Preoperative Diagnosis of Xanthogranulomatous Pyelonephritis

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Introduction: The aim of this study was to evaluate the possibility of differentiating xanthogranulomatous pyelonephritis (XGPN) preoperatively from chronic pyelonephritis on the basis of demographic data, clinical parameters, and biochemical, microbiological, and radiological workups.

Materials and Methods: Between 1995 and 2005, a total of 239 patients were diagnosed to have pyelonephritis at our center, of which, 56 underwent nephrectomy. Forty-five (80.4%) of the nephrectomy specimens showed diagnosis of chronic pyelonephritis and 11 (19.6%) showed XGPN.

Results: Compared to chronic pyelonephritis, XGPN was more likely to occur in the middle-aged women (91%) with diabetes mellitus (64%) and a history of recurrent UTI was more frequently noted. The disease is likely to present with flank pain and tenderness in 100.0% and 90.9% of the patients with XGPN, respectively. Anemia (81.8%), hematuria (81.8%), and bacteriuria (90.9%) were more frequent in these patients than in those with chronic pyelonephritis. The mean blood hemoglobin was 7.0 g/dL in the patients with XGPN. *Proteus mirabilis* was detected in 6 patients (55%) of the XGPN group and only 2 of the chronic pyelonephritis group ($P < .001$). Renomegaly and kidney calculus were more frequently noted in the patients with XGPN. Finally, XGPN led to a higher rate of postoperative complications.

Conclusion: Demographic data, comorbidities, predisposing factors, and biochemical as well as roentgenological features are significant but nonspecific indicators of preoperative diagnosis of XGPN.

Keywords: kidney diseases, pyelonephritis, infection, nephrectomy, xanthogranulomatous pyelonephritis, diagnosis

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INTRODUCTION

Xanthogranulomatous pyelonephritis (XGPN) is a rare chronic inflammatory disorder which was initially described over 90 years ago by Schlagenhaufer.[1] It is characterized by diffuse renal parenchymal destruction and its replacement by lipid-laden macrophages (foamy cells) which imparts a yellowish tan to the tissue. These changes were found in 0.6% to 1.4% of patients with kidney inflammation and in 1% to 8% of all inflammatory conditions requiring nephrectomy.[2,3] The disease is classically seen in middle-aged diabetic women in the presence of urolithiasis, nonfunctioning kidneys, and urinary tract infection (UTI) especially with *Proteus mirabilis*.[4]

It is difficult to make a preoperative differential diagnosis of XGPN from other forms of chronic inflammatory conditions. However, clinically, it is very important to diagnose the disease early and differentiate it from chronic pyelonephritis which has a potentially benign course. Early diagnosis helps prevent inevitable loss of kidney

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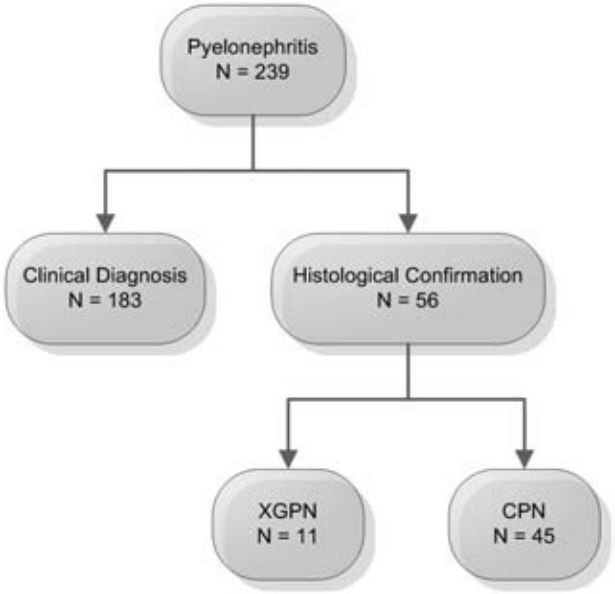
function.[5] Clinical features, imaging, urine cytology, and kidney biopsy are helpful in making a diagnosis.[6-9] However, urine cytology is nonspecific and follow-up studies have not supported its accuracy, yet.[7,9] Kidney biopsy is invasive and also accompanied by the risk of spreading the tumor through the needle tract in case of malignancy and the risk of sinus formation or spread of infection in XGPN.[10-12] Percutaneous biopsy does not generally provide adequate specimen for diagnosis of XGPN or kidney neoplasms in some cases.[13]

Although difficult to diagnose preoperatively, XGPN can be diagnosed using improved diagnostic tools if there is a high suspicion of the disease. Preoperative diagnosis provide the chance of its management by parenteral antibiotic therapy and nephrostomy for drainage of the pus which leads to overall better survival and decreases postoperative morbidities such as bleeding, infection, and fistula.[14] We evaluated the impact of various clinical, laboratory, and radiological parameters in differentiating XGPN from chronic pyelonephritis (CPN).

