Radiology Case Reports 19 (2024) 6373–6379

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Case Report

Stage III xanthogranulomatous pyelonephritis with sarcomatoid degeneration ☆

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ARTICLE INFO

Article history:
Received 10 April 2024
Revised 16 September 2024
Accepted 17 September 2024

Keywords:
Xanthogranulomatous pyelonephritis
Sarcomatoid degeneration
Cancer
Nephrectomy
Ceus
Us
Acute abdominal pain
Fistula
Bear paw sign
Pyonephrosis
Great imitator

ABSTRACT

Xanthogranulomatous pyelonephritis (XGP) is an uncommon chronic condition characterized by destructive granulomatous disease of the kidney with uncertain etiology. Significant risk factors for XGP are represented by the coexistence of history of nephrolithiasis, diabetes mellitus, recurrent urinary tract infections and other immunocompromised conditions. It is also associated with higher risk of malignancy, reported in up to 11% of patients. We report a case of a 76-year-old female who presented to the emergency department with an insidious onset of abdominal and right lower back pain. She had a history of renal stones and diabetes mellitus. On physical examination, a painful fistulous orifice in skin on the right lumbar region was found. CT images showed a nonfunctioning right kidney replaced by multiple necrotic cavities with inflammatory involvement of the right hepatic lobe and a nephrocutaneous fistula. These CT findings were strongly suggestive of XGP (III state). CT images obtained before and after the administration of intravenous contrast material showed also a hyper-vascularized renal mass with irregularly thickened walls confirmed by a targeted CEUS examination and suspicious for malignancy. Pathologic examination confirmed the chronic pyelonephritis and revealed evidence of a concomitant sarcomatoid lesion. This case underlines the central role of a multimodality imaging approach in the emergency department and how this affects the correct management and treatment of patients. In fact, MDCT is considered the current gold standard for the diagnosis and the staging of XPG but

☆ Competing Interests: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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https://doi.org/10.1016/j.radcr.2024.09.090

the contrast-enhanced ultrasound (CEUS) in selected patients can increase the diagnostic accuracy in the uncertain small renal masses detected on CT scans.

Introduction

Xanthogranulomatous pyelonephritis (XGP) represents an uncommon condition that accounts for 0.6%-1% of pyelonephritis. It is characterized by suppurative granulomatous inflammation and progressive destruction of the renal parenchyma. The association with history of nephrolithiasis is reported in more than 80% of patients [1–7]. Many patients present nonspecific symptoms [8] such as flank or abdominal pain, palpable mass, dysuria, weight loss and macroscopic hematuria. According to Pais et al. [3], fever occurs in less than 50% of patients, despite the inflammatory process that led to the formulation of the hypothesis that the pathological agent develops in symbiosis with the host organism.

XGP is usually described as the "great imitator" because it can mimic other pathological conditions like renal cell carcinoma or renal tuberculosis. The prognosis of XGP is usually excellent, with no recurrences after treatment but it is associated with higher risk of malignancy, reported in 10%-11% of patients [4,5,9,10]. The carcinogenesis mechanism is still debated: it is not clear if a malignant focus promotes XGP response or vice versa [4]. CT imaging is considered the diagnostic gold standard for XGP although the radiologist's diagnostic confidence can be reduced by nonspecific imaging features and concomitant solid renal masses that can be difficult to detect in preoperatory settings [4,5]. For these reasons nephrectomy is considered the first line therapy. Herein, we report a case of XGP underlying the central role of a multimodality imaging approach in the emergency department and how this affects the correct management and treatment of patients

