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## Case Report

# Imaging features of renal complications after crizotinib treatment for non–small-cell lung cancer: a case report

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## ABSTRACT

Crizotinib has been approved for the treatment of advanced ALK-positive non–small cell lung cancer. Its use is associated with the development of complex renal cysts. However, there is limited literature regarding imaging features of renal cystic disease during crizotinib therapy and its complications or progression. Here, we describe a case of a patient with ALK-positive advanced non–small cell lung cancer who developed complex renal cyst during crizotinib treatment. The renal cyst is complicated by infection and abscess formation. Subsequent renal biopsy, antibiotics treatment, and open drainage of loculated renal abscess showed no malignant cells and contributed to the diagnosis. The imaging features should be recognized as renal cystic disease of crizotinib treatment and not to be mistaken as new metastasis and disease progression.

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## Introduction

Non–small-cell lung cancer comprises of 85% of all lung cancer diagnosed [1]. The identification of EML4-ALK fusion gene in 4%–5% of lung adenocarcinoma [2] promotes a new class of drugs, which selectively targets this subset of non-small cell lung cancer (NSCLC).

Crizotinib is a first-generation orally active ALK inhibitor, which received Food and Drug Administration approval for

use in ALK-positive NSCLC in November 2013. Randomized control trials report positive progression-free survival and overall response in patients with disease progression after conventional chemotherapy. However, recent literature has reported complication of crizotinib with development of complex renal cysts [3–5].

Here, we report imaging findings of a patient with ALK-positive NSCLC who developed complex renal cyst during crizotinib therapy necessitating open drainage and cessation of therapy.

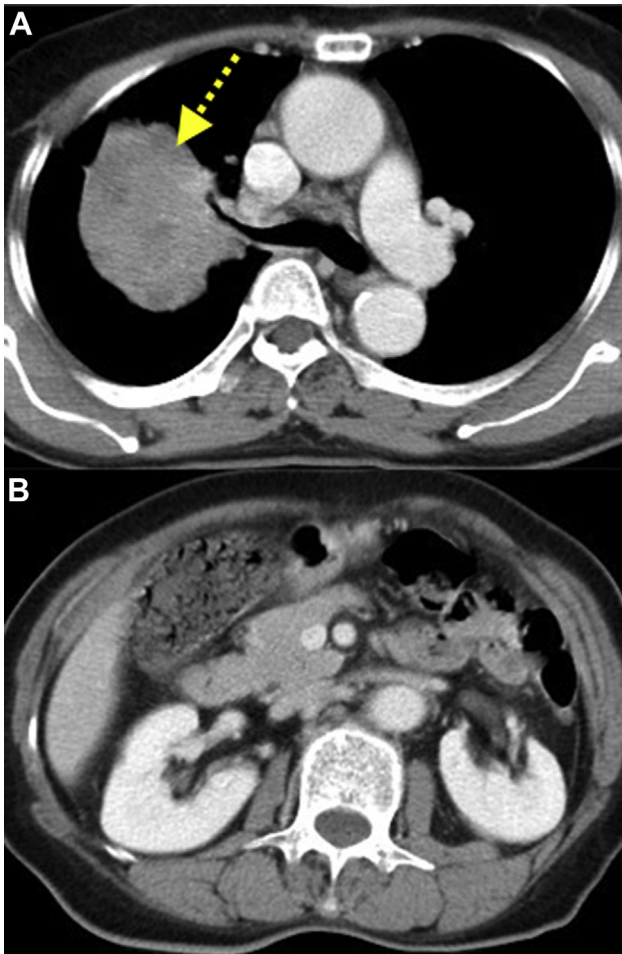
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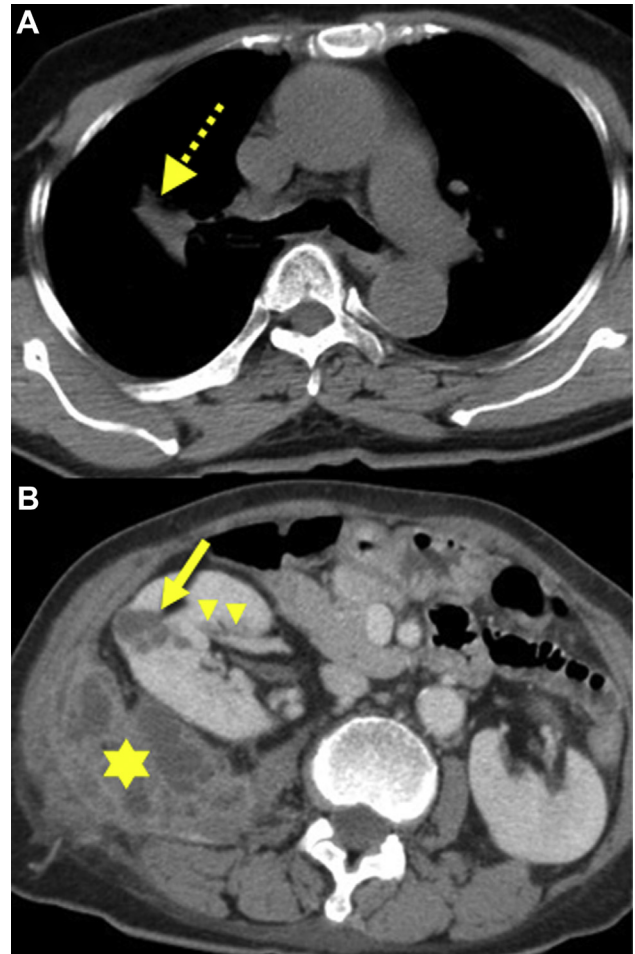
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**Fig. 1** – Axial CT scan before crizotinib therapy. (A) Right lung tumor (dotted arrow) and (B) normal kidneys. CT, computed tomography.



