A Resected Primary Angiosarcoma of the Pancreas Presenting Aggressive Metastatic Liver Recurrence with Uncontrollable Intra-abdominal Bleeding: a Case Report

Shota Igaue1 · Hiroki Kudo1 · Yusuke Kyoden1 · Mayumi Hoshikawa1 · Ken Koyama2 · Hitoaki Saitoh3 · Tatsuo Iijima3 · Toru Motoi4 · Fuyo Yoshimi1 · Junji Yamamoto1

Accepted: 3 October 2021 / Published online: 14 October 2021
© Springer Science+Business Media, LLC, part of Springer Nature 2021

Introduction

Angiosarcoma is a rare and aggressive vascular tumor that accounts for less than 2% of all sarcomas [1, 2] and that can surge in any part of the body, appearing most frequently in the head and the neck. Only a few cases of primary angiosarcoma of the pancreas have been reported so far, and most of them have shown a poor prognosis. The following article presents a primary angiosarcoma of the pancreas with a rapid and aggressive course with recurrent multiple liver metastases and peritoneal dissemination in spite of complete resection.

Case Report

A 74-year-old man with a medical history of hypertension had been diagnosed with obstructive jaundice due to a pancreatic head tumor (38 mm × 32 mm) and was referred to our institution for surgical resection. The initial computed tomography (CT) scan revealed a tumor with heterogeneous density on plain imaging and an enhanced nodular component during portal phase imaging (Fig. 1a, b). Previously, he had smoked 30 cigarettes per day but had indeed quit smoking for 30 years and currently consumes 40 g/day of ethanol daily. He had no significant family history. Notably, 6 months before the current presentation, a cyst 11 mm in diameter in the pancreas was incidentally identified with no other abnormal findings in abdominal ultrasound (US) examination at a medical checkup. The patient showed a slight anemia with hemoglobin level of 12.7 g/dl and jaundice with serum total bilirubin level of 11.4 mg/dl (normal range: 0.4–1.5 mg/dl).

Given the attempt to perform endoscopic nasal biliary drainage ended in failure, percutaneous transhepatic gallbladder drainage was done and an attempt at curative resection was postponed due to economic reasons. A dynamic contrast-enhanced CT (CE-CT) scan performed with 10-week interval revealed the enlarging tumor (49 mm × 46 mm) (Fig. 1c). The tumor showed expansile growth and compressed the portal and superior mesenteric vein without any evidence of distant or lymph node metastases nor of peritoneal dissemination. Although the superior mesenteric artery (SMA) and the right hepatic artery (RHA) were also compressed, these vessels could be preserved by resecting the extrapancreatic nerve plexus because they were not encased (Fig. 1d).

Gadoxetic acid-enhanced magnetic resonance imaging (EOB-MRI) revealed the tumor had the same enhancement pattern as the CT and high signal intensity in diffusion-weighted image. In addition, no evidence of liver metastases was obtained from MRI. Fluorodeoxyglucose-positron emission tomography CT (FDG-PET-CT) also revealed high uptake nodular areas corresponding with the area later enhanced on CT, which suggests the viable cells in this tumor (Fig. 1e).

We had planned surgery, on the previous day, but the patient complained of severe upper abdominal pain and showed clouding of his consciousness, which immediate CE-CT demonstrated a markedly dilated common bile duct that contained a high-density substance that indicated...
hemobilia (Fig. 2). Transcatheter arterial coil embolization (TAE) of the anterior/posterior pancreaticoduodenal artery was performed in order to control the bleeding before the surgery, and we performed on the same day an emergency operation. There was no evidence of liver metastases and peritoneal dissemination on laparotomy with upper to middle midline incision. Instead, the tumor had invaded the superior mesenteric and the portal vein, enteric artery (SMA) and the right hepatic artery (RHA) were compressed by the tumor but no encasement was observed (d). Fluorodeoxyglucose-positron emission tomography CT (FDG-PET-CT) showed high uptake in the marginal region (e).