Case

A 76-year-old woman presented to the emergency department with acute abdominal pain. She had a history of diabetes mellitus, recurrent urinary tract infections and right renal stones that had been surgically treated. She was afebrile and hemodynamically stable. At physical examination, a painful fistulous orifice in skin and a palpable on the right lumbar region mass were found. Physical examination also revealed lower limbs edema. Blood test results showed anemia (Hb 7.9 g/dL, reference range 12.0-16.0 g/dL), high values of white cell count (1449×10^3 /mm^3, n.v. 4.2-10.5; neutrophils 81.8, n.v 40,0-75), PCR (12.37 mg/dL, reference range 0.0-0.5 mg/dL) and creatinine (1.53 mg/dL, reference range 0.40-0.95 mg/dL). Based on clinical and laboratory findings, firstly abdominal-pelvic MDCT scan was performed before and after the administration of intravenous contrast material (1.0-1.5 mL/kg with a flow rate of 3-5 mL/s, depending on the vein access) using the *Aquilion Prime 160 channels system* (Toshiba Medical Systems, Otawara City, Japan).
The CT protocol included:

- Unenhanced scan to detect renal stones, intralesional fat and the UH values.
- Corticomedullary phase (with a delay of 25 s) acquired with bolus tracking technique and the region of interest (ROI) within the abdominal aorta before renal artery origins with a threshold of 120 HU
- Nephrogenic phase (with a delay of 90 s) in order to detect the optimal enhancement of the renal parenchyma and to underline the enhancement and washout of renal lesions
- A delayed excretory phase performed after at least 8 min (400 500 s). In cases of suspected urothelial carcinoma or extra renal extension of renal cancer, a delayed phase is acquired after at least 20/30 min in supine or prone position depending on the localization of the suspected carcinoma [5].

CT images showed an enlarged right kidney without any obstructing calculi (Fig. 1), replaced by multiple necrotic cavities that extended into the right hypochondrium causing liver infiltration and into the lateral abdominal wall, leading to the formation of a nephron-cutaneous fistula (Fig. 2). The right ureter had an irregularly thickened wall. The pelvis was contracted with some lithiasis formations in the lower calyces and the "bear sign" was not recognizable. These CT findings, in particular the invasiveness aspect of the renal inflammatory disease, were strongly suggestive of XGP (III state) [5,7,11]. CT images also showed a lobulated renal mass within the lower pole of the right kidney, measuring 12 × 8 cm, with irregular margins and gradual contrast enhancement (Fig. 3). The renal mass deserved further investigation so, after a CT, was performed a target contrast-enhanced ultrasound (CEUS) in ER settings. At US B-mode, the lesion appeared pluri-loculated, with thick and irregular walls and nonhomogeneous echotexture. After contrast agent administration (24 mL of Sonovue followed by 10 mL of saline injected manually through an antecubital vein on the right arm), the examination showed a solid avid enhancement and multiple septations and mural nodules that had rapid wash-in and wash-out pattern compared to the renal cortex (Fig. 4). These US findings, and the lesion pattern enhancement relative to the adjacent renal cortex suggested the diagnosis of concurrent neoplastic degeneration.

The patient was admitted and after 3 days a TBCT was performed to completed the imaging investigation, that excluded any pathological lymph nodes or metastasis to distant organs. She underwent percutaneous nephrostomy for urinary drainage that revealed the presence of ESBL-producing E. coli and Acinetobacter Baumanni and received intravenous targeted antibiotic therapy with Ceftazidime-avibactam (Zavicefta).

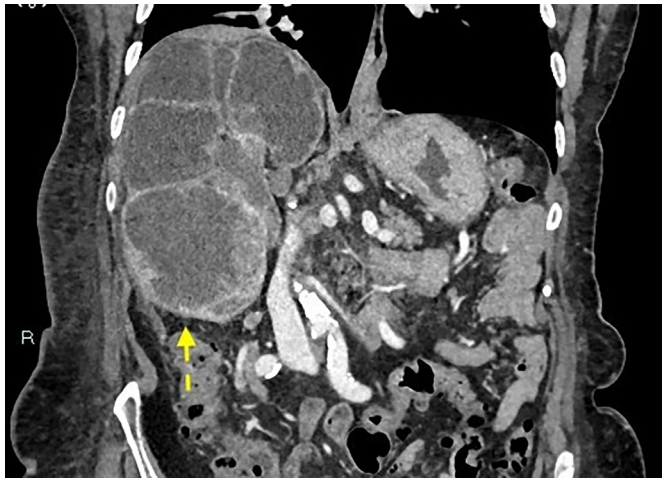

Fig. 1 – Enhanced coronal CT image in portal phase shows an enlarged right kidney, replaced by multiple fluid-filled cavities. At the lower pole of the right kidney 1 fluid-cavity has thickened walls with gradual postcontrast enhancement, suspicious for malignancy (yellow arrow).

