Rare disease

Xanthogranulomatous pyelonephritis presenting as a pseudotumour in a 5-year-old boy

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Summary

Xanthogranulomatous pyelonephritis (XGPN) is a rare, severe and atypical form of chronic pyelonephritis. It is characterised by destruction of the renal parenchyma and replacement with a chronic inflammatory infiltrate and lipid-laden macrophages resulting in a non-functional kidney. The authors report a case of a 5-year-old boy presented with a history of abdominal pain, malaise, anorexia and weight loss for 2 months. Physical examination revealed a large flank mass and the child was directed to the oncology unit on suspicion of renal tumour. Based on clinical examination and imaging, the presumptive diagnosis of XGPN of the left kidney was made. A left transperitoneal nephrectomy was performed and the histology confirmed the diagnosis. Although rare, XGPN is a clinically important entity that should be considered in the differential diagnosis of an atypical-appearance renal mass in paediatric age.

BACKGROUND

Xanthogranulomatous pyelonephritis (XGPN) is a rare, severe and atypical form of chronic pyelonephritis. The aetiology is poorly understood. The most common associated factors are urinary tract obstruction and infection, not always present. It is presumed to be related to chronic bacterial infection, renal or lymphatic obstruction, alterations in lipid metabolism or an ineffective immune response. Most occurrences of XGPN are unilateral and diffuse in form. Mostly common in middle-aged women, it is important to recognise this rare entity in children because it may be confused with childhood renal malignancies particularly Wilms' tumour.

CASE PRESENTATION

A 5-year-old Caucasian boy with a 2-month history of unclear abdominal pain, malaise, anorexia, weight loss and pale skin was examined by his primary care physician. There was no significant family history. His parents confirmed no prior urinary symptoms, fever, history of urinary obstruction, renal calculi or urinary tract infections. Physical exam revealed a large flank mass and the child was directed to the oncology unit of our paediatric department with suspected renal tumour. On arrival the physical exam showed a temperature of 36.5°C, a pulse rate of 90 beats/min and a blood pressure of 100/53 mm Hg (50th–75th percentile). He was clinically pale in good nutrition status. A palpable left flank mass with poorly defined limits, estimated dimensions of 10×10 cm, slightly tender to the touch, a rubbery texture and dull to percussion was noted. The liver and spleen were not enlarged and there was no clinical evidence of ascites. Systemic examination was otherwise normal. No congenital anomalies were noted such as aniridia, hemihypertrophy or cryptorchidism.

INVESTIGATIONS

Blood investigations revealed microcytic hypochromic anaemia (Hb 8.1 g/dl), leucocytosis ($21.4 \times 10^3/\text{ul}$) and thrombocytosis ($823 \times 10^3/\text{ul}$). C reactive protein (11 mg/dl) and erythrocyte sedimentation rate (108 mm) were raised. Urinalysis demonstrated pyuria (1550/ul) and urine culture was positive for *Proteus mirabilis*. Tumour markers were negative and immunological study was unremarkable. Abdominal ultrasound was obtained showing a left kidney enlargement with pelvicaliceal dilatation, parenchyma destruction and the presence of calcifications (figure 1). Based on the imaging features, the diagnostic hypothesis were medullary sponge kidney, mesoblastic nephroma or unilateral nephroblastomatosis. An abdominal CT was ordered and it confirmed global renal enlargement,

Figure 1 Kidney ultrasound: enlarged left kidney, with bosselated surface and loss of corticomedullary differentiation. Multiple hyperechoic foci with posterior acoustic shadowing suggestive of calculi. There was no adrenal or renal space occupying lesions.

parenchyma destruction, presence of calculi, spread of infiltration into the fat capsule, thickening of Gerota's fascia and multifocal areas of varying density. The affected kidney was non-functional. The right kidney was normal (figure 2).

Renal scintigraphy with technetium-99m dimercaptosuccinic acid (^{99m}Tc -DMSA) confirmed the presence of no functional left renal parenchyma. Right kidney had normal dimensions and morphology, regular borders and a homogeneous distribution of radioactive tracer. The presumptive diagnosis of XGPN of the left kidney was made.

TREATMENT

In view of a symptomatic child admitted on suspicion of a renal tumour, in which the laboratory and imaging revealed a non-functional, diffuse, enlarged kidney suggestive of an inflammatory condition (but impossible to rule out the hypothesis of renal neoplasm) a transperitoneal left nephrectomy was performed. Preoperative broad spectrum antibiotherapy was administered. During surgery, adhesences to descendent colon were noted.

