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# Pazopanib-Induced Severe Acute Pancreatitis

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# **Key Words**

Angiosarcoma · Pazopanib · Drug-induced acute pancreatitis

#### Abstract

Pazopanib is an oral angiogenesis inhibitor targeting vascular endothelial growth factor receptors, platelet-derived growth factor receptors, and c-Kit approved for the treatment of renal cell carcinoma and soft tissue sarcoma. Nonselective kinase inhibitors, such as sunitinib and sorafenib, are known to be associated with acute pancreatitis. There are few case reports of severe acute pancreatitis induced by pazopanib treatment. We present a case of severe acute pancreatitis caused by pazopanib treatment for cutaneous angiosarcoma. The patient was an 82-year-old female diagnosed with cutaneous angiosarcoma. She had been refractory to docetaxel treatment and began pazopanib therapy. Three months after pazopanib treatment, CT imaging of the abdomen showed the swelling of the pancreas and surrounding soft tissue inflammation without abdominal pain. After she continued pazopanib treatment for 2 months, she presented with nausea and appetite loss. Abdominal CT showed the worsening of the surrounding soft tissue inflammation of the pancreas. Serum amylase and lipase levels were 296 and 177 IU/I, respectively. She was diagnosed with acute pancreatitis induced by pazopanib treatment and was managed conservatively with discontinuation of pazopanib, but the symptoms did not improve. Subsequently, an abdominal CT scan demonstrated the appearance of a pancreatic pseudocyst. She underwent endoscopic ultrasound-guided pseudocyst drainage using a flared-end fully covered self-expandable metallic stent. Then, the symptoms resolved without recurrence. Due to the remarkable progress of molecular targeted therapy, the oncologist should know that acute pancreatitis was recognized as a potential adverse event of pazopanib treatment and could proceed to severe acute pancreatitis.

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Kawakubo et al.: Pazopanib-Induced Severe Acute Pancreatitis

#### Introduction

Pazopanib is an oral angiogenesis inhibitor targeting vascular endothelial growth factor receptors, platelet-derived growth factor receptors, and c-Kit approved for the treatment of renal cell carcinoma and soft tissue sarcoma [1, 2]. Nonselective kinase inhibitors, such as sunitinib and sorafenib, are known to be associated with acute pancreatitis [3]. There are few case reports of severe acute pancreatitis induced by pazopanib treatment. We present a case of severe acute pancreatitis caused by pazopanib treatment for cutaneous angiosarcoma.

## **Case Report**

The patient was an 82-year-old female diagnosed with cutaneous angiosarcoma. She had been refractory to docetaxel treatment and began pazopanib therapy. Three months after pazopanib treatment, CT imaging of the abdomen showed the swelling of the pancreas and surrounding soft tissue inflammation without abdominal pain. After she continued pazopanib treatment for 2 months, she presented with nausea and appetite loss. Abdominal CT showed the worsening of the surrounding soft tissue inflammation of the pancreas. Serum amylase and lipase levels were 296 and 177 IU/l, respectively. She was diagnosed with acute pancreatitis induced by pazopanib treatment. She was managed conservatively with discontinuation of pazopanib, but the symptoms did not improve. Subsequently, an abdominal CT scan demonstrated the appearance of a pancreatic pseudocyst (fig. 1). She underwent endoscopic ultrasound-guided pseudocyst drainage using a flared-end fully covered self-expandable metallic stent. Then, the symptoms resolved without recurrence.

# Discussion

Hyperamylasemia and hyperlipasemia are well-known adverse events of multikinase inhibitors, but little is known about the association to acute pancreatitis [4]. Although the severity of pancreatitis is usually mild, focal, and managed conservatively by discontinuation of treatment [5, 6], our case progressed to severe acute pancreatitis requiring endoscopic drainage in spite of the discontinuation of pazopanib. The diagnosis of drug-induced pancreatitis is sometimes difficult [7]. Due to the remarkable progress of molecular targeted therapy, the oncologist should know that acute pancreatitis was recognized as a potential adverse event of pazopanib treatment and could proceed to severe acute pancreatitis.

### **Statement of Ethics**

The authors have no ethical conflicts to disclose.

## **Disclosure Statement**

The authors have no conflicts of interest or funding to disclose.





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#### References

- van der Graaf WT, Blay JY, Chawla SP, Kim DW, Bui-Nguyen B, Casali PG, Schoffski P, Aglietta M, Staddon AP, Beppu Y, Le Cesne A, Gelderblom H, Judson IR, Araki N, Ouali M, Marreaud S, Hodge R, Dewji MR, Coens C, Demetri GD, Fletcher CD, Dei Tos AP, Hohenberger P: Pazopanib for metastatic soft-tissue sarcoma (palette): a randomised, double-blind, placebo-controlled phase 3 trial. Lancet 2012;379:1879–1886.
- Motzer RJ, Hutson TE, Cella D, Reeves J, Hawkins R, Guo J, Nathan P, Staehler M, de Souza P, Merchan JR, Boleti E, Fife K, Jin J, Jones R, Uemura H, De Giorgi U, Harmenberg U, Wang J, Sternberg CN, Deen K, McCann L, Hackshaw MD, Crescenzo R, Pandite LN, Choueiri TK: Pazopanib versus sunitinib in metastatic renal-cell carcinoma. N Engl J Med 2013;369:722–731.
- Ghatalia P, Morgan CJ, Choueiri TK, Rocha P, Naik G, Sonpavde G: Pancreatitis with vascular endothelial growth factor receptor tyrosine kinase inhibitors. Crit Rev Oncol Hematol 2015;94:136–145.
- 4 Pezzilli R, Corinaldesi R, Morselli-Labate AM: Tyrosine kinase inhibitors and acute pancreatitis. JOP 2010;11:291–293.
- 5 Tirumani SH, Jagannathan JP, Shinagare AB, Kim K, Krajewski KM, Ramaiya NH: Acute pancreatitis associated with molecular targeted therapies: a retrospective review of the clinico-radiological features, management and outcome. Pancreatology 2013;13:461–467.
- 6 Howard SA, Krajewski KM, Thornton E, Jagannathan JP, O'Regan K, Cleary J, Ramaiya N: Decade of molecular targeted therapy: abdominal manifestations of drug toxicities what radiologists should know. AJR Am J Roentgenol 2012;199:58–64.
- Nitsche C, Maertin S, Scheiber J, Ritter CA, Lerch MM, Mayerle J: Drug-induced pancreatitis. Curr Gastroenterol Rep 2012;14:131–138.



**Fig. 1.** Abdominal CT scan showing a pseudocyst (arrows) in the head and tail of the pancreas.