Fig. 1 The initial computed tomography (CT) scan showed a tumor with heterogenous density on plain image (a) and late enhancement in contrast-enhanced (CE)-CT (b). CT scan performed 8 days before surgery and after an interval of 10 weeks revealed an enlarging tumor. There was no evidence of liver metastases (c). The superior mesenteric artery (SMA) and the right hepatic artery (RHA) were compressed by the tumor but no encasement was observed (d). Fluorodeoxyglucose-positron emission tomography CT (FDG-PET-CT) showed high uptake in the marginal region (e).

Fig. 2  a, b CT scan done the day before planned surgery showed larger tumor than 8 days before, compressing the portal and superior mesenteric vein (a early arterial phase; b portal phase). There was no evidence of liver metastases. c CT scan performed 8 days before the surgery showed biliary dilatation (arrowhead). d CT scan acquired the day before planned surgery showed high-density substance within the common bile duct, suggesting hemobilia.
so we performed pylorus-preserving pancreatoduodenectomy with superior mesenterico-portal vein resection and reconstruction. The operation lasted 5 h and 23 min, and the blood loss amounted to 2752 ml. A gross examination of the surgical specimen showed a tumor that contained hemorrhagic necrosis in the pancreatic head whose size was 90×65×60 mm in dimension (Fig. 3a, b), and pathological examination demonstrated the viable tumor tissue was composed of sinusoid cells, epithelioid cells, and spindle cells with large ill-shaped nuclei and prominent nucleolus. Moreover, epithelioid and sinusoid cells form vascular figures suggested that this tumor had the character of differentiation toward the vascular structure (Fig. 4a), and spindle cells surrounding sinusoid cells also proved there were transitive cells between those cells. An immunohistochemical examination of atypical cells tested positive for CD31 (Fig. 4b) and CD34 and a pathological diagnosis showed a pancreatic angiosarcoma. The invasion into the superior mesenteric vein (SMV) was pathologically confirmed; however, R0-resection was achieved through SMV resection and reconstruction. Additionally, the tumor had extended into the lumen of the intrahepatic bile duct, which we thought was the reason for hemobilia induction. He presented after surgery a grade B [3] delayed gastric emptying but managed to recover and was thus discharged on postoperative day 33. However, he was emergently transferred to our hospital 4 days after said discharge due to weakness and an inability to move, which laboratory data proved to be due to severe anemia (hemoglobin level of 5.1 g/dl). CE-CT scan demonstrated, in its turn, numerous liver nodules with enhancement and massive ascites with spotty high-density area (Fig. 5a, b), and abdominocentesis revealed bloody serous ascites, and for that reason, abdominal drainage tubes were inserted. The emergency angiography showed a cotton-wool-like look in the right hemiliver (Fig. 5c) and TAE with gelfoam particles for the RHA was performed so as to control the bleeding. After this procedure, bloody serous output from the drainage tubes did decrease but nevertheless continued. The anemia progressed slowly, and blood transfusion was needed several times, and he expired 10 days after re-admission. An autopsy revealed numerous metastases in the liver, small intestine, lungs, left adrenal gland, and spleen, accompanied by disseminated lesions in the peritoneal cavity that were friable and russet brown (Fig. 6a, b).
Discussion

Angiosarcoma is a rare and aggressive type of tumor with a differentiation toward vascular endothelium, accounting for 2% of soft tissue sarcomas [1]. Angiosarcomas can arise in any part of the body but are found most commonly in cutaneous lesions and rarely arise from visceral organs [2]. Specifically, a primary angiosarcoma of the pancreas is extremely rare with only six cases reported till date (Table 1) [4–9]. Thus, this is the seventh case of primary angiosarcoma of the pancreas. Five out of seven cases (including ours) expired within 2 months after the initial diagnosis or surgery. In this case, multiple liver metastases and dissemination appeared within 2 months after surgery in spite of gross complete resection, indicating the extremely aggressive feature of this tumor.

The correct diagnosis of angiosarcoma is challenging as it is an exceedingly rare disease related to the pancreas with most patients showing signs and symptoms, such as abdominal pain, anemia, gastrointestinal bleeding, melena, or obstructive jaundice. According to the pathological findings, the tumor had extended into the lumen of the intrahepatic bile duct; therefore, in the present case, we thought that hemobilia was induced by the implosion of the tumor into
the intrapancreatic bile duct. Kim KH et al. had previously reported two cases of hemobilia induced by pancreatic cancer [10], but pancreatic tumor is a rare cause for hemobilia [11]. Here, hemobilia was thought to be caused by the invasion of the angiosarcoma into the intrapancreatic bile duct; this aspect of angiosarcomas is noteworthy.