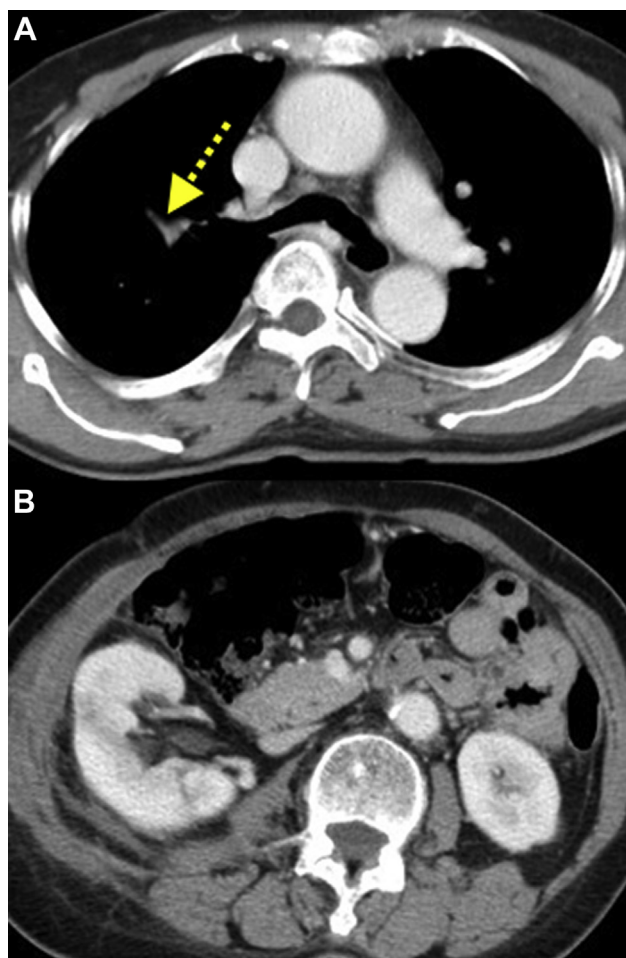
**Fig. 2** – CT scan during crizotinib therapy. (A) Significant decrease in size of right lung tumor and (B) new infected right kidney middle pole renal cyst (arrow) complicated by extension to renal pelvis (arrowheads) into the retroperitoneum with retroperitoneal abscess (\*) 11 months after treatment. CT, computed tomography.