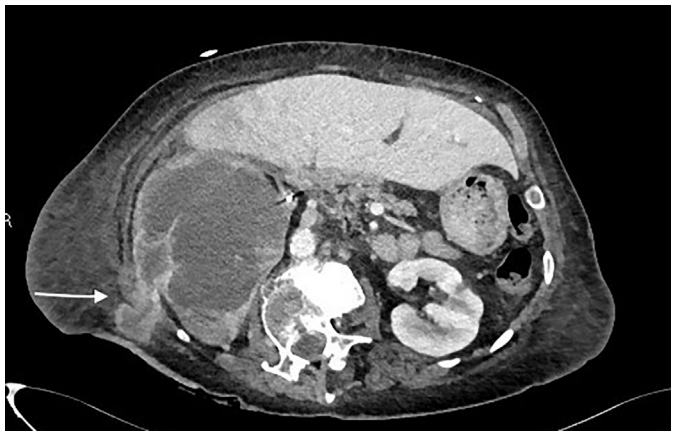

Fig. 2 – Enhanced axial CT image in portal phase shows the nephron-cutaneous right fistula (Arrow).

Then, the patient underwent a right open nephrectomy and pathologic examination of the gross nephrectomy specimen showed a renal carcinoma with probable origin from the collecting ducts (Bellini carcinoma), with sarcomatoid features while the remaining parenchyma appeared hydronephrotic with chronic XGP. The patient was discharged after 2 weeks.

Multidisciplinary team agreed on the immunotherapy therapeutic plan, but the patient's relatives refused the treatment due to her advanced age. A month later, positron emission tomography/computed tomography (PET/CT) showed a diffuse metabolic activity in the right hepatic lobe (with a SUV max 12) and in segments VIII, VI-VII and III (with a SUV max 7.7), correlated to focal hypodense hepatic lesions on CT scan. It showed also an increased glucose metabolism with a target-like appearance at the hepatic hilum (with a SUV max 10) and less pronounced in the intercaval-aortic region and in the mesenteric adipose tissue as well, correlated to pathological lymph nodes on CT scan. High metabolic activity was found also in the upper lobe of the left lung, lingula (with a SUV max 1.8), subcarinal and hilar lung region (with SUV max 3.7), correlated to parenchymal nodules on CT scan. An extensive pleural effusion on the right side was present without significant radiopharmaceutical hyperaccumulation (Fig. 5).

Three months later the patient died.

Discussion

XGP is a rare variant of pyelonephritis characterized by locally invasive granulomatous inflammation that arises in the renal pelvis, causing progressive destruction of the renal parenchymal. Despite the local spread, it has a lower mortality rate [2,5]. It occurs more frequently in females, with greater incidence in the fourth and fifth decades, but it has been reported also in children [12].

The etiology is still unknown. Significant risk factors are diabetes mellitus, rheumatoid arthritis, chronic viral hepatitis C, cirrhosis and obesity [5,13,14].

