

## Case Report

# A case of xanthogranulomatous pyelonephritis leading to nephrobronchial fistula and lung abscess: does it always manifest with respiratory symptoms?

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**Abstract:** Xanthogranulomatous pyelonephritis (XGP) is a serious manifestation of chronic kidney inflammation that can expand to adjacent structures. Here we report a case of XGP extending beyond the diaphragm through a nephrobronchial fistula to form a lung abscess in a 70-year-old man. The patient presented to the emergency department with severe right flank colic pain, nausea, vomiting and nonspecific constitutional symptoms for the past 4 months. Although the patient did not complain of any respiratory symptoms, initial evaluations revealed severe right-sided hydronephrosis with debris, as well as an area of infiltration in the right lung lower lobe (RLL). Given the patient's condition, a thorough work-up was expedited to investigate the potential association between the symptoms. Ultimately, a diagnosis of XGP with expansion to the RLL through the right hemidiaphragm was developed. A right radical nephrectomy, right lower lobectomy and right hemidiaphragm resection were carried out. XGP was confirmed on the basis of the pathological evaluation of the resected specimens.

**Keywords:** Xanthogranulomatous pyelonephritis, nephrobronchial fistula, lung abscess, nephrectomy

## Introduction

Xanthogranulomatous pyelonephritis (XGP) is an invasive, chronic inflammation of the kidney in which lipid-laden (foamy) macrophages of granulomatous tissue cause substantial destruction of the normal renal parenchyma. It accounts for up to 20% of pyelonephritis cases managed with nephrectomy [1] and often presents with flank and/or abdominal pain, fever, anorexia and malaise [2]. XGP is staged based on the degree of involvement of adjacent tissues and can be divided into 3 stages: stage 1 or nephric in which the infection is confined to the kidney; stage 2 or perinephric involving the kidney and Gerota's fascia; and stage 3 or paranephric, with widespread extension to retroperitoneal space and nearby structures [3]. Two of the most important, albeit rare, complications of XGP are fistulation and abscess formation. Fistulous tracts can develop in the setting of ischemia, necrosis or chronic inflammation. As in stage 3 of XGP, an intrarenal inflammatory process may spread beyond the renal capsule

and take the path of least resistance to form a fistula between the infected kidney and the adjacent organs [4]. Fistulas most commonly involve the colon, diaphragm and thoracic cavity. A nephrobronchial fistula results in the dissemination of inflammation into the lungs and the formation of an abscess [5]. An important feature of XGP is its ability to mimic the characteristics of renal tumors, particularly renal cell carcinoma (RCC) [6].

Regarding the fact that XGP often presents with nonspecific constitutional symptoms, its expansive nature, the probability of fistula formation and existence of RCC as an important differential diagnosis, clinical suspicion of XGP in the first place, and accordance recognition and management of the disease is of great importance. Therefore, the purpose of this case report is to lead the audience's mind toward this disease as one of the rare but important underlying causes of lung abscess to be able to provide timely relevant treatment.

## XGP leading to nephrobronchial fistula and lung abscess

Here we report a case of XGP that led to nephrobronchial fistula and lung abscess in a 70-year-old man who presented with flank colic pain but did not complain of any respiratory symptoms.

### Case history

A 70-year-old man, a resident of a rural area in Iran, was admitted to the emergency department affiliated with Isfahan university of medical sciences, complaining of severe right flank colic pain, nausea and vomiting. The symptoms had started 4 months ago and worsened over time. He also referred to repeated episodes of hyperpyrexia and chills in this duration, with the last episode occurring 3 days ago. He denied any lower urinary tract symptoms (LUTS) or gross hematuria. The patient suffered from loss of appetite and significant weight loss since the beginning of the symptoms. He had a past medical history of nephrolithiasis and had undergone transurethral lithotripsy (TUL) surgery but was otherwise healthy.

A physical examination noted an emaciated individual compatible with his age. He was afebrile and had a body temperature of 36.9°C. Other vital signs were within the normal range. There was tenderness in the right costovertebral angle, decreased respiratory sounds and dullness of percussion over the right lung lower lobe (RLL). Laboratory data included hemoglobin of 7.5 g/dL, a total leukocyte count of 18700/ $\mu$ L with differential leukocyte counts as neutrophils 87.8% and lymphocytes 6.1%, a serum creatinine level of 1.5 mg/dL and 1-hour erythrocyte sedimentation rate (ESR) of 121 mm/hr. Analysis of the midstream urine sample suggested amorphous and urate crystals, 1-2 WBC, 6-8 RBCs in each high-power field and few bacteria. Urinary nitrite was negative and urine culture did not reveal any bacterial growth after 24 h.