MATERIALS AND METHODS

In this case-control study between January 1995 and October 2004, a total of 239 patients with the diagnosis of pyelonephritis (based on the International Classification of Diseases, 9th edition, Clinical Modification data indexing and coding system) were evaluated.[15] Those patients with proven histological diagnosis were included in the study including 11 with XGPN and 45 with CPN (Figure). Carcinoma and other forms of pyelonephritis such as tuberculous pyelonephritis were excluded. Preoperative workup was performed using routine biochemical and hematological tests. Radiological evaluations included plain abdominal radiography, ultrasonography, intravenous urography (IVU), computerized tomography (CT), or a combination of these (Table 1). Nephrectomy was performed under general anesthesia through lumbar, extraperitoneal, or extrapleural approach.

The demographic data, comorbidities, etiologic factors, mode of presentation, clinical and radiological features, blood chemistry, and urine cultures were noted. The histological features and postoperative complications were also recorded and reviewed. The data were analyzed using the chi-square test and the *t* test for nominal and numerical/interval data. A *P* value of less than .05 was considered statistically significant.



Schematic representation of patients distribution in various groups is shown.

Table 1. Radiological Findings of Patients with XGPN and CPN*

Investigations	Patients With Pyelonephritis	
	XGPN	CPN
Plain abdominal radiography		
Number of patients	7 (63.6)	8 (17.8)
Kidney calculi	7 (100.0)	8 (100.0)
Intravenous urography		
Number of patients	8 (72.7)	22 (48.9)
Nonfunctioning kidney	4 (50.0)	8 (36.4)
Ultrasonography		
Number of patients	7 (63.6)	23 (51.1)
Renomegaly	6 (85.7)	4 (17.4)
Kidney calculi	5 (71.4)	14 (60.9)
Computed tomography		
Number of patients	6 (54.5)	10 (22.2)
Renomegaly	5 (83.3)	1 (10.0)
Kidney calculi	5 (83.3)	3 (33.3)

*Values in parentheses are percents. XGPN indicates xanthogranulomatous pyelonephritis and CPN, chronic pyelonephritis.

RESULTS

A total of 56 patients underwent nephrectomy for nonfunctioning or poor-functioning kidney with chronic pyelonephritis, of which, 11 had histologically proven XGPN and the remainders had CPN. Demographic and clinical characteristics of the

patients are outlined in Table 2. The mean age of the patients at the time of diagnosis of XGPN was 48.4 ± 9.7 years (range, 15 to 65 years) and it was 41.6 ± 11.3 (range, 17 to 65 years) in the patients with CPN. Male-female ratio was 1:10 and 2:1 in the patients with XGPN and CPN, respectively. All patients had unilateral disease predominantly affecting the left kidney except 1 in the CPN group. Seven of 11 patients in XGPN group (63.6%) and 7 of 45 patients in the CPN group (15.6%) had diabetes mellitus (DM).

In the patients with XGPN, anemia (hemoglobin of less than 10 g/dL), hematuria, and bacteriuria were more frequent than those in the patients with CPN (Table 2). The mean hemoglobin was 7.0 g/dL in the patients with XGPN. *Proteus mirabilis* was detected in 6 patients (54.5%) of the XGPN group and only 2 of the CPN group ($P < .001$). *Escherichia coli* was found to be the most common affecting organism in the CPN group.

Finally, the patients in the XGPN group had a higher rate of a positive history of UTI (Table 2) and they faced a higher rate of postoperative complications. The observed complications are shown in Table 3.