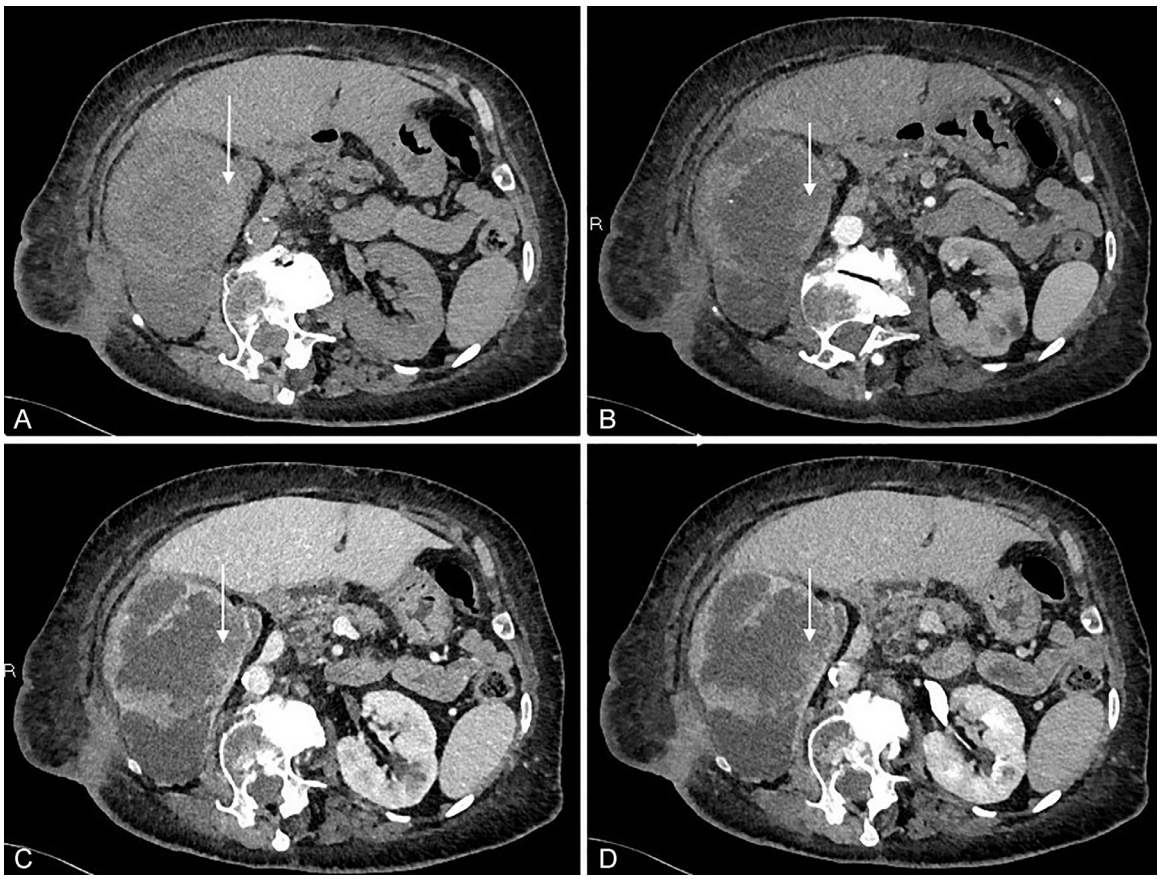

Fig. 3 – (A-D) Unenhanced axial CT image (A, arrow) shows a disorganized and enlarged right kidney; enhanced axial CT image in arterial phase (B, arrow) shows hypodense cavities with enhancement of the walls, increasing in the nephrographic phase (C, arrow) and a gradual wash-out in excretory phase (D, arrow).

Three forms of XGP are recognized:

I) stage I-the lesion is confined to the renal parenchyma.

II) stage II-the lesion involves the perirenal space.

III) stage III-the lesion extends into perirenal and pararenal spaces [5,7,11].

It is usually monoliteral with diffuse, segmental, or focal involvement of the kidney, but bilateral forms have been reported too.

MDCT is considered the current gold standard for the diagnosis and the staging of XPG. Typical CT findings include the presence of staghorn calculi, "bear paw sign", xanthomas, pyonephrosis, air in the collecting system due to anaerobic infection, fat stranding and local complications such as abscesses (renal or in adjacent organs) and fistulas.

In advanced cases, pleural effusion, lung atelectasis and dysventilation are frequently found and transdiaphragmatic inflammatory extension has been reported as well [8,15].

The coexistence of nonfunctioning enlarged kidney, a central calculus within a contracted renal pelvis, fluid filled cavities, hydronephrosis and inflammatory changes in the perinephric space, that may involve and extend beyond the Gerota's fascia, are suggestive of XGP [7].