With regard to the clinical and paraclinical findings, primary imaging studies were conducted at the emergency department. Abdominal ultrasound detected an enlarged right kidney, a heterogeneous hypoechoic area in the right kidney's upper pole, and severe hydronephrosis with debris. We conducted a chest X-ray (CXR) film because of the suspicious findings in the physical examination of the lungs. The CXR revealed an area of infiltration in the

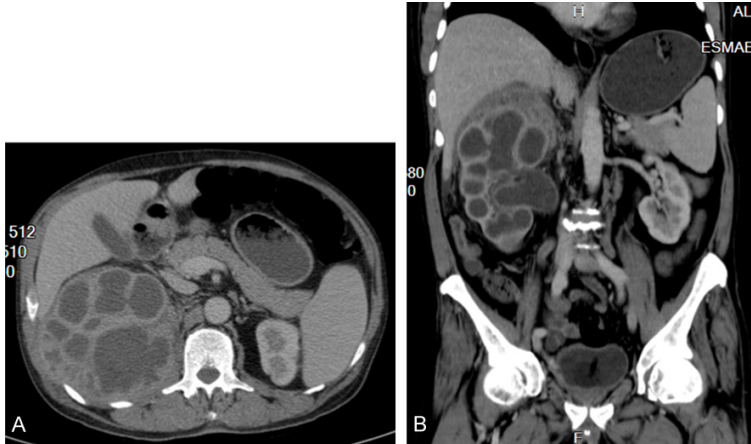
RLL with minimal right-sided pleural effusion and a blunt right hemidiaphragm. This was an interesting finding as the patient did not complain of any respiratory symptoms.

The patient was then transferred to the urology service where besides managing the patient's chief complaint, work-up was initiated to find the cause of the pulmonary findings simultaneously. As a result, multi-detector row computed tomography (MDCT) of the chest, abdomen and pelvis with and without the administration of contrast medium injection was performed to further investigate the pathologies visualized by prior ultrasound and CXR. In addition to confirming previous results, the CT scan revealed a multiloculated abscess in the size of 145\*115 in the right perinephric area with external extension and fat stranding, dilated pyelocaliceal system with fluid accumulation and thinning of cortical parenchyma-the classic appearance called "bear's paw sign", which is often associated with XGP (**Figure 1**). Additionally, a thick wall cavitary lesion in the size of 92\*82 mm was detected in RLL containing air bubbles, associated with parenchymal alveolar infiltration and ground glass opacity. The findings were in favor of a lung abscess (**Figure 2**). Since the admission occurred during the COVID-19 pandemic, a reverse transcription polymerase chain reaction (RT-PCR) test was ordered to determine whether the lung abscess was associated with COVID-19 infection; however, the result was negative.

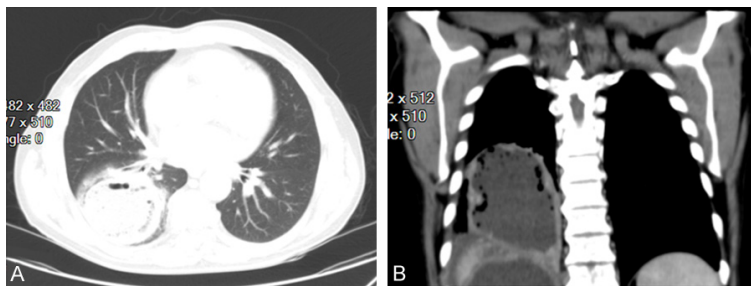
Given the patient's clinical symptoms, recent weight loss and the results of the CT scan, we ultimately suspected two important differential diagnoses: Renal malignancy with lung metastasis and paranephric XGP with extension to the RLL. In order to distinguish between the two differential diagnosis, we performed a urine cytology test, which was not conclusive for either malignancy or XGP and a second urine culture, again, did not reveal any bacterial growth. Nevertheless, *Proteus mirabilis*, a common urinary tract pathogen, grew from the sputum culture. At this point, XGP was favored over RCC; but the latter could not yet be positively ruled out without histopathological confirmation.