Table 2. Demographic and Clinical Features of Patients With XGPN and CPN*

	Patients With Pyelonephritis		
Variables	**XGPN**	**CPN**	***P***
Mean age, y	48.4	41.6	.03
Male/female	1/10	30/15	.001
Diabetes Mellitus	7 (63.6)	7 (15.6)	.001
Lower urinary tract symptoms	6 (54.5)	22 (48.9)	.73
Fever	7 (63.6)	20 (44.4)	.32
Flank pain	11 (100.0)	40 (88.9)	.57
Flank tenderness	10 (90.9)	28 (62.2)	.08
Anemia	9 (81.8)	20 (44.4)	.04
Leukocytosis	7 (63.6)	17 (37.8)	.18
Pyuria	10 (90.9)	29 (65.9)†	.146
Hematuria	9 (81.8)	17 (38.6)†	.01
Bacteriuria	10 (90.9)	18 (40.9)†	.001
Proteus mirabilis	6 (54.5)	2 (4.4)	< .001
History of UTI	8 (72.7)	11 (24.4)	.001
History of urologic instrumentation	8 (72.7)	22 (48.9)	.19
History of calculus	5 (45.5)	18 (40.0)	.74

*Values in parentheses are percents. XGPN indicates xanthogranulomatous pyelonephritis and CPN, chronic pyelonephritis.
†These were assessed in 44 patients.

Table 3. Postoperative Complications in Patients With XGPN and CPN*

	Patients With Pyelonephritis	
Complications	**XGPN**	**CPN**
Respiratory complications	2 (18.2)	2 (4.4)
Wound infections	2 (18.2)	6 (13.3)
Hemorrhage and sepsis	0	1 (2.2)
Postoperative ileus	0	1 (2.2)
Overall complications	4 (36.4)	10 (22.2)

*Values in parentheses are percents. XGPN indicates xanthogranulomatous pyelonephritis and CPN, chronic pyelonephritis.

DISCUSSION

Review of the literature as well as our results revealed XGPN to mostly affect women in their 4th to 5th decades of life.[9] The patients most prone to this disease are those with prior history of DM, urolithiasis, recurrent UTI (especially with *Proteus mirabilis*), and urological instrumentation.[4,14] Although multiple theories have been proposed to explain the development of this peculiar type of pyelonephritis, the etiology still remains obscure. The probable predisposing factors include recurrent UTI, obstruction, malnutrition, abnormal lipid metabolism, altered immunological response, lymphatic blockage, and congenital urinary abnormalities.[16,17] The condition has been described as great imitator due its variant clinical nonspecific symptoms and signs.[9,18] Lower urinary tract symptoms, fever and chills, flank pain, tenderness, and palpable mass are the symptoms commonly observed. Therefore, a patient presenting with urolithiasis, recurrent UTI, and prior urological instrumentation in a poor-functioning kidney has a high index for suspicion of XGPN.[14] In our patients with XGPN, flank tenderness, recurrent UTI, DM, fever, and lower urinary tract symptoms were the dominant findings in the primary examinations.

To date, imaging modalities such as CT, ultrasonography, and magnetic resonance imaging (MRI) have potential ability to identify this fulminant kidney infection preoperatively.[19] It has been stated that XGPN has no specific ultrasonographic features, but is suggested by parenchymal thinning and hydronephrosis, ultrasonographic signs of chronic obstructive uropathy caused by the calculi, echoes in the dilated collecting system, and a perinephric fluid collection. Also, CT, needle biopsy, or both are recommended for further evaluations and confirmation of the suspected cases of XGPN.

Verswijvel and colleagues reported early findings on the use of diffusion-weighted MRI in kidney infections including XGPN.[20] However, nowadays, CT is still considered as the gold standard method in the preoperative radiological evaluation of XGPN.

Laboratory findings noted leukocytosis in 63.6% and anemia in 81.8% of the patients with XGPN in our series. Goodman and associates suggested that anemia might be due to defects in iron reutilization.[21] In our study, no data was available for serum iron and total iron binding capacity, but all of our patients had hypochromic microcytic anemia suggesting iron deficiency. Microscopic hematuria normally is not a cause of anemia; however, if prolonged and associated with other risk factors such as nutritional deficiency, it may lead to iron deficiency.