Furthermore, hepatic or splenic origin is common among angiosarcomas in visceral organs. A heterogeneous look that reflects hemorrhage, fibrosis, and necrosis is common within the imaging features in visceral angiosarcoma according to the previous review [12]. In this case, the CT and MRI showed an expansile and well-circumscribed tumor with a heterogeneous internal density which is clearly different from invasive ductal carcinoma of the pancreas. Hypervascular component indicated other primary pancreatic tumors, such as acinar cell carcinoma, adenosquamous cell carcinoma, solid pseudopapillary tumor, and pancreatic neuroendocrine tumor as differential diagnoses. Histological features of angiosarcoma are various among cases, and as Darre reported biopsy should be a possible way to definitive diagnose of this tumor [8]. Tumor cells may present rounded, polygonal, or spindle-shaped configurations, and immunohistochemistry is needed to confirm its differentiation in relation to vascular epithelium. Typically, angiosarcomas express Factor-VII, CD31, CD34, and vascular endothelial growth factor (VEGF) [13].

Even though there is limited data regarding the treatment of angiosarcoma and there is no consensus as to its algorithm, surgery with complete resection is thought to be the primary and most reliable treatment for local diseases [14], whereas radiotherapy or chemotherapy is considered to conduct for unresectable angiosarcoma. The 5-year overall survival (OS) rate in all angiosarcoma is about 30–40% [15,16]. The 5-year OS rate of visceral angiosarcoma is under 20%, while that of angiosarcoma arising in the other location is about 60%. Moreover, the 5-year OS of angiosarcoma with metastases is reported nil [14]. Worth et al. reported a case of 1-year survivor without recurrence after robotic-assisted distal pancreatectomy for a 31×24-mm lesion in the pancreatic tail [7]. Metastases at presentation, visceral, or deep soft tissue tumor location, tumor size > 5 cm, presence of tumor necrosis, and the absence of surgical resection are reportedly associated with a poor prognosis [16]. In this case, metastases had developed within 2 months and patient died 42 days after surgery. The rupture of the liver metastases might have resulted in peritoneal dissemination.

It is worth pointing out that Seth et al. have described the case of another patient who died 15 days after surgery. Notably, that patient also showed hemobilia and aggressive intransperitoneal bleeding from multiple liver metastases [4]. The hemobilia in the patient studied by Seth et al. and in our patient may suggest an aggressive character and hemorrhagic disposition of the tumor. Although this is the
first report of TAE being performed for metastases from a primary angiosarcoma of the pancreas, a previous study has suggested the use of emergent TAE as the primary procedure to stop acute intra-abdominal bleeding [17].

To summarize, in the present study, we report a primary angiosarcoma of the pancreas, primary and recurrent lesions, which presented fatal bleeding, which indicate a tumor of this nature should be accounted for in the presence of hemobilia and a visible and heterogeneous look. The remarkable angiogram of multiple liver metastases and detailed description of the aggressive clinical course, including autopsy, provide unique and instructive information about the management of such tumors.

Author Contribution SI, HK, and JY are responsible for the conception of the study, participation in the study design, and writing the paper. SI, HK, KK, and FY were involved in the clinical and therapeutic management of the patient. YK, MH, FY, and JY contributed in the critical revision of the manuscript and providing important intellectual content. HS, TI, and TM contributed in the interpretation of the pathological findings. All the authors have read and approved the final paper submitted for publication.

Availability of Data and Material Not applicable.

Declarations

Ethics Approval All procedures performed in the study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Consent to Participate Not applicable.

Consent for Publication Written informed consent from the patient’s wife and son was obtained for the publication of this case report.

Conflict of Interest The authors declare no competing interests.

References

1. Coindre JM, Terrier P, Guillou L, et al. Predictive value of grade for metastasis development in the main histologic types of adult soft tissue sarcomas: a study of 1240 patients from the French Federation of Cancer Centers Sarcoma Group. Cancer. 2001;91:1914–26. https://doi.org/10.1002/1097-0142(20010515)91:10%3c1914::aid-cncr1214%3e3.0.co;2-3.

