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Case Report

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SEVERE ACUTE PANCREATITIS SECONDARY TO ALECTINIB IN A PATIENT WITH METASTATIC BRONCHIAL ADENOCARCARCINOMAWITH ALK REARRANGEMENT: A CASE REPORT

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SUMMARY

Oral targeted therapies represent an essential weapon in the therapeutic arsenal of non-small cell lung cancer (NSCLC) with detected oncogenic addiction. Anti-ALK tyrosine kinase inhibitors are seeing their indications expand in the different therapeutic lines of metastatic NSCLC with ALK rearrangement. These are generally well tolerated molecules with known and manageable side effects, however, some complications are still unknown and can be serious or even fatal. Clinical case: We report the case of a young patient with an ALK-positive bronchial adenocarcinoma (ADK) initially treated with Crizotinib for 8 months, discontinued for a rare toxicity such as bilateral osteonecrosis of the legs, then replaced by Alectinib for 3 months. He presented to the emergency room for severe abdominal pain with jaundice, vomiting and fever. Abdominal CT showed acute pancreatitis (AP) stage E of BALTHAZAR with superinfection of necrosis flows, lipasemia was elevated to 3 times the normal value with biological signs of infection and hepatocellular insufficiency. The patient was put on digestive rest with parenteral antibiotic and symptomatic treatment. The evolution at 48h was made towards clinical, biological and radiological worsening, no surgical or percutaneous drainage of the infected castings was possible due to the diffusion of the infiltration, the hemodynamic instability and the increased bleeding risk in this patient. Despite the intensification of medical treatment and resuscitation measures, his condition progressed to death from septic shock. Conclusion: Alectinib was incriminated in the occurrence of this complication after the elimination of other causes of AP, despite the absence of data from the literature reporting such cases : is it the same mechanism as acute pancreatitis by hypertriglyceridemia already described? While waiting to elucidate its pathophysiology, careful monitoring of patients under these molecules remains the only means of prevention.

KEYWORDS: NSCLC, Alectinib, ALK rearrangement, pancreatitis, side effect.

INTRODUCTION

Alectinib is a highly selective tyrosine kinase inhibitor with anti-AnaplasticLymphoma Kinase (ALK) activity.[1] it is indicated from the first line of treatment for bronchial adenocarcinoma with rearrangement of the ALK gene, its profile of tolerance is usually good with generally manageable side effects. Monitoring this oral targeted therapy is essential, particularly at the start of treatment, to assess compliance, tolerance and above all to detect side effects and possible druginteractions.[2] The main reported complications of this molecule are allergic reactions, edemas, transit disorders, or headaches. Others are rarer and more serious if not treated early, such as visual disturbances, heart rhythm disorders, liver or kidney damage, and gastrointestinal perforations.[3] In this article, we describe the occurrence of fatal acute pancreatitis during the treatment of metastatic bronchial ADK with ALK rearrangement with Alectinib.

Clinical observation

This is a young 33-year-old patient, with nopathological history, followed since December 2020 for bronchial adenocarcinoma with ALK rearrangement, immediately metastatic to the cervical, mediastinal, and thoracic lymph nodes withperitoneal and pericardial effusion. He was initially put on Crizotinib, a first-generation ALK inhibitor, with an excellent response at3 months, but this molecule was stopped for unusual toxicity such as bilateral osteonecrosis of the legs for which it was changed to Alectinib at the dose of 600 mg/12h continuously. He presented to the emergency room on 12/12/2021 for an array of intense abdominal pain with febrilejaundice and vomiting, of acute onset.

Admission abdominal CT showed thickening of the pancreatic head and D3 with peri-lesional lymphadenopathy and an appearance of peritoneal carcinomatosis. (Figure 1).

Given the neoplastic background of our case, the pancreatic thickening was initially taken for a tumor lesion raising fears of progression.

The patient benefited from conditioning with symptomatic treatments before carrying out a complete biological assessment showing white blood cells at 14,600 elements/mm3 with neutrophils at 11,610 elements/mm3, platelets at 399,000 elements/mm3, Hemoglobin at 12.1 g/dl, PT at 35%, CRP was at 248 g/l, lipasemia at 228 IU/l, the lipid assessment was normal, in particular the triglyceridemia, factor V was at 153%.

In view of this clinical, biological and radiological presentation, acute pancreatitis was strongly suspected. Medical treatment based on antibiotics, analgesics, symptomatic treatment and digestive rest was instituted, with armed surveillance of the patient's parameters. The biological control assessment carried out 48 hours after admission objectified a worsening of the infectious syndrome with an increase in white blood cells, CRP, worsening of cholestasis and hepatic cytolysis, hypoglycemia at 0.46 g/l and a drop in PT at 17% with no decrease in factor V.