Urinalysis in patients with XGPN often reveals bacteriuria, pyuria, and hematuria.[12,14] Nine out of our 11 patients had hematuria and 10 had bacteriuria, figures that were not that frequent in the patients with CPN. Urine culture of 6 patients showed *Proteus mirabilis* which is in agreement with most of the reports.[4, 5] *Proteus* species are implicated as serious causes of infections in humans along with *Escherichia coli, Klebsiella, Enterobacter,* and *Serratia* species. *Proteus* species are most commonly found in the human intestinal tract as a part of the normal human intestinal flora along with *Escherichia coli* and *Klebsiella* species. Patients with recurrent infections, structural abnormalities of the urinary tract, those who have had urethral instrumentation, and those whose infections are acquired in the hospital have an increased frequency of infection caused by *Proteus* species and other organisms such as *Klebsiella*, *Enterobacter*, *Pseudomonas*, *Enterococcus*, and *Staphylococcus* species. Bacterial production of urease has also been shown to increase the risk of pyelonephritis in experimental animals. Urease production, together with the presence of bacterial motility and fimbriae, may favor the production of upper urinary tract infections by organisms such as *Proteus mirabilis*. The ability of *Proteus* organisms to produce urease and to alkalinize the urine by hydrolyzing urea to ammonia makes it effective in producing an environment to survive. This leads to precipitation of organic and inorganic compounds leading to struvite calculus formation composed of magnesium ammonium phosphate (struvite) and calcium carbonate apatite.[5]

Ballesteros and associates found presence of xanthoma cells in the urine to be helpful for the primary diagnosis.[7] In our series, data were not available for urine and fine needle aspiration cytologies. However, reports have revealed that urine cytology is nonspecific and has a high false-positive rate. In a study, the investigators detected urine foam cells by serial urine cytology and reported an 80% preoperative accuracy in diagnosing XGPN with this method; however, these results could not be duplicated in later studies.[7,9] Kidney biopsy has remote chances of spreading the tumor through the needle tract in case of malignancy as well as being invasive.[10,11] Also, percutaneous biopsy increases the risk of sinus formation or spread of infection and does not provide adequate specimen for diagnosis of XGPN or kidney neoplasms in some cases.[12,13] The use of fluoroscopic guidance is also accompanied by an approximately 10% false-negative rate.[18]

Xanthogranulomatous pyelonephritis has several characteristic features on imaging. Plain abdominal radiographies reveal urinary tract calculus and renomegaly with ill-defined outline due to perinephric extension of inflammation which is in agreement to our study (all of our patients who had undergone plain abdominal radiography with XGPN had calculus).[8] Poor-functioning or nonfunctioning systems on the IVU are a common finding.[9] Ultrasonography reveals renomegaly, typical central echogenic area due to calculi, and multiple parenchymal hypoechogenic areas due to multiple necrotic foci.[18] Computed tomography demonstrates an enlarged kidney with calculus and multiple water-density areas representing dilated calyxes and abscess cavities filled with varying amounts of pus and debris. Although they are prominently enhanced in CPN and tumors, these cavities fail to enhance in XGPN.[2,3] In our study, on kidney ultrasonography, renomegaly and calculus were present in 71.4% and 85.7% of the patients with XGPN with a significant difference from those in the CPN group. On CT scan, 83.3% of the patients had renomegaly and calculus in the XGPN group. Data on calculus analyses were inconclusive as the majority had calcium oxalate calculi and 2 of 5 patients in the XGPN and 4 of 14 in the CPN had struvite calculi (Table 4). As it has been mentioned before, preoperative diagnosis is difficult, but some characteristic findings can be used for this purpose.[3] In a study by Hammadeh and

Table 4. Calculi Composition in Patients With XGPN and CPN*

Calculus Composition	Patients With Pyelonephritis	
	XGPN (n = 5)	CPN (n = 14)
Calcium oxalate	2	7
Struvite	2	4
Uric acid	1	3

*XGPN indicates xanthogranulomatous pyelonephritis and CPN, chronic pyelonephritis.

coworkers, 9 of 11 patients (82%) were diagnosed preoperatively on the basis of clinical and radiological features.[6] Imaging is therefore considered the paramount for preoperative diagnosis of XGPN.[22]

CONCLUSION

Demographic data (age, gender distribution), comorbidities, predisposing factors, biochemical analysis, and roentgenological features, in combination, can be highly suggestive of XGPN in the patients with pyelonephritis and are therefore the crucial means for preoperative diagnosis of this disease.

CONFLICT OF INTEREST

None declared.

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