Pre-operative renal biopsy was not indicated because the gold standard treatment for both of our differential diagnoses was radical ne-

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**Figure 1.** CT scan of the abdomen and pelvis demonstrating XGP. A. Axial section showing a noticeably large and abnormal right kidney with a radial arrangement of multiple low-attenuation dilated calyces surrounded by thin renal parenchyma with higher contrast enhancement, mimicking a “bear’s paw”. B. Coronal section confirming aforementioned changes in the right kidney.

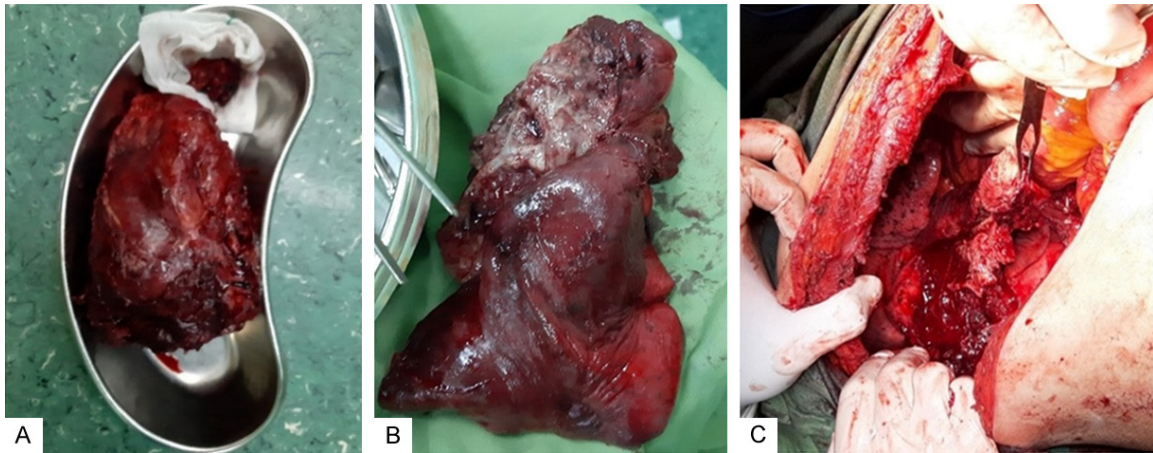


**Figure 2.** Thoracic CT scan revealing a large irregular bordered cavitating lesion occupying the RLL. A. Axial section. B. Coronal section. Note the lesion extending through the ipsilateral hemidiaphragm.

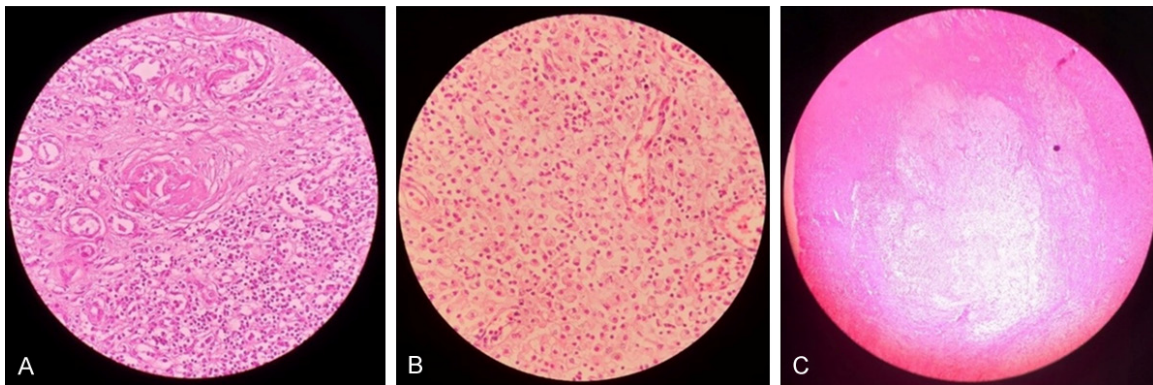
phrectomy. In addition, the size of the lung abscess was large enough to require surgical removal. As a result, we planned a surgical intervention of right radical nephrectomy, RLL abscess resection and right hemidiaphragm resection, in combination with an antibiotic therapy. After consulting the infectious disease department, we immediately initiated intravenous meropenem (1 g, q 8 h) and vancomycin (1 g, q 12 h) and the patient was prepared for the surgery. After general anesthesia, in the right semi-flank position, a right thoraco-abdominal incision was made from the mid axillary line toward the umbilicus. The 10th rib was subperiosteally resected with a bone cutter. The right kidney appeared deformed and tumorous and the Gerota’s fascia showed severe adhesions to the liver, colon, duodenum, psoas