2. Young RJ, Brown NJ, Reed MW, et al. Angiosarcoma. Lancet Oncol. 2010;11:983–91. https://doi.org/10.1016/s1470-2045(10)70023-1.

3. Bassi C, Marchegiani G, Dervenis C, et al. The 2016 update of the International Study Group (ISGPS) definition and grading of post-operative pancreatic fistula: 11 Years After. Surgery. 2017;161:584–91. https://doi.org/10.1016/j.surge.2016.11.014.

4. Seth AK, Argani P, Campbell KA. Angiosarcoma of the pancreas: discussion of a rare epithelioid neoplasm. Pancreases. 2008;37:230–1. https://doi.org/10.1007/MPA.8b013e318164a1c9.

5. Csiszkó A, László I, Palatka K, et al. Primary angiosarcoma of the pancreas mimicking severe acute pancreatitis—case report. Panreatology. 2015;15:84–7. https://doi.org/10.1016/j.pan.2014.11.008.

6. Meeks M, Grace S, Veerapong J, et al. Primary angiosarcoma of the pancreas. J Gastrointest Cancer. 2017;48:369–72. https://doi.org/10.1007/s12029-016-9837-1.

7. Worth PJ, Turner M, Hammill CW. Incidental angiosarcoma of the pancreas: a case report of a rare, asymptomatic tumor. J Pancreat Cancer. 2017;3:24–7. https://doi.org/10.1089/pancan.2017.0007.

8. Darré T, Tchaou M, Tchang F, et al. Primary angiosarcoma pancreas: a case report of an exceptional localization. J Gastrointest Cancer. 2019;50:935–8. https://doi.org/10.1007/s12029-018-0123-2.

9. Faria A, Lopes F, Figueira A, et al. Pancreas angiosarcoma—case report of a rare cause of abdominal pain. Int J Surg Case Rep. 2020;76:116–20. https://doi.org/10.1016/j.ijscr.2020.09.131.

10. Kim KH, Kim TN (2012) Etiology, clinical features, and endoscopic management of hemobilia: a retrospective analysis of 37 cases. Korean J Gastroenterol = Taehan Sohagwi Hakhoe. chi 59:296–302. https://doi.org/10.4166/kjg.2012.59.4.296.

11. Berry R, Han JY, Kardashhan AA, et al. Hemobilia: etiology, diagnosis, and treatment. Liver Res. 2018;2:200–8. https://doi.org/10.1016/j.livres.2018.09.007.

12. Gaballah AH, Jensen CT, Palmquist S, et al. Angiosarcoma: clinical and imaging features from head to toe. Br J Radiol. 2017;90:20170039. https://doi.org/10.1259/bjr.20170039.

13. Ohsawa M, Naka N, Tomiita Y, et al. Use of immunohistochemical procedures in diagnosing angiosarcoma. Evaluation of 98 cases. Cancer. 1995;75:2567–74. https://doi.org/10.1002/1097-0142(19950615)75:12%3c2567::aid-cncr2820751212%3e3.0. co;2-8.

14. Cao J, Wang J, He C, et al. Angiosarcoma: a review of diagnosis and current treatment. Am J Cancer Res. 2019;9:2303–13.

15. Fayette J, Martin E, Piperno-Neumann S, et al. Angiosarcomas, a heterogeneous group of sarcomas with specific behavior depending on primary site: a retrospective study of 161 cases. Ann Oncol: official journal of the European Society for Medical Oncology. 2007;18:2030–6. https://doi.org/10.1093/annonc/mdm3381.

16. Buehler D, Rice SR, Moody JS, et al. Angiosarcoma outcomes and prognostic factors: a 25-year single institution experience. Am J Clin Oncol. 2014;37:473–9. https://doi.org/10.1097/COC.0b013e31827e4e7b.

17. Maeyashiki C, Nagata N, Uemura N. Angiosarcoma involving solid organs and the gastrointestinal tract with life-threatening bleeding. Case Rep Gastroenterol. 2012;6:772–7. https://doi.org/10.1159/000346398.

Publisher’s Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.