilateral calculi and hugely dilated left renal pelvis suggestive of uretero-pelvic junction obstruction.

Figure 2 Coronal view of the CT scan showing bilateral multiple cysts and features of Lt uretero-pelvic junction obstruction.

Europe and 7–9 per million in the USA, accounting for up to 10% of chronic dialysis population.³ All renal manifestations are directly related to the development and enlargement of renal cysts. Most of the cases of ADPKD are caused by mutations in either of the two

Figure 3 CT-urogram showing hugely dilated left extrarenal pelvis caused by pelvi-ureteric junction obstruction.

genes encoding polycystin 1 and polycystin 2 (*PKD1* and *PKD2*, respectively).⁴ The presence of a third gene (*PKD3*) is now accepted as the cause of disease in a very small percentage of patients who are negative both for *PKD1* and *PKD2* gene, however the locus is yet to be identified.⁵ The polycystins regulate tubular and vascular development in the kidneys and other organs (liver, brain, heart and pancreas).⁴ Nephrolithiasis occurs in 20–30% of patients with ADPKD, and nearly one half of them are symptomatic. The aetiology of stone formation in ADPKD is a combination of metabolic abnormalities and local urinary stasis.² Like hypertension and infection, nephrolithiasis has also been proposed to hasten the onset of renal failure.

Extrarenal manifestations of ADPKD include cysts in liver, spleen, pancreas and seminal vesicles, valvular cardiac defects, colonic diverticulosis, intracranial Berry aneurysms and inguinal hernias.⁴ Apart from all these frequent manifestations, infantile hypertrophic pyloric stenosis (IHPS) has been reported in association with ADPKD.^{6,7} a finding that has not been linked to polycystin proteins. Loh *et al*⁷ reported this association, in a set of identical twins and their father. The association of dominantly inherited polycystic kidneys and IHPS in this family was thought to be due to chance. However, the authors speculated that the autosomal gene for polycystic kidney might occur at one of several loci that carry the genetic liability for IHPS.⁷ Later, molecular research in ADPKD localised this disease to two heterogeneous genetic foci: *PKD1* (chromosome region 16p13.3; around 85% cases) and *PKD2* (4q21; around 15% cases). Similarly, one of five genetic loci associated with IHPS has been localised to 16p13-p12, which is in close vicinity to *PKD1* that is, chromosome region 16p13.3.⁸ This appears to be in accordance with the speculation made by Loh *et al*.

In the present case, PUJ obstruction has been noted in association with ADPKD. Going back to the pathogenesis, neither polycystin gene mutation nor related genetic loci have been implicated in PUJ obstruction. Hereditary hydronephrosis due to unilateral or bilateral PUJ obstruction has been reported as an autosomal-dominant trait by Izquierdo *et al*.⁹ Linkage analysis was undertaken in five families with hereditary PUJ obstruction using the major histocompatibility complex locus as a test marker. Their data supported the assignment of one of the loci for hereditary hydronephrosis to chromosome 6p. So no such genetic linkage seems to exist between ADPKD and PUJ obstruction. This co-association of ADPKD and PUJ obstruction has been reported only once in the literature.¹⁰ But in that case PUJ obstruction was a retrospective histological diagnosis in a nephrectomy specimen, performed for renal trauma. Keeping in view, that PUJ obstruction is a functional diagnosis, histological finding of narrowing or kinking of the ureteral segment does not signify functional obstruction. In our case, a symptomatic patient was confirmed to have PUJ obstruction on structural and functional studies. Although, this merely appears to be a co-existence of two different pathological conditions, but this co-association bears significant clinical implications regarding the overlapping presentation and difficulty in diagnosis and treatment of these two entities.

Learning points

- ▶ Autosomal-dominant polycystic kidney disease (ADPKD) is the most common genetic renal cystic disease invariably leading to the renal failure and need for renal replacement therapy later in life.
- ▶ Stone disease in ADPKD is usually caused by associated metabolic abnormalities, but needs to be appropriately managed as it accelerates the ongoing renal damage through several mechanisms.
- ▶ Pelvi-ureteric junction (PUJ) obstruction is a congenital disease with poorly understood genetic basis. The present case is the first report of PUJ obstruction diagnosed appropriately in a patient of ADPKD. This condition causes diagnostic difficulties in the presence of polycystic kidney.
- ▶ PUJ obstruction needs to be timely diagnosed and appropriately managed using minimally invasive surgery as it will add an obstructive component to these compromised kidneys with progressive renal failure.

Competing interests None.

Patient consent Obtained.

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