Case report

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XANTHOGRANULOMATOUS PYELONEPHRITIS AND DIAGNOSTIC APPROACH: A CASE REPORT

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Xanthogranulomatous pyelonephritis (XGPN) is an uncommon chronic granulomatous process that can result in significant destruction of renal parenchyma and propagation of inflammation into adjacent pararenal tissues. The presented patient had xanthogranulomatous inflammation of renal pelvis, peri- and paranephritic tissue, with formation of a large tumor-like mass which was in close relation to the base of urinary bladder. The findings of pathognomonic foamy macrophages and multinucleated giant cells showing diffuse positivity for CD68 confirmed the precise diagnosis. Having in mind that XGPN can mimic various clinically and pathologically benign and malignant conditions, a multidisciplinary diagnostic approach is required. Sometimes, careful clinical, imaging, nuclear and histopathological examinations are necessary to determine the type and degree of renal damage, which will dictate surgical approach, especially if nephrectomy is not planned. *Acta Medica Medianae 2023;62(3):75-80.*

Key words: *xanthogranulomatous pyelonephritis, diagnostic approach, histopathology*

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Introduction

Xanthogranulomatous pyelonephritis (XGP) is an unusual, unilateral and very rare form of chronic granulomatous pyelonephritis due to infection (*E. coli, Proteus*) or stones. Nephrolithiasis, most often with the staghorn-type calculus, is not a prerequisite, nevertheless remains a well-established predisposition for XGP (1). Kidney involvement in XGP can be diffuse, segmental or focal with inflammation localized within the cortex of the kidney (2, 3). The precise pathogenetic mechanism remains incompletely understood in XGP. Associations between XGPN and calyceal stones and staghorn calculi, with pyelo-ureteral junction obstruction, ureteropelvic duplication, ureteral schistosomiasis and tumours (including renal cell and urothelial carcinomas) are well known, but obstruction may be incomplete, and renal parenchymal destruction and subsequent renal impairment occur secondary to the chronic inflammation and macrophage infiltration (3 - 5). The combination of obstruction and infection is presumed the primary initiator, resulting in an interstitial pyelonephritis, followed by chronic granulomatous immune response which is the result of incomplete eradication of the inciting agent (5). Granulomatous inflammation is a response induced primarily by bacteria presence within the granulomas, in both intra-and extracellular locations. The failure to completely degrade the bacterial products provokes a chronic inflammatory response, but also suggests a limited/incomplete host immune response (6).

XGPN starts from the renal pelvis and calyces, spreading to the renal parenchyma, extends beyond the kidney into the perinephric and pararenal spaces, and finally, adjacent organs such as the liver, spleen, duodenum, pancreas, and great vessels can be involved if left untreated (7–9). The typical gross pathological appearance is that of an enlarged kidney with capsular thickening and replacement of parenchyma with yellow tissue, with necrosis and a dilated pelvicalyceal system containing stones/debris and variable volumes of pus. The microscopic examination of a XGPN shows three distinct zones centered by a calyx. The inner zone consists of leukocytes, lymphocytes, plasma cells, histiocytes

or macrophages, and necrosis. In the middle zone, we can see granulation tissues surrounded by hemorrhage. Giant cells, cholesterol clefts, and fibrous tissues are characteristics of the outer zone. The pathognomonic feature in XGPN is the presence of lipid-laden foamy macrophages (xanthoma cells) that give a yellow color to the tissue (10, 11).

In this case report, we present a patient with XGPN that presented as pseudotumor on radiological and gross pathological examination, with an emphasis on diagnostic dilemmas.