Abdominal CT was in favor of BALTHAZAR stage E acute pancreatitis, with the onset of superinfection, necrosis flows, gallbladder sludge and peritoneal carcinomatosis. (Figure 2)

The patient's clinical condition continued to worsen with signs of hepatic encephalopathy, a pattern of sepsis resistant to the antibiotic treatments administered.

No radiological or surgical drainage technique was possible due to the diffuse pancreatic inflammation and the high risk of bleeding.

The evolution was quickly made towards the occurrence of a septic shock resistant to resuscitation measures taken with a multi-organ failure carrying the patient, and his death was announced.

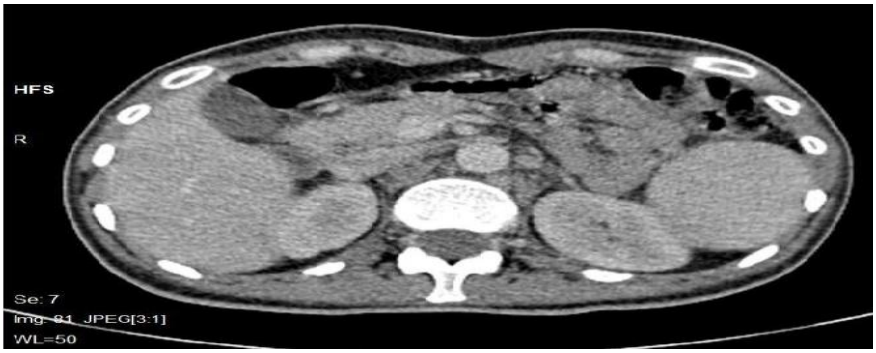
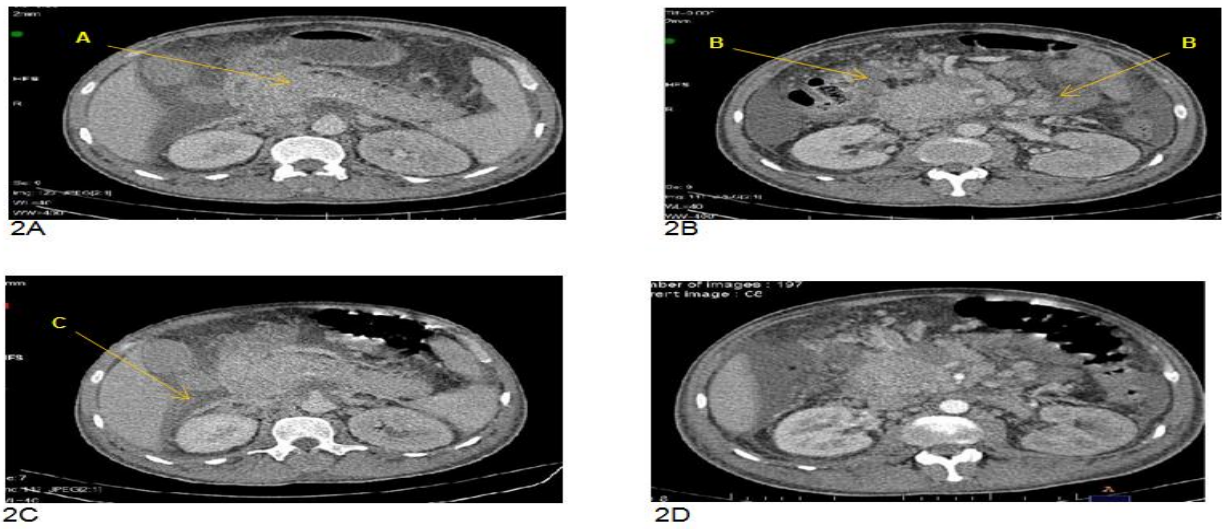


Figure 1: Section of the initial abdominal CT scan in portal phase showing thickening of the pancreatic head with slight infiltration of peripancreatic fat.



Figures 2: Sections of the abdominal CT scan in the portal phase performed after 48 hours: Swollen appearance of the head of the pancreas (2A) necrosis flows with infiltration of peripancreatic fat (2B), and peritoneal effusion (2C), Accentuation of necrosis and pancreatic thickening (2D).

DISCUSSION

Acute pancreatitis is an acute inflammation of the pancreas, which can be mild in its edematous form or necrotic with a reserved prognosis. Its main causes are cholelithiasis.[4] and chronic alcoholism,[5] followed by pancreatic tumoral causes, post-endoscopic or post-operative iatrogenic trauma,[6,7] metabolic causes, essentially hypertriglyceridemia.[8,9] and hypercalcemia, infections,[10] autoimmune causes,[11,12] and finally drug's side effects.[13,14,15]

In our case, the patient had no obvious cause responsible for this acute pancreatitis apart from taking Alectinib the ALK gene inhibitor.

