

Xanthogranulomatous pyelonephritis in childhood

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Abstract

Background—Xanthogranulomatous pyelonephritis is a severe, atypical form of chronic renal parenchymal infection accounting for 6/1000 surgically proved cases of chronic pyelonephritis. Its manifestations mimic those of neoplastic and other inflammatory renal parenchymal diseases and, consequently, it is often misdiagnosed preoperatively.

Aim—To examine the relation between clinical history and the results of renal investigations performed in children with xanthogranulomatous pyelonephritis.

Method—A retrospective review of 31 cases presenting with the histopathological diagnosis of xanthogranulomatous pyelonephritis between 1963 and 1999.

Results—The mean follow up was 8.2 years. The male:female ratio was 1:1.1. The left kidney was affected in 26 of the 31 patients. The positive findings on examination and investigation at presentation were: fever, 16 children; pyuria, 26 children; positive urine culture, 16 children. A haemoglobin of < 100 g/l was measured in 27 of 31 patients and 15 of 18 patients tested had a raised erythrocyte sedimentation rate of > 20 mm in the first hour. Twenty six children had renal calculi, with a large reduction in the function of the affected kidney on isotope scintigraphy in 27 of the 29 patients tested. Hypertrophy of the contralateral kidney, shown on imaging, was present in 17 of 31 patients.

Conclusions—Increasing awareness of this condition should lead to the diagnosis being suspected preoperatively.

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Keywords: nephrectomy; xanthogranulomatous pyelonephritis

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Xanthogranulomatous pyelonephritis is a severe, atypical form of chronic renal parenchymal infection accounting for six/1000 surgically proved cases of chronic pyelonephritis.¹ Its manifestations mimic those of neoplastic and other inflammatory renal parenchymal diseases and, consequently, it is often misdiagnosed clinically.

Women are affected more frequently than men, with a peak incidence in the 6th and 7th decades.² Up until 1982, only single case reports were described in children and, in all incidences, these were girls.³⁻¹² Since then, larger series of several cases have been reported.¹³⁻¹⁴ Nephrectomy has been curative in all cases, with no long term sequelae. To date, no large series of xanthogranulomatous pyelonephritis in children has been reported.

We report a retrospective review of 31 patients presenting to this unit between 1963 and 1999, the largest series of children with this disease to be reported to date.

Patients and methods

The hospital records of all 31 patients presenting to our unit with xanthogranulomatous pyelonephritis between 1963 and 1999 were examined. There were 16 girls and 15 boys aged between 7 months and 14 years at presentation. Details of symptoms at presentation, investigations, operative findings, and histological findings of the affected kidney were recorded. The mean follow up was 8.2 years (range, 2 months to 20 years).

Results

There was a history of previous urinary tract infection in only eight patients and the symptoms were of relatively short duration (less than three weeks in all cases). Diagnosis was made preoperatively in 20 of the last 21 patients presenting with xanthogranulomatous pyelonephritis. Before that, the preoperative clinical diagnoses were very varied: Wilms's tumour (2), splenomegaly as a result of leukaemia (2), intestinal obstruction (1), perinephric abscess (2), hepatomegaly (1), osteomyelitis (1), and failure to thrive (1).

Sixteen of the 31 children had fever at the time of presentation. Only four patients had a haemoglobin > 100 g/l and 11 had a haemoglobin of < 80 g/l. The erythrocyte sedimentation rate (ESR) was raised to > 30 mm in the first hour in 15 of 18 patients in whom this test was performed (range, 20-145 mm in the first hour). Nineteen children had a polymorph leucocytosis. In 15 patients the urine was sterile but appreciable pyuria was present in 10 of these. Of the 16 children with bacteriuria, *Proteus* strains grew in eight, *Escherichia coli* strains in five, and there was a mixed growth of bacteria in the remaining three patients.