Case report

A 61-year-old female presented with abdominal pain and leukocytosis. The native graphics of urinary tract detected a calcium intensity shadow measuring 21 x 16 mm on the left side, at the height of L2/L3. Distally, ipsilaterally, at the level of the transverse process of L4, there was another shadow of calcium density with a diameter of 6.5 mm. As well as a soft tissue shadow, from the lower pole of the left kidney to the base of the urinary bladder, probably a cyst or tumor was detected with the largest diameter of 12 cm. CT scans of left kidney showed multiple cystic changes of diameter from 25 mm to 150 mm and compression on the blood vessels without infiltration, as well as a calculus of diameter 20 mm with hydronephrosis grade III-IV. Static renal scintigraphy with 99mTc-DMSA detected that the distal pole of the left kidney was displaced laterally and irregularly shaped. The cortical parenchyma was markedly reduced and scarred. A large number of photo-deficient fields were observed which according to their scintigraphic characteristics corresponded to calculosis and cysts. Individually, the left kidney participated with 27% and the right with 73% in the total renal function (Figure 1A).

The gross pathology showed pyonephrotic left kidney 20.5 x 14 x 8 cm, with the staghorn-type calculus in the pelvis and calculus in the proximal part of the ureter with complete obstruction. The renal parenchyma was atrophic with a thickness of 1 mm, with the exception of the lower pole where it was up to 15 mm focally. Tumor-like adrenal gland tissue, 92 x 55 x 37 mm was detected in the peripelvic space and extended below the lower pole of the kidney. A cavity 105 x 75 mm, filled with blood and pus was localized in peripelvic fat, and was in contact with the yellow tumor-like mass. Microscopic examination showed renal parenchymal destruction with obstructive uropathy and XGPN in pelvis and peripelvic adipose tissue, including sections sampled from a tumor-like mass. XGPN was characterized by a granulomatous mixed inflammatory infiltrate with fibrosis and cholesterol clefts in the background (Figure 1B). The inflammatory infiltrate was composed of xanthomatous histiocytes with foamy cytoplasm, which showed diffuse positivity for CD68, neutrophils, lymphocytes, and plasma cells (Figure 1C, 1D). Microscopic findings included the presence of abscess in perinephritic fat.

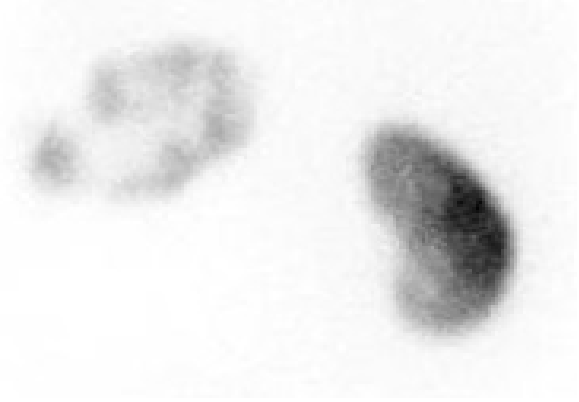

Figure 1A. Static renal scintigraphy with ^{99m}Tc-DMSA, posterior projection, markedly reduced cortical parenchyma of the left kidney with scarring changes

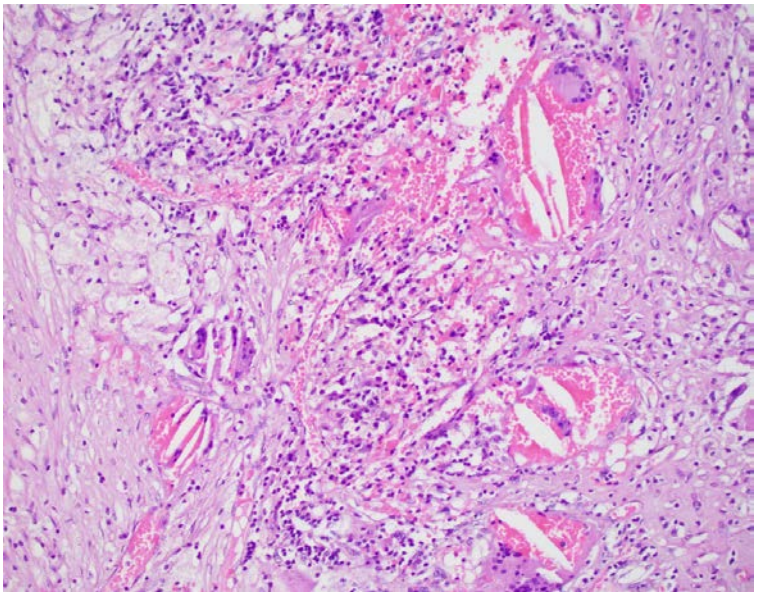

Figure 1B. Cholesterol clefts, xanthomatous histiocytes, and granulomatous inflammatory infiltrate in xanthogranulomatous pyelonephritis (H&E, original magnification ×20)