muscle, and diaphragm. A thorough dissection of all adhesions was performed. While releasing the upper and lower poles, a large volume of purulent secretion gushed out of the kidney, diaphragm and pleura. We noticed a fistulous tract between the infected kidney and the diaphragm that extended to the RLL. The involved part of the diaphragm was resected. Since the abscess had destroyed a large part of the RLL, a total lobectomy was required. Finally, the diaphragm and pleura were repaired and the incision was closed after inserting a 32-F chest tube and a hemovac drain in the right renal space.

The resected kidney and RLL specimens were sent to the pathology department for further assessment, culture and antibiogram (**Figure 3**). Gross surgical pathology demonstrated a brownish/tan purulent mass in the size of 18\*13\*7 cm occupying the entire kidney that contained areas of necrosis and bleeding. Histological analysis reported the replacement of renal parenchyma with granuloma-like structures, foamy histiocytes (xanthoma cells) with cholesterol clefts, occasional multinucleated giant cells and inflammatory cells with an extension to perinephric fat. Necrosis and renovation tissue were seen in some foci (**Figure 4**). A section of the RLL showed infiltration of acute inflammatory cells, cell debris and necrosis. Staining for CD68 and vimentin was also strongly positive in the immunohistochemical analysis. *Proteus mirabilis* was cultured from the purulent secretion and no histopathological evidence was reported in favor of RCC. Considering all of the above, the diagnosis of XGP was confirmed. After the surgery, intravenous antibiotic therapy was modified to meropenem alone (1 g, q 8 h) and vancomycin was discontinued, based on the result of the antibiogram. The patient experienced an uneventful



**Figure 3.** A. Specimen of right radical nephrectomy including right kidney, adrenal gland tissues and surrounding perinephric fat. B. Specimen of the resected RLL. C. Surgical procedure of resecting the infected kidney.



**Figure 4.** Histopathological examination of the surgical specimen with hematoxylin and eosin staining demonstrating microscopic features of XGP. A. A detailed image of glomerular sclerosis in the context of XGP. B. Replacement of renal parenchyma with foamy histiocytes. C. A section of a granuloma within the renal parenchyma.

postoperative course and progressive recuperation. 11 days later, in order to search for any potential infection or abnormality in the operated areas and adjacent structures, we conducted a spiral CT scan of the chest and abdomen, which did not show any abnormality. On the 17th postoperative day, the patient's symptoms had been completely resolved and he was successfully discharged from the hospital with a hemoglobin level of 10.1 g/dL, a serum creatinine level of 0.8 mg/dL and an ESR of 36 mm/hr. We asked the patient to come back 3 months later to evaluate his general, urinary and respiratory status. On the outpatient follow-up visit, he was asymptomatic with negative physical exam and all of the previously abnormal laboratory findings were reported within the normal range.

#### Discussion

XGP is a distinct clinicopathological entity described as chronic xanthogranulomatous renal infection. Contrary to our case, it mostly affects middle aged women. XGP can present with a variable spectrum of symptoms, but most frequently manifests as flank pain, palpable mass, weight loss, chills and fever [7]. Characteristic laboratory findings include anemia, typically in the form of chronic disease, leukocytosis, increased ESR and C-reactive protein (CRP) and elevated serum creatinine levels in cases of renal injury. An enlarged kidney may cause mild biliary retention; hence, alkaline phosphatase and liver aminotransferase enzymes may also be elevated in some patients, but will most definitely come back to normal after the treatment [8]. Urinary symptoms such as LUTS

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and hematuria may not always be present, but if observed, can be very helpful in proposing the diagnosis [2]. One of the tricky aspects of our case was the absence of any urinary symptoms, so it was hard to think of XGP as one of the differential diagnoses, in the first place. However, XGP must be considered in all patient with flank pain and constitutional symptoms.

Although the pathogenesis of XGP is not exactly known, recurrent urinary tract infection (UTI), nephrolithiasis and obstruction are reported to be the predisposing factors [9].