Radiological investigation revealed multiple renal calculi in 26 patients and in one patient there was a ureteric stone associated with multiple renal calculi. In 17 patients intravenous urography and an ultrasound scan of the kidneys revealed hypertrophy of the contralateral non-affected kidney. In 29 patients DTPA (diethylenetriamine pentaacetic acid) renography was performed. In 23 of these, there was no function in the affected kidney and poor function (< 10% relative function) was found in four of the remaining six patients. The left kidney was affected in 26 of the 31 children.

At surgery, the affected kidney was enlarged in 21 patients and densely adherent to the surrounding tissues in all patients. In three instances, the kidney was adherent to the

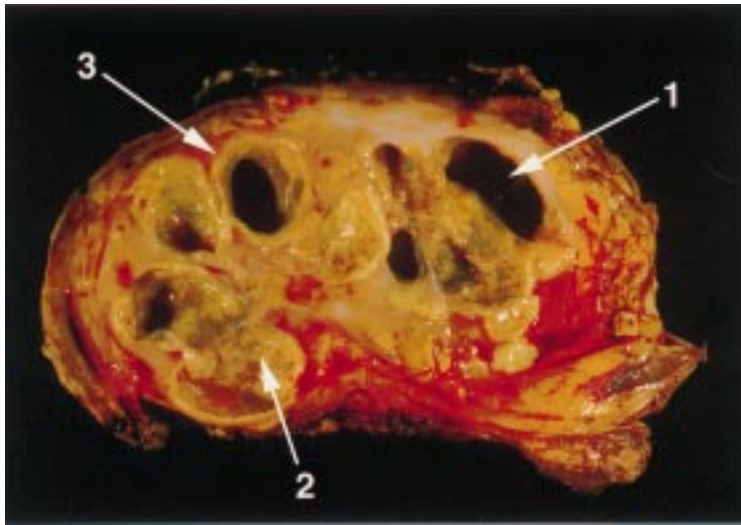


Figure 1 Macroscopic features of xanthogranulomatous pyelonephritis: dilated calyx (1); dilated calyx filled with pus (2); yellow tinge of fat laden macrophage layer (3).

descending colon, necessitating a partial colonic resection with the kidney in one patient; in another patient, the small intestine was adherent to an abscess at the lower pole of the affected kidney, causing intestinal obstruction. Perinephric abscess cavities were present in four children. Total nephrectomy was performed in 29 children. In one girl, the disease process was confined to the upper pole of a duplex kidney, and an upper pole nephrectomy was achieved. In another, an area of focal disease was identified as an abnormality on an

ultrasound scan and confirmed by biopsy. A limited resection was performed to remove the focal area of inflammation. In three patients there was clear evidence of pelviureteric junction obstruction.

In all instances, the cut surface of the kidney showed diffuse cortical scarring with considerable effacement of the normal renal architecture. Areas with the distinctly yellow tinge, which give the condition its name, were seen grossly in most patients, either as scattered foci or as a discrete rim around dilated, pus filled calyces or other cystic spaces (fig 1).

Microscopically, the kidneys showed a mixed acute and chronic inflammatory cell infiltrate with giant cells and lipid laden macrophages (fig 2). Such foci were usually surrounded by dense fibrous tissue and both inflammation and fibrosis clearly extended beyond the renal capsule in most of the cases examined. Contiguous, less severely affected areas of the kidney frequently showed more conventional histological features of chronic pyelonephritis.

In the intervening time after nephrectomy, one child had a lower pole nephrectomy on the contralateral side as a result of reflux nephropathy and urolithiasis in the lower pole of a duplex kidney. Three years after nephrectomy, at the age of 7 years, a further child developed renal failure. Renal biopsy at this stage showed evidence of amyloid in the remaining kidney. On reviewing previous histology, amyloid had not been present at the time of the nephrectomy.