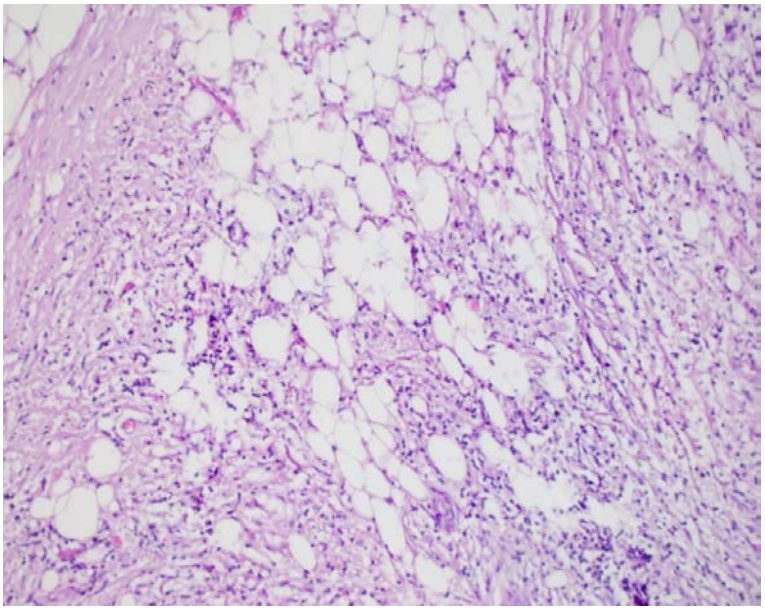

Figure 1C. Fibrous background and xanthogranulomatous inflammation in peripelvic adipose tissue (H&E, original magnification ×20)

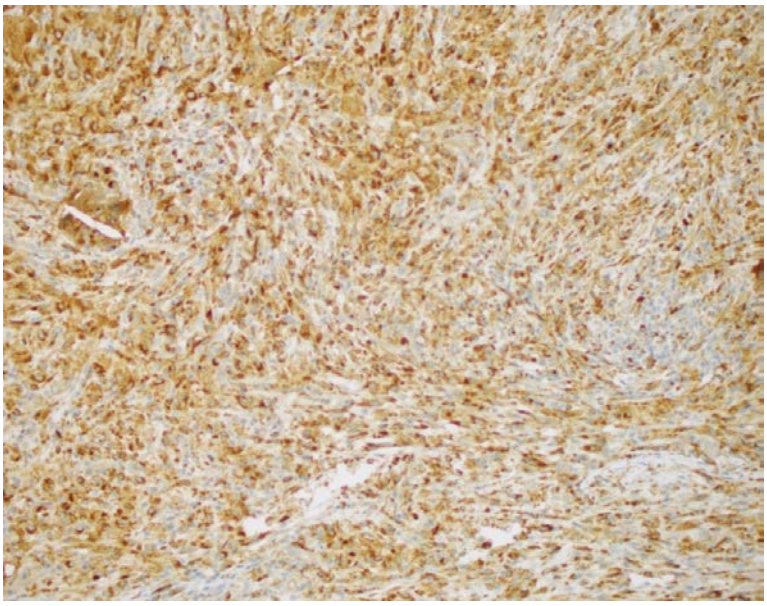

Figure 1D. The xanthomatous cells and multinucleated giant cells are positive for CD68 (IHC staining, original magnification ×20)

Discussion

XGPN is well known as the "great imitator" or pseudotumor because of the overlap of imaging features with other conditions in kidney, including renal cell carcinoma (RCC), urothelial carcinoma, tuberculosis and malakoplakia, which can lead to serious misdiagnosis. In some cases, the presence of synchronous XGPN and renal malignant tumor creates an additional diagnostic dilemma (12, 13).