Nephrolithiasis, frequently staghorn stones, is observed in up to 100% of the cases published in the literature [10]. It is a very strong predisposing factor, to the extent that Goldman et al. claimed it is almost impossible to diagnose XGP in the absence of obstructing calculi [11]. De Souza et al. described a case with untreated renal calculi that led to recurrent episodes of renal colic during an 8-year period and ultimately XGP. He had presented with cough, dyspnea, and purulent expectoration. A nephrobronchial fistula was suggested and the patient underwent nephrectomy with drainage of the subphrenic abscess [12]. In our study, although the patient had a past history of nephrolithiasis, calculi were found neither on the CT scan nor in the surgical procedure. This could be due to the point that the duration of obstruction plays an important role in the development of the chronic inflammation process. XGP is usually linked to long-standing presence of calculi and a single episode alone may not be able to cause the disease [13]; however, this claim has not yet been positively confirmed.

60% of XGP cases show features associated with UTI, including pyuria, bacteriuria or hematuria in their urinalysis and in 90% of the patients, at least one of the following organisms is isolated in the urine culture: *Proteus mirabilis*, *Escherichia coli*, *Pseudomonas*, *Enterococcus faecalis* or *Klebsiella* [14]. Much to our interest, our patient denied any history of UTI and continued to have negative urine culture throughout our diagnostic work-up period.

Due to the variable and nonspecific findings, clinical suspicion of XGP is complex, and the formation of a fistulous tract intensifies this complexity by spreading the infection to other organs. Sometimes the disease merely mani-

festes as symptoms related to the affected organ, while the underlying XGP is indolent. For instance, a nephrobronchial fistula secondary to XGP can present with respiratory symptoms including chest pain, cough and foul-smelling sputum, in the absence of any clinical presentation of the renal infection. Uppe et al. reported a case admitted with non-productive cough and anemia for 15 days with no history of urinary symptoms [15]. A similar case was described by Pandya et al. whose patient presented with productive cough, right-sided chest pain, dyspnea and fever for a 3-day duration [16]. In both of these cases, XGP was only suspected when a work-up was initiated to find the cause of the anemia. This circumstance can be complicated as it could lead the mind to a sole pathology in the fistulated organ, completely ignoring the underlying XGP. In contrast, sometimes there are no clinical symptoms suggestive of the involvement of another organ, and if imaging fails to identify the fistulous tract, it would be very difficult to associate different data to offer a conclusion. This was an obstacle we faced in our case. Although our patient did not complain of any respiratory symptoms nor was the fistula detected by the CT scan, we suspected the presence of a fistulous tract on account of our previous experience with a complicated XGP that caused nephrocutaneous fistula [17]. The key is to perform a comprehensive physical exam and thorough work-up to associate all the findings and investigate the common places of fistulation in the paranephric form of XGP.

No definitive diagnostic criteria have been established for XGP; however, the diagnosis is initially made radiographically and later confirmed by histopathology [18]. CT scan has been the imaging of choice. The most distinctive finding of XGP in CT scan is the “bear’s paw sign”, which is an important pathognomonic feature described as an atypical kidney contour along with dilated calyces and a contracted pelvis. Besides, CT scan can demonstrate the degree of extrarenal invasion of the disease which is crucial for surgical planning [19]. Although the clinical suspicion of XGP was challenging in our patient, radiological findings, including the classical “bear’s paw sign”, were suggestive of XGP and helped in considering it as one of the differential diagnoses. Fistulous tracts are usually detected in the CT scan, but

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in our case it was not found until the surgical procedure. Histopathological examination of the resected specimen demonstrates substitution of renal parenchyma by nodular collections of lipid-laden (foamy) histiocytes, often containing cholesterol clefts, focal calcification and occasional central necrotizing changes. Chronic infiltration of inflammatory cells such as lymphocytes, macrophages and plasma cells is also identifiable [20].

XGP has the ability to mimic the clinical, radiological and even histological features of renal malignancies, in particular RCC; thus, the diagnosis is not regularly fulfilled preoperatively. Our patients' age and symptoms of decreased appetite and significant weight loss were compatible with renal malignancy which could also explain the pulmonary findings, considering its invasion through the lymphatic and blood system. Elevated levels of ESR and CRP could be indicative of both a chronic inflammatory process and carcinoma. Leukocytosis was more in favor of XGP and is rarely observed in RCC. Urine cytology can be indicative of carcinoma by identifying cytological atypia or can suggest XGP by detecting xanthoma cells in the urine specimen; however, it is not completely reliable. This point was well illustrated in an article by Inouye et al. who described a 16-year-old boy with a 2-year history of daily gross hematuria. Preoperatively, he was assumed to have RCC based on the urine cytology findings, but was then diagnosed as XGP after the histopathological evaluation of the resected kidney [21]. The best way of distinguishing between XGP and carcinoma is by histopathological analysis of the tissue; although, there is still small potential for misdiagnosis as lipid-laden histiocytes can resemble the characteristic clear cells of RCC [22]. We did not perform a preoperative needle biopsy because its indications and necessity are still a matter of debate [13]. Besides, it was an invasive procedure that could not change our treatment decision, which included radical nephrectomy in both cases.