At CT, the diagnosis of renal inflammatory disease can be ruled out in most patients but the diagnostic confidence is reduced in nonadvanced stages.

The "bear paw " sign", reported in more than 70% of patients, has been described as a finding specific for XGP. Xanthomas are pathognomonic of XGP but less frequently reported (5.6%) [5].

In focal and segmental XGP, the renal parenchyma is replaced by hypodense areas with nonhomogeneous contrast enhancement and extrarenal extension, similar to what happens in local spread of renal cancer. Focal XGP can be considered a diagnostic challenge for radiologists [13,16–18,19] even in the era of multimodality imaging, indeed mistaken diagnoses are therefore frequently reported [22]. In fact, US findings are nonspecific [13,20], at US the kidney usually appears enlarged, there are areas of hyperechogenicity and cystic abnormalities that are indicative of necrosis and inflammation [13,20].

The sensitivity of spin-echo T1-weighted images in magnetic resonance (MRI) depends on the amount of lipid-laden foamy macrophages, for evaluating the degree of soft tissue involvement, in particular, MRI can offer improved tissue contrast. Patchy enhancement on postcontrast sequences and hypointense patches on T2-weighted images are indicative of sarcomatoid degeneration [21].

PET/CT imaging doesn't improve the diagnostic accuracy [21]. For these reasons, XGP has been described as the "great imitator" because it can mimic clinically and radiologically