The pathological examination confirmed the diagnosis. A left kidney measuring $14 \times 11 \times 7$ cm was received. Macroscopic examination (figure 3) revealed an enlarged kidney with a thickened capsule. Renal pelvis was dilated and filled with debris and purulent fluid (figure 4). The renal parenchyma had an atrophic appearance with diminished consistency yellow areas (figure 5). Microscopic examination (figure 6) showed destruction of renal parenchyma by an acute and chronic inflammatory cell infiltrate with giant cells and lipid-laden macrophages. The final diagnosis of XGPN was made.

The differential diagnosis based on clinical presentation included neoplastic processes such as Wilms's tumour, nephroblastoma or renal cell carcinoma, lymphoma, germ cell tumour or an inflammatory process. The pathological differential diagnosis included renal malakoplakia but after periodic acid Schiff (PAS) staining identification of Michaelis-Gutmann bodies was not possible (foamy

Figure 2 Abdominal CT scan with contrast: renal asymmetry with global left renal enlargement ($13.7 \times 8.8 \times 7$ cm) with bosselated surface. Left kidney was non-functional with multifocal areas of varying density, intraparenchymal and pelvis calculi surrounded by parenchyma destruction. Dilated calices—'Bear paw sign'. Normal right kidney.

Figure 3 Pathology. Macroscopic examination: enlarged left kidney with bosselated surface.

macrophages with pale cytoplasm containing PAS positive basophilic inclusions, figures 7 and 8).

OUTCOME AND FOLLOW-UP

At the 3-year follow-up visit, the patient was still asymptomatic.

DISCUSSION

XGPN is a chronic destructive granulomatous inflammation of renal parenchyma.¹ The first descriptions of the distinctive gross and macroscopic features of this disease

Figure 4 Pathology. Macroscopic examination: in cut surface the renal pelvis was dilated and filled with debris and purulent fluid.

Figure 5 Pathology. Macroscopic examination. The renal parenchyma had an atrophic appearance. Adjacent to the pelvis and calyces, yellow areas were seen.

were made by Schlagenhaufen in 1916¹⁻³ but it was Oberlin who introduced the term XGPN in 1935.^{3 4} In 1978, Malek and Elder classified and staged the disease.^{3 5} The first paediatric case was described in 1963 by Avnet and Friedenber.^{3 6 7} It is an uncommon entity, accounting for between 0.6% of histologically documented cases of chronic pyelonephritis and 19.2% of nephrectomies performed for pyelonephritis.¹

XGPN most frequently occurs in middle-aged women with a history of recurrent urinary tract infection.^{1 4 8-11} A review of recently published data indicates that about 250 cases of XGPN have been reported for paediatric age.¹² The earliest presentation age reported so far has been 21 days¹³ even though 60–75% of cases have been diagnosed before 5 years of age.¹² Boys and girls of paediatric age are equally affected and the disorder in the left kidney is slightly more common than in the right.^{4 12}

Figure 6 Pathology. Microscopic examination (H&E stain). Infiltration of renal parenchyma by acute and chronic inflammatory cells.

Figure 7 Pathology. Microscopic examination (H&E stain). Presence of some foci of dystrophic calcification.

The exact aetiology of XGPN is unknown, but is generally accepted that the disease process is associated with long-term obstruction and infection.^{1 3 4 10 14-16} Other factors have also been implicated and include altered immune response and intrinsic disturbance of leucocyte function, alterations of lipid metabolism, lymphatic obstruction, malnutrition, arterial insufficiency and venous occlusion.^{4 10 16}

Two forms of XGPN have been described, a diffuse or global form (84.6%) as is this case, and a focal form (15.4%).^{1 4 10 16} It is further classified into three stages: stage I, the lesion is confined to the kidney (nephric), stage II, when it extends to Gerota's space as is this case (perinephric) and stage III, the extension to the perinephric space or retroperitoneal structures (paranephric).^{4 10}

XGPN has been termed as the great imitator because it may be misdiagnosed as a renal neoplasm, special focal lesions.^{4 10} The most common presenting features are intermittent fever, flank pain or flank tenderness, weight loss and palpable mass. This clinical presentation is similar among the reported cases and was also found in this case.