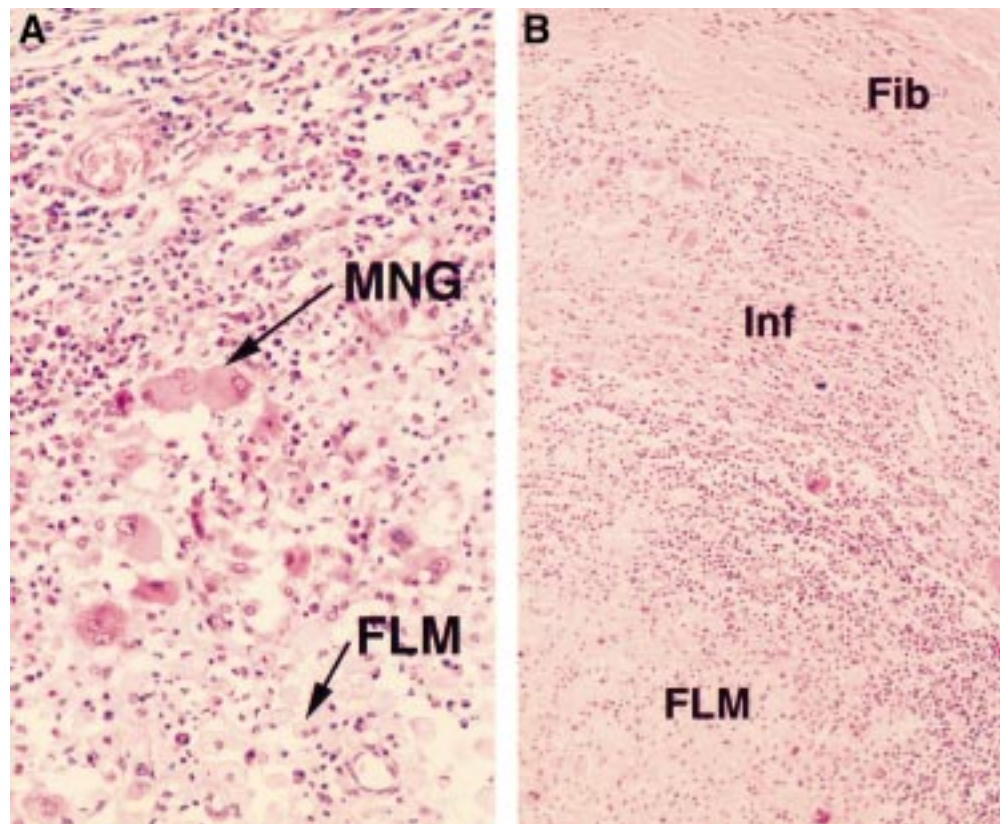


Figure 2 (A) Histological features of xanthogranulomatous pyelonephritis ($\times 20$ magnification) showing multinucleated giant cells (MNG) and fat laden macrophages (FLM). (B) Histological features of xanthogranulomatous pyelonephritis ($\times 4$ magnification) showing fibrosis (Fib), inflammatory infiltrate (Inf), and fat laden macrophages (FLM).

Discussion

Several interrelated aetiological features are thought to be responsible for the pathogenesis of xanthogranulomatous pyelonephritis. They include calculus or non-calculus urinary obstruction, ineffectively treated urosepsis, chronic renal ischaemia causing localised alterations in renal metabolism, lymphatic obstruction, alterations in lipid metabolism, and finally an altered immune response. The extent of the pathological process within the affected kidney varies. In the rare localised form, the lesion can be confined to one or other pole, as was seen in one part of a duplex kidney in our series. More commonly, a diffuse process is seen involving the whole kidney, leading in most cases to a decrease in renal function. The inflammatory process with extension into the perirenal tissues and adjacent organs causes great variety in the clinical presentations of xanthogranulomatous pyelonephritis.

Many reports on this disease conclude that preoperative diagnosis is not easy and this viewpoint seems to have been generally accepted, given the protean manifestations of the disease. However, we think that because of the increasing awareness of the condition, this is a diagnosis that can and should be made preoperatively. Indeed, in 20 of our last 21 cases the diagnosis was made before surgery. The characteristics of the condition that might help in a preoperative diagnosis of xanthogranulomatous pyelonephritis include: disease is usually unilateral (although very rare bilateral cases have been reported); renal function is absent or grossly impaired on the involved side; large, often numerous, renal calculi are present; anaemia, raised ESR, and leucocytosis are often present.