The exclusion of all causes of acute pancreatitis led us to consider it as a side effect of treatment with Alectinib. Unfortunately, the serious presentation and the rapid evolution of this complication as well as the delay in consultation led to the death of the patient after one month of his hospitalization despite all the medical measures.

In the literature, there is a single reported case of acute pancreatitis induced by hypertriglyceridemia secondary to taking Alectinib in a patient with metastatic bronchial adenocarcinoma with an ALK rearrangement.[16] and which evolved well under medical treatment lowering triglyceride levels.

The pathophysiological mechanism of this acute pancreatitis secondary to Alectinib turns out to be different from that induced by the hypertriglyceridemia previously described, in the absence of elevation of triglycerides in our case. Is it a specifictoxicity targeting pancreatic cells? the answer is still unknown, requiring more research to elucidate this mechanism and to implement effective means of preventionthat can prevent the occurrence of this fatalsecondary event.

CONCLUSION

The search for therapeutic targets has now become a diagnostic standard in the management of cancers, particularly in non-small cell lung cancers. The marketing of new targeted therapies requires more vigilance in prescribing and monitoring to detect any unrecognized complications at an early stage.

REFERENCES

1. Sakamoto H, Tsukaguchi T, Hiroshima S, Kodama T, Kobayashi T, Fukami TA, et al. CH5424802, a selective ALK inhibitor capable of blocking the resistant gatekeeper mutant. *Cancer Cell*, 2011. 19:67990.10.1016/j.ccr.2011.04.004.
2. Hida T, Nokihara H, Kondo M, Kim YH, Azuma K, Seto T, et al. Alectinib versus crizotinib in patients with ALK-positive non-small-cell lung cancer (J-ALEX): an open-label, randomized phase 3 trial. *Lancet*, 2017; 390: 29-39. 10.1016/S0140-6736(17)30565-2.
3. Kinoshita K, Asoh K, Furuichi N, et al. Design and synthesis of a highly selective, orally active and potent anaplastic lymphoma kinase inhibitor (CH5424802) *Bioorg Med Chem*, 2012; 20(3): 1271- 1280.
4. Cohen ME. Gallstone size and risk for pancreatitis. *Arch Intern Med*, 1998; 158: 543–544.
5. Robles-Diaz G, Gorelick FS. Alcohol and Pancreatitis. *Yale J Bio Med*, 1997; 70: 77–87.
6. Kahaleh M, Freeman M. Prevention and management of post-endoscopic retrograde cholangiopancreatography complications. *Clin Endosc*, 2012; 45: 305–312.
7. Masci E, Toti G, Mariani A, Curioni S, Lomazzi A, Dinelli M, Minoli G, Crosta C, Comin U, Fertitta A, Prada A, Passoni GR, Testoni PA. Complications of diagnostic and therapeutic ERCP: a prospective multicenter study. *Am J Gastroenterol*, 2001; 96: 417–423.
8. Nagayama D, Shirai K. [Hypertriglyceridemia-induced pancreatitis] *Nihon Rinsho*, 2013; 71: 1602–1605.
9. Havel RJ. Pathogenesis, differentiation and management of hypertriglyceridemia. *Adv Intern Med*, 1969; 15: 117–154.
10. Rawla P, Bandaru SS, Vellipuram AR. Review of Infectious Etiology of Acute Pancreatitis. *Gastroenterology Res.* 2017; 10: 153–158.
11. Chari ST, Smyrk TC, Levy MJ, Topazian MD, Takahashi N, Zhang L, Clain JE, Pearson RK, Petersen BT, Vege SS, Farnell MB. Diagnosis of autoimmune pancreatitis: the Mayo Clinic experience. Clin Gastroenterol Hepatol. 2006; 4: 1010–6: 934.
12. Kamisawa T, Egawa N, Nakajima H. Autoimmune pancreatitis is a systemic autoimmune disease. *Am J Gastroenterol*, 2003; 98: 2811–2812.
13. Wang GJ, Gao CF, Wei D, Wang C, Ding SQ. Acute pancreatitis: etiology and common pathogenesis. *World J Gastroenterol*, 2009; 15: 1427– 1430.
14. Wilmink T, Frick TW. Drug-induced pancreatitis. *Drug Saf.*, 1996; 14: 406–423.
15. Badalov N, Baradarian R, Iswara K, Li J, Steinberg W, Tenner S. Drug-induced acute pancreatitis: an evidence-based review. *Clin Gastroenterol Hepatol*, 2007; 5: 648–61: 644.
16. A.Rao and all. Life-threatening hypertriglyceridemia-induced pancreatitis related to alectinib successfully treated by plasmapheresis: A review of the literature on metabolic toxicities associated with anaplastic lymphoma kinase inhibitors.J Oncol Pharm Pract., 2020 Sep; 26(6): 1533- 153.