Haematological evaluation frequently shows microcytic anaemia and systemic inflammatory reaction (leucocytosis,

Figure 8 Pathology. Microscopic examination (H&E stain). Sheets of lipid-laden macrophages (foamy cells) and occasional multinucleated giant cells.

thrombocytosis, increased C reactive protein and erythrocyte sedimentation rate) as this case reported.^{1 3 4 17} Urinalysis often reveals pyuria and proteinuria.^{1 3 4} The percentage of positive urine cultures ranges from 61% to 88%.¹ The most common organisms are *Escherichia coli* and *Proteus mirabilis*. Others include *Staphylococcus aureus*, group B *Streptococcus*, *Candida* sp., *Klebsiella* and *Bacteroides*.¹ In this case, the urinalysis showed pyuria and *P. mirabilis* was isolated in urine culture.

There are no pathognomonic clinical or imagiological signs of this entity. Distinctive ultrasound and CT appearances of XGPN have been reported.^{1 3 9 11 16 18–20} Ultrasound of diffuse XGPN usually shows an enlarged kidney with a large amorphous central echogenicity that corresponds to renal pelvis staghorn calculus, irregular thinned parenchyma, dilated collecting system and multiple hypoechoic fluid-filled masses. In focal XGPN the findings are virtually impossible to differentiate from renal abscess or neoplasm. CT is the mainstay of diagnostic imaging for XGPN, and shows diffuse disease in most cases. The findings include hydronephrosis, renal calculi, pyonephrosis, intraparenchymatous collections, cortical renal atrophy and abscesses. However, the combination of a non-functioning enlarged kidney, a central calculus within a contracted renal pelvis, expansion of the calices and inflammatory changes in perinephric fat is strongly suggestive of XGPN.¹ It may also show the classic ‘bear paw sign’⁹ of dilated caliceal spaces, as this case reported.

Tc-DMSA renal scanning may be used to evaluate and confirm differential renal function.¹¹

The final diagnosis should be determined by histopathological examination.^{1 3 4 8 20} Macroscopic findings include an enlarged kidney with a thickened capsule, yellow nodules with or without central necrosis in the renal parenchyma and the renal pelvis may be dilated and filled with stones, debris or purulent fluid.^{1 20} Microscopic findings include mixed acute and chronic inflammatory cell infiltrate with giant cells and lipid-laden macrophages (foam cells). Misinterpretation of ‘foamy cells’ as ‘clear cells’ consistent with renal carcinoma is the most important diagnostic challenge in histological terms.²⁰ In this situation, an immunohistochemistry study plays an essential role in differential diagnosis.¹ Two benign closely related entities are malakoplakia and megalocytic interstitial nephritis. The hallmark of both lesions is the periodic acid-shift diastase-positive material in the cytoplasm of the macrophages while in malakoplakia Michaelis-Gutmann bodies are characteristic of the lesion.^{1 21}

Nephrectomy remains the standard care for the diffuse disease but partial nephrectomy is advocated whenever possible (focal or bilateral lesions).^{1 3 4 10 18 22 23} An anterolateral transperitoneal approach has been recommended instead of standard lumbar incisions to provide better exposure and facilitate dissection.^{11 20} Preoperative and postoperative broad-spectrum antibiotics are also key factors for successful management of this condition.

XGPN is a relatively rare entity. The resultant unawareness often delays diagnosis and therapy. It should be included in the differential diagnosis of children with a renal mass. Previously, XGPN diagnosis was normally based on pathological assessment after nephrectomy. Over the last decade, clinical awareness combined with increasingly sensitive radiological investigation has made

preoperative diagnosis possible. Once the diagnosis is made, the prognosis is excellent after appropriate treatment.^{1 12 20}

Learning points

- ▶ Xanthogranulomatous pyelonephritis is a rare disease in children.
- ▶ The symptoms are often vague and non-specific.
- ▶ It should be included in the differential diagnosis of children with a renal mass, anaemia and elevated inflammatory markers.
- ▶ CT is the mainstay of diagnostic imaging.
- ▶ Histopathological examination is necessary to confirm the diagnosis and exclude other benign and malignant diseases.
- ▶ Surgical intervention still remains the cornerstone of treatment for this uncommon disease and is a curative procedure.

Competing interests None.

Patient consent Obtained.

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