These characteristics might not all be present—for example, no stones were found in five of our 31 patients, but combinations of most of these findings suggest a diagnosis of xanthogranulomatous pyelonephritis. However, confirmation of this diagnosis depends on histological examination of the resected kidney.

Treatment of this disease is surgical excision of the diseased tissue. In most cases this will mean a total nephrectomy. However, in the relatively rare cases where the localised form of the disease is found, which involves only a single pole of the kidney, it might be possible to carry out a partial nephrectomy (as was the case in one of our patients). When performing surgery, it is very useful if the correct preoperative diagnosis has been made because surgery in this condition can be extremely difficult as a result of the inflammatory process extending beyond the boundaries of the kidney. In many cases, the kidney will have to be dissected off the major vessels. Therefore, it is unusual for the kidney to be able to be removed without opening the peritoneum, and an extensive anterolateral transperitoneal approach, such as that used in resection of a Wilms's tumour, is recommended rather than the standard lumbar renal incisions for nephrectomy.

It is generally accepted that once the diseased kidney has been removed the future prognosis for the affected child is excellent.

When a patient loses a kidney, the opposite kidney's compensatory response is remarkable. In infancy and childhood, the remaining solitary kidney undergoes hypertrophy and can even double in size to the extent that the mass of the solitary kidney will nearly equal the original combined mass of both kidneys.¹⁵⁻¹⁷ At the time of surgery, 17 of the 31 patients had hypertrophy of the contralateral kidney, suggesting chronic poor function of the diseased kidney. At follow up, 12 of the 16 patients examined had an easily palpable contralateral solitary kidney. This was confirmed on ultrasound scan in many cases. Although reports on both adults and children suggest that there is no predilection for any particular side,^{18,19} our study suggests that there is a large bias towards the left side. In the adult form of the disease, there is no predilection for any particular side and there is no clinical, anatomical, or pathological reason for this bias towards the left side. In the only other large series of this condition in children there is no bias towards any one side.¹⁹ Our results challenge previous claims that the focal variety of the disease is more common in children,^{8,12,20,21} because only one of 31 patients in our series had focal disease. Even in the patient in whom xanthogranulomatous pyelonephritis was confined to one pole of a duplex system, histology confirmed a diffuse inflammatory process throughout the whole pole. This is in agreement with many recent series.^{9,22}

One child in our series appeared to have normal renal function based on the single remaining kidney at the time of nephrectomy. However, he has shown a serious deterioration in renal function in the succeeding years secondary to amyloid, which affected the remaining kidney. Amyloidosis has been described previously in association with xanthogranulomatous pyelonephritis in four patients,²³⁻²⁵ including one child.²⁵ Nephrectomy does not seem to halt the progression of the secondary amyloidosis in these patients. For this reason, it is strongly recommended that children who have had surgical intervention for xanthogranulomatous pyelonephritis should be retained on a long term follow up basis.

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APEC

Paediatricians and dermatologists in the Aquitaine region of France were informed of the clinical features of asymmetric periflexural exanthem of childhood (APEC) and asked to report cases to paediatric dermatologists in Bordeaux (Didier Coustou and colleagues. *Archives of Dermatology* 1999;135:799–803). They came up with 67 cases (37 girls) between April 1994 and December 1996.

The condition affected mainly toddlers (mean age 28 months, range 1–5 years). Peak onset was in September, 90% of cases presenting between February and September. There were no cases in relatives or contacts. There was an erythematous rash consisting of convergent micropapules and starting usually on one side of the trunk near the axilla but later spreading centrifugally. Both sides of the body were eventually involved in 70% of cases. A prodrome involving the upper respiratory or gastrointestinal tracts was noted in 60% and fever in 40%. Itching (65%) and lymphadenopathy (70%) were common. The rash lasted typically for two or three weeks but it persisted for seven weeks or more in eight children. Skin biopsy specimens in nine cases had infiltration with T lymphocytes predominantly around sweat glands.

APEC, which is said to have been described first in 1962, appears to be a specific and fairly common childhood exanthem. Its cause is unknown but infection seems probable.

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