CASE REPORT

Crizotinib-induced pancreatic pseudocyst: a novel adverse event

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Accepted 28 August 2015

SUMMARY

Crizotinib is a tyrosine kinase inhibitor that demonstrates a dramatic tumour response in patients with advanced non-small cell lung cancers harbouring anaplastic lymphoma kinase (ALK) rearrangement. The pancreatic cyst has never been reported in patients who received crizotinib, whereas crizotinib-induced renal cysts developed in 4% of patients who were enrolled in clinical trials. We present the case of a 54-year-old man who was diagnosed with non-small cell lung cancer harbouring ALK rearrangement. After the start of treatment with crizotinib, we accidentally encountered the pancreatic pseudocyst without abdominal symptom and elevated serum pancreatic enzymes. In this report, we describe a case of pancreatic pseudocyst that appeared after starting treatment with crizotinib and regressed after treatment withdrawal.

TREATMENT

Treatment with crizotinib (250 mg twice daily) was started in September 2014. Grade 3 elevations of transaminase levels appeared 9 days after starting treatment with crizotinib, and the drug was discontinued. After improvement of the grade 1 elevations, crizotinib was restarted on day 23 at a dose of 200 mg twice daily. However, crizotinib was withdrawn again because of recurrent hepatic toxicity on day 41. Although the patient had no abdominal symptoms at the time of discontinuing crizotinib, CT of the abdomen revealed the development of cystic lesions in the body and tail of the pancreas (figure 2A). Serum amylase and lipase levels were within the normal range. Five months after the withdrawal of crizotinib, CT showed regression of the pancreatic cyst (figure 2B).

BACKGROUND

Crizotinib is a tyrosine kinase inhibitor that inhibits anaplastic lymphoma kinases (ALKs).¹ Crizotinib can potentially lead to a dramatic tumour response in patients with advanced non-small cell lung cancers harbouring ALK rearrangements.^{2 3} The package insert for crizotinib approved by the US Food and Drug Administration states that crizotinib-induced renal cysts developed in 4% of patients who were enrolled in clinical trials. To the best of our knowledge, however, a case of crizotinib-induced pancreatic pseudocyst has not been reported previously. We describe a pancreatic pseudocyst that appeared after starting treatment with crizotinib and regressed after treatment withdrawal.

CASE PRESENTATION

A 54-year-old man was referred to our hospital because of postoperative recurrence of lung cancer. He had undergone surgery in another hospital 7 years previously. Because pathological stage IA disease was diagnosed, the patient received no adjuvant therapy. Two months previously, he had right back pain. At initial presentation, he reported severe back pain. CT scan showed metastases to the right pleura, with thoracic vertebral invasion (figure 1A). This time, CT of the abdomen revealed no abnormal finding of the pancreas (figure 1B). A CT-guided biopsy of the involved thoracic vertebra was performed, and the pathological diagnosis on immunohistochemical analysis was adenocarcinoma with ALK protein expression.

Figure 1 CT scans obtained before the administration of crizotinib, showing pleural and thoracic vertebral metastases (A) and no abnormality in the abdomen (B).

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To cite: Ishida H, Ichikawa W, Sasaki Y. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2015-211556

Figure 2 CT scans showing newly developed cysts in the pancreatic body and tail (arrowheads) 6 weeks after starting treatment with crizotinib (A) and regression of the pancreatic cyst 5 months after the discontinuation of crizotinib (B).

OUTCOME AND FOLLOW-UP

Alectinib was started after the withdrawal of crizotinib. The patient had been receiving alectinib for 6 months at the last follow-up, and had experienced no pancreatic pseudocyst recurrence during that time.

DISCUSSION

Crizotinib-induced renal cysts have been reported to develop in 4% of patients who receive crizotinib.² These renal cysts generally resolve after discontinuation of the drug.^{4 5} To the best of our knowledge, we have described the first reported case of crizotinib-induced pancreatic pseudocyst. In our patient, the pancreatic pseudocyst appeared after starting treatment with crizotinib and regressed on withdrawal of the drug. We therefore concluded that the pseudocyst was induced by crizotinib.

Pancreatic pseudocysts induced by anticancer drugs are considered rare adverse events. L-Asparaginase-induced pancreatic cysts have been reported in patients with acute lymphocytic lymphoma.⁶ L-Asparaginase-induced pancreatic pseudocysts are

generally mild and self-limiting, and rarely cause acute pancreatitis. However, restarting of the drug must be carefully considered because pancreatic pseudocyst recurrence has been reported after resuming treatment with L-asparaginase.⁶ On the contrary, the relative risk of pancreatitis associated with multitargeted vascular endothelial growth factor receptor (VEGFR) tyrosine kinase inhibitors such as sunitinib, sorafenib, pazopanib, axitinib, vandetanib, cabozantinib, ponatinib and regorafenib has been reported.⁷ Treatment with tyrosine kinase inhibitors can cause acute pancreatitis, although the development of pancreatic pseudocysts is rare.

In conclusion, we reported a case of crizotinib-induced pancreatic pseudocyst, considered a unique adverse event. The incidence of crizotinib-induced pancreatic cyst is unknown. Caution should be exercised in patients given crizotinib who have abdominal pain, elevated serum amylase and lipase levels, or abnormal CT findings of the abdomen.

Learning points

- ▶ A pancreatic pseudocyst induced by anticancer drugs is a rare adverse event.
- ▶ In this case, pancreatic pseudocysts appeared after starting treatment with crizotinib and regressed after treatment withdrawal.
- ▶ Caution should be exercised in patients given crizotinib who have abdominal pain, elevated serum amylase and lipase levels, or abnormal CT findings of the abdomen.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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