### Case report

A 68-year-old Asian woman was diagnosed with T2N2M0 ALK-positive lung adenocarcinoma (Fig. 1A). Of note, baseline computed tomography (CT) demonstrated a 1.4-cm cyst in segment V of the liver and 2 subcentimeter cysts in the lower pole of the right kidney but otherwise normal kidneys (Fig. 1B). She was not suitable for curative surgery or radiotherapy due to borderline lung function. As part of an ongoing clinical trial, she was commenced on first-line oral crizotinib tablets. Subsequent chest CT after 2 months of crizotinib demonstrated partial response of lung tumor (Fig. 2A).

Seven months after initiation of crizotinib, follow-up CT scan showed 2 new cystic lesions in middle and lower poles of the right kidney. She underwent percutaneous drainage of the cystic lesions, which was negative for malignancy and infection, and then commenced on empirical tuberculosis therapy after consultation with the infectious diseases team. Tuberculosis therapy was stopped due to negative cultures, as well as lack of response. She was admitted again (9 months after crizotinib initiation) for further drainage, which was once

again negative for malignancy and infection, and trialed on various antibiotics as well as antifungals without improvement. In July 2013, her condition deteriorated with extension of the cystic masses to her back with fistulation through to the skin and secondary infection. CT performed showed stable lung tumor; however, interval increase in size of the retroperitoneal loculated septated collection with involvement of the right posterolateral abdominal wall and psoas muscle with a lower right posterior back subcutaneous collection opening to the skin (Fig. 2B). In view of the likely relationship of crizotinib with renal cysts, and the exclusion of other etiology, crizotinib was discontinued. She eventually underwent open drainage of these cystic collections. Intraoperatively, multiloculated abscesses involving the right posterior abdominal wall, psoas, right posterior liver lobe, and the right kidney interpolar region were noted. All cultures were negative, and there was no evidence of malignancy. Postoperative CT scans demonstrated resolution of the abscess and complex renal cysts (Fig. 3).



**Fig. 3 – CT scan 3 months after stopping crizotinib therapy. (A) Barely perceivable right lung tumor (dotted arrow) and (B) interval resolution of right middle pole renal cyst. Postsurgical drainage and complete resolution of retroperitoneum abscess is also seen. CT, computed tomography.**

## Discussion

Crizotinib has been associated with development of renal cysts [3–5], however, limited literature is available to describe its progression and imaging features due to novelty of this class of drug. Although crizotinib is used as a targeted selective inhibitor of ALK, it is a multikinase inhibitor of c-MET and ROS1 oncogenic tyrosine kinases. C-MET receptors are normally present in renal tubular epithelium [6]. It is unknown if its target of c-MET may explain for crizotinib influence on

renal cysts production, either de novo or increase risk of complex transformation of existing renal cysts. Further studies are needed to confirm this hypothesis.

Our case report indicated that these renal cysts can be complex and complicated by infection, rupture, and abscess formation. Renal cysts are classified by Bosniak's category by their imaging features and complexity [7]. Complex renal cysts (Bosniak III and IV) are associated with higher malignant potential and standard guidelines recommend surgery. In this case, the imaging features are indistinguishable from Bosniak III lesions, which include cystic renal cell carcinoma or renal metastasis, which prompts further procedures for histopathologic confirmation.

This case highlights the importance of recognizing the imaging features of renal cystic disease as a complication of crizotinib treatment. Erroneous interpretation of such complex cysts as new metastasis and disease progression may lead to invasive investigations and patients quality of life. Isolated case reports in the literature [3,8] suggested that stopping crizotinib will lead to spontaneous regression of these renal cysts. Invasive investigative procedures and surgery, as demonstrated in our case, can be avoided.

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