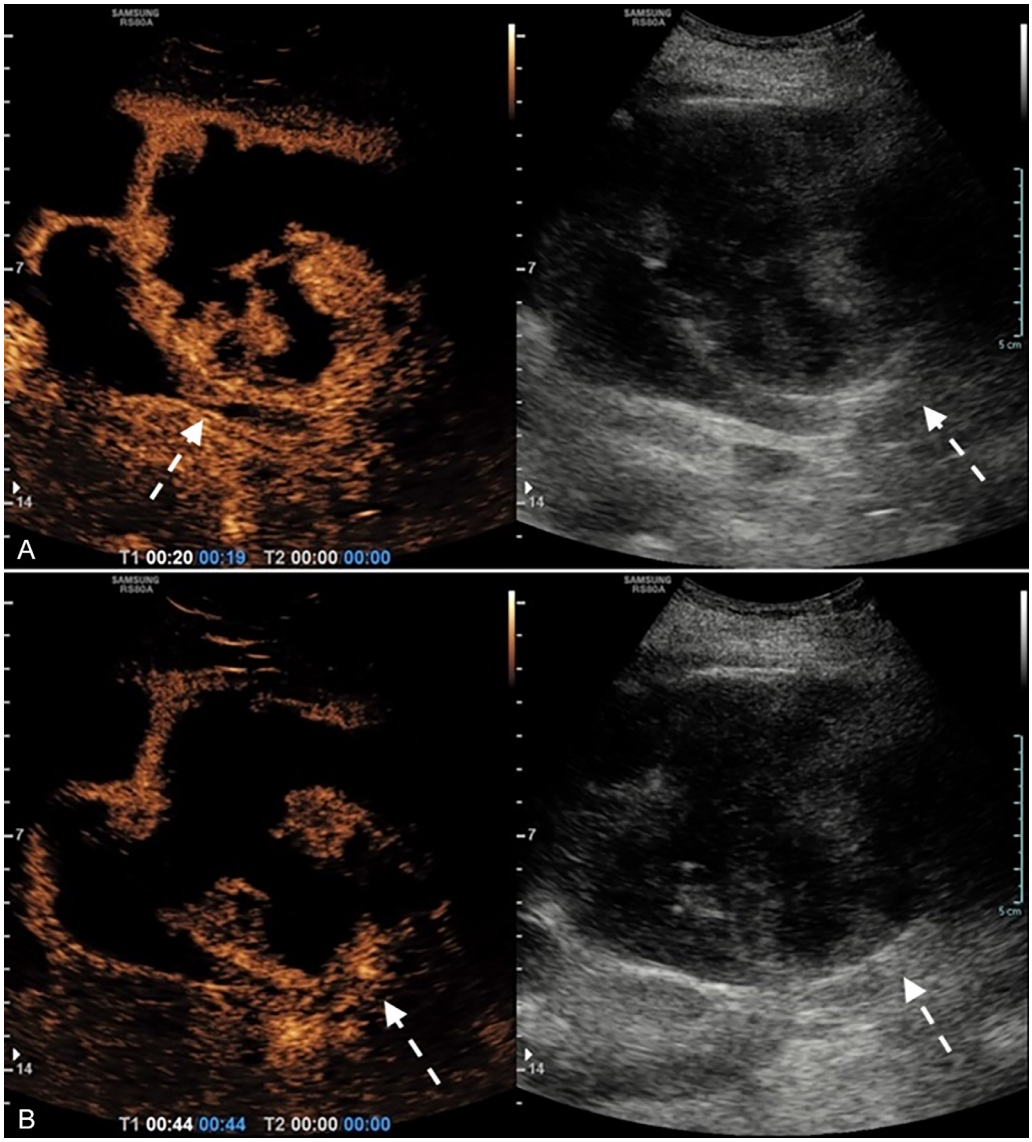

Fig. 4 – (A, B) on CEUS examination: at 19 seconds after the administration of Sonovue (A), the nodular thickening of the wall shows rapid and inhomogeneous enhancement compared to the normal renal cortex parenchyma; at 44 seconds after contrast agent administration (B) the lesion shows a fast-out pattern compared to the renal cortex (white arrows).

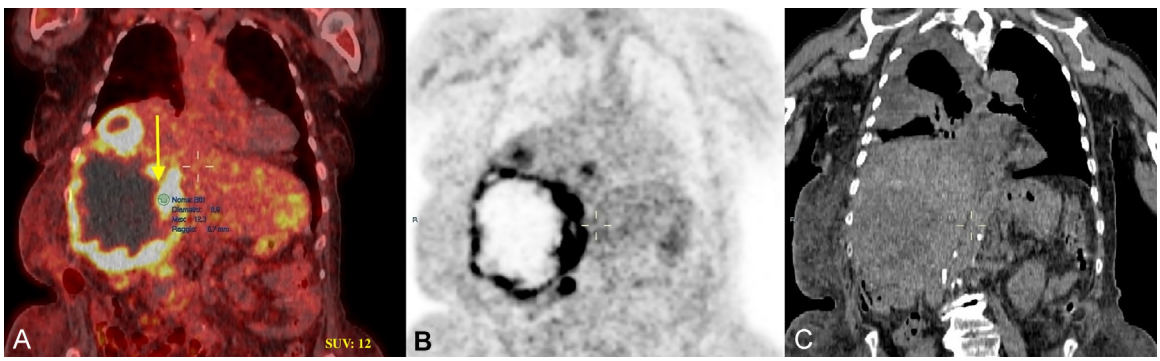

Fig. 5 – (A-C) Whole-body FDG PET maximum projection image shows a diffuse metabolic activity in the liver and in the right renal lodge (yellow arrow, SUVmax 10).

both neoplastic and inflammatory renal disorders [13,5,25]. Differential diagnosis includes RCC, leiomyosarcoma, malakoplakia, megalocytic interstitial nephritis, Wilms tumor [12], pyonephrosis, renal tuberculosis, renal abscess, angiomyolipoma, extrapulmonary sarcoidosis, and actinomycosis [7].

Concomitant carcinoma is found at autopsy in 11.1% of diffuse forms of XGP, and it is usually not recognizable prospectively and retrospectively in CT scans [4,5,21–24].

Histopathology is an important diagnostic tool but the reliability of histopathological evaluation is limited by the fact that xanthomatous cells (with a foamy cytoplasm) may mimic the clear cytoplasm of clear cell RCC cells, foamy histiocytes may be present extensively in papillary RCC and XGP with prominent spindle cell proliferation also mimic sarcomatoid RCC. Therefore, erroneous histopathological diagnoses can occur [26,27]. Immunohistochemistry can help to make a more confident diagnosis because XGP is diffusely positive for CD68, while CD10 and epithelial membrane antigens are usually positive in RCC and in sarcomatoid RCC together with cytokeratins [12,27,28]. As reguard on imaging, RCC, especially the papillary subtype, can resemble XGP; however, RCC is more vascularized and usually does not have the large regions of necrosis that are present in XGP. Diagnosis may be complicated by sarcomatoid differentiation in RCC presenting similarly to sarcomatoid degeneration in XGP [4,5,21–24].