The diagnostic algorithm includes conventional radiographs of the abdomen, ultrasound, and CT for DDg with tumors especially in focal/segmental form of XGPN and in detection of associated complications (14).

Therefore, early identification and treatment are required to decrease the morbidity and mortality associated with this condition. Although antibiotics can be given in acute infection, the treatment of choice for XGP is nephrectomy for a nonfunctional kidney (15). 99mTc-DTPA and 99mTc-MAG3 can show the degree of residual renal function, and this finding will dictate surgical approach, renal salvage or nephron-sparing surgery if feasible, especially in the setting of focal XGP (16, 17).

On the one hand, multiple yellow nodules around calyces may form a mass and be infiltrative which may be suspicious of neoplastic proliferation. In our case, XGPN with extension of xanthogranulomatous inflammation to the peri- and paranephritic tissue forms a large tumor-like mass, which was the main Ddg dilemma intraoperatively and during macroscopic examination.

The most important diagnostic challenge is misinterpretation of foam cells in XGPN as clear cells in clear cell RCC (cRCC). Characteristic histology and immunohistochemistry stains usually lead to the right diagnosis. Our staining showed diffuse cytoplasmic CD68 positivity in foamy macrophages and multinucleated giant cells, and on the other hand, characteristic immunohistochemical finding in cRCC is expression of Vimentin, CD10, and RCC (12). Foamy macrophages can be seen in papillary RCC, especially in type 1, with characteristic localization in cores of tumor papillae, and ICH findings are similar with cRCC because of their origin from proximal tubules epithelium (18).

Malakoplakia is a rare histiocytic disease that is clinically presented as a single or multiple white-yellow soft raised plaques on the mucosal surface in the pelvis, ureter and most often in the urinary bladder. Microscopy finding detected foamy epithelioid histiocytes with PAS+ granular eosinophilic cytoplasm in lamina propria, some lymphocytes and occasional giant cells (19).

Conclusion

In evaluation of XGPN, it is necessary to integrate the clinical presentation of the disease with the findings of radiological and nuclear diagnostic methods, and differentiate with respect to other malignant and non-malignant conditions. Multidisciplinary diagnostic approach, including radiological, nuclear, and histopathological examinations, is necessary in XGPN especially if nephrectomy is not planned.

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KSANTOGRANULOMATOZNI PIJELONEFRITIS I DIJAGNOSTIČKI PRISTUP: PRIKAZ SLUČAJA

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Ksantogranulomatozni pijelonefritis (KSGPN) je redak hronični granulomatozni proces, koji može dovesti do značajne destrukcije bubrežnog parenhima i propagacije zapaljenja u susedna pararenalna tkiva. Prikazani bolesnik imao je ksantogranulomatozno zapaljenje bubrežne karlice, perinefritičnog i paranefritičnog tkiva, sa formiranjem velike tumorolike mase, koja se pružala do baze mokraćne bešike. Nalaz patognomoničnih penastih makrofaga i multinuklearnih džinovskih ćelija, koje su bile difuzno pozitivne na CD68, potvrdio je preciznu dijagnozu. Budući da KSGPN može oponašati različita klinički i patološki benigna i maligna stanja, potreban je multidisciplinarni dijagnostički pristup. Ponekad su neophodna pažljiva klinička, radiološka, nuklearna i patohistološka ispitivanja, kako bi se utvrdio tip i stepen oštećenja bubrega, što će odrediti hirurški pristup, posebno ako nefrektomija nije planirana. *Acta Medica Medianae 2023;62(3):75-80.*

Ključne reči: *ksantogranulomatozni pijelonefritis, dijagnostički pristup, histopatologija*