XGP is a surgically managed disease. Radical nephrectomy is the cornerstone of treatment. Certain cases of stage 1 or 2 of XGP, when the function of the kidney is preserved, could be amenable to partial nephrectomy [23]. Closure of all the fistulas as well as dissection of the granulomatous tissues and adhesions should

be carried out to avoid any fistula formation in the future [24]. Pre and post-operative antibiotics must be prescribed in all cases, but medical therapy alone rarely suffices for treatment. A number of articles reported successful management by antibiotic therapy alone, although it is not considered as a standard treatment [25]. Provided that XGP is unilateral, treated early and the infection is successfully controlled by antibiotics, the prognosis of nephrectomy is good [26]. Due to the symptomatic management, opt for the early standard surgical intervention and careful eradication of infection with broad-spectrum antibiotics, our patient did not experience any operative-related complications and was healthy in the follow-up visit.

Fistulas most commonly affect the gastrointestinal tract, thoracic cavity, urinary organs, and skin. Nephrobronchial fistula and the subsequent lung abscess are very rare [27]. For the first time, Parson et al. reported a nephrodiaphragmatic fistula secondary to XGP [28] and since then, very few cases of the similar condition have been described in the literature [5, 12, 15, 16, 27, 29, 30]. The anatomic explanation for the extension of a suppurative process up through the diaphragm was first explained by Evans et al. who claimed that the lumbocostal triangle (Bochdalek foramen), a relatively weak part of the diaphragm, is culpable for directing the exudate into the thoracic cavity, because parietal pleura and renal capsule come in contact in this space [31]. Although it is unclear why XGP tends to fistulate in some cases, a review of the literature indicated that certain conditions such as diabetes mellitus, immunodeficiency, microvascular diseases and lower socioeconomic status might contribute to the development of complicated XGP [22, 28]. Alifano et al. reported a nephrobronchial fistula secondary to XGP, in a 31-year-old man infected with human immunodeficiency virus (HIV). It cannot be overlooked that HIV might have been a concurrent cause for the evolution of the nephrobronchial fistula [27]. Al-Ghazo et al. published an article about their experience with 18 XGP patients. They reported that all of the fistulated cases had a lower socioeconomic status [22]. Our patient did not suffer from any notable concomitant medical condition and was otherwise healthy; even so, one could not be sure that his advanced age or lower socio-

economic status had no effect on complicating the disease.

Looking back at our clinical approach, we think that there are two limitations in this study that could be addressed in the future. First, we did not perform a renal scan to accurately assess the renal function. Although this could have idealized the clinical work-up, we did not consider it to be mandatory as we planned on performing the gold standard treatment option, which was radical nephrectomy. Nevertheless, it is better to perform the renal scan in cases where a nephron sparing surgery is considered, for instance having a single kidney. Second, our patient was not followed-up after the 3-months outpatient appointment. The long distance between his hometown and the hospital may have been the reason of his non-attendance. Anyhow, it is better to perform annual imaging of the contralateral urinary tract after radical nephrectomy.

In summary, contrary to the prior reported cases, the distinguishing feature of our study is the absence of any respiratory symptoms at the time of admission. Our patient was a healthy immunocompetent male with no history of predisposing factors responsible for causing the XGP, except for an episode of nephrolithiasis. We assume that this could have played a role in causing the initial renal infection, which then developed to fistulate and form a lung abscess. We speculate that the patient's advanced age or lower socioeconomic status might have contributed to the fistulation of XGP. This article emphasizes the importance of timely identification of XGP and having a holistic view while managing the patient's disease. One should search for XGP complications by examining common places of fistulation, even in the absence of clinical symptoms. It's crucial to keep in mind that XGP could be a rare, yet important underlying cause of lung abscess, especially in cases of concurrent renal and pulmonary involvement.

### Disclosure of conflict of interest

None.

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