Other frequent differential diagnoses may include inflammatory processes affecting the kidney [7]. Pyonephrosis, an infection-related disorder that can manifest as renal hypertrophy and abscess formation, is another alternative diagnosis. XGP is characterized by chronic granulomatous inflammation and fibrosis, whereas pyonephrosis has an abrupt beginning [7].

Although it is not a characteristic of XGP, gas development inside the renal parenchyma can be caused by a severe infection or emphysematous pyelonephritis [7].

Last but not least, although renal scarring and parenchymal thinning may be present, chronic pyelonephritis does not usually exhibit the widespread necrotic alterations and inflammatory masses associated with XGP [7].

Therefore, fine-needle aspiration cytology can be useful in the diagnosis of focal or segmental XGP. Surgical treatment associated with pre- and postoperative broad-spectrum antibiotic therapy is considered the first line therapy in diffuse forms. The multidisciplinary discussion (MDD) suggests which surgical treatment is more suitable according to the patient's characteristics (open, laparoscopic and robotic assisted nephrectomy or nephroureterectomy) and allows a low rate of surgical reconversion [4,25]. Conservative treatment with antibiotic therapy is indicated in focal XGP and bilateral XGP, when the diagnosis can be based on clinic-radiological and histologic findings [12]. However, XGP can become a life-threatening condition because of the diagnostic delay, which also increases the risk of malignant degeneration, with greater incidence of transitional cell carcinoma and RCC.

Our patient had a Bellini carcinoma with sarcomatoid components, which are associated with a poor prognosis and a median survival of less than 1 year.

The sarcomatoid components, reported in 1%-6.5% of renal carcinoma, are related to the proliferation of pleomorphic spindle cells with marked cellular atypia, resembling sarcoma tumors. According to recent trials, the immune checkpoint therapy (ICT) can be considered a promising treatment for sarcomatoid dedifferentiation tumor [29,30]. The collecting duct carcinoma represents 3% of renal tumors and is a rare variant with aggressive clinical phenotype and a poor prognosis, which is more similar to urothelial-origin tumors than RCC [29,30].

According to Guglin et al. [4], the radiologist should be aware that the diagnosis of XGP cannot exclude other diagnoses, in particular overlapping malignancy. It follows that chronic inflammatory disease even in asymptomatic patients should not be underestimated.

Conclusion

Histopathological investigation is still the gold standard for verifying XGP and sarcomatoid degeneration, even though imaging is essential for diagnosis. While CT and MRI are valuable diagnostic instruments, their ability to distinguish benign inflammatory tumors from malignant degeneration based purely on imaging features is limited. For greater characterization, more sophisticated imaging methods like PET-CT could be used.

Our case underlines the central role of multimodality imaging in ER settings, including contrast-enhanced ultrasound (CEUS). In fact, CEUS is a promising technique that shows a wide range of application in different settings such as oncological, vascular, pediatric and even in emergency, allowing rapid bedside diagnoses. The potential use of CEUS involves also the study of uncertain small renal masses detected by CT, as it is shown. CEUS examination can be performed immediately after the CT-exam with administration of intravenous contrast material without any kidney failure risk for the patient. Moreover, in both elective and emergency settings, CEUS can be a valid alternative to RM in noncooperative patients, or in those with contraindications. Our case report also highlights the importance of the multidisciplinary discussion that improves the diagnostic confidence among specialists and influences the management and the treatment, respecting the patient's choices.

Limitations

The study focuses on a single patient, further studies with larger populations are needed to understand the full spectrum of sarcomatoid degeneration in XGP and confirm the data reported here.

Patient consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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