

# Duodenal Angiosarcoma: An Unusual Cause of Severe Gastrointestinal Bleeding

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Angiosarcoma is a rare soft-tissue neoplasm that occurs most often in the skin and the subcutaneous tissues but very rarely in the gastrointestinal tract. We report a case of primary intestinal angiosarcoma with severe gastrointestinal bleeding. This patient was referred to our institute for shock with tarry-bloody stool and severe anemia. Panendoscopy revealed multiple duodenal polypoid tumors, and initial biopsy specimen showed poorly differentiated adenocarcinoma. The tumors were treated with pancreaticoduodenectomy, but the patient died 2 weeks after the operation as a result of acute respiratory distress syndrome. The pathology was consistent with angiosarcoma of the duodenum. In our experience, this tumor may cause severe bleeding, and surgery should be performed as soon as possible to prevent complications of hypovolemic shock. [*J Chin Med Assoc* 2007;70(8):352–355]

**Key Words:** angiosarcoma, immunohistochemistry, intestinal neoplasm

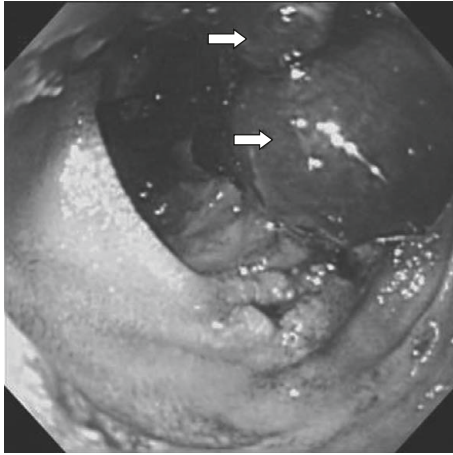
## Introduction

Angiosarcomas are rare soft-tissue neoplasms, comprising 1–2% of all sarcomas. They occur mainly in superficial soft tissues, but they may also affect internal organs such as the heart, liver, spleen, and, rarely, the gastrointestinal tract.<sup>1</sup> The etiology is unclear, although some risk factors have been reported, including irradiation exposure and foreign body retained for a prolonged period or arteriovenous shunts.<sup>2–5</sup> Histologically, angiosarcoma may have well-differentiated forms where the vascular nature of the tumor is easily recognized. However, its poorly differentiated forms may resemble undifferentiated neoplasms, and factor VIII-related antigen is traditionally considered a valuable tool for the diagnosis of angiosarcoma.<sup>6</sup> Treatment options include surgery, sometimes followed by adjuvant chemotherapy, but the prognosis is believed to be very poor.<sup>3</sup> We recently diagnosed an elderly man with angiosarcoma involving the duodenum and herein report its catastrophic clinical presentation.

## Case Report

A 79-year-old male with a medical history of hypertension presented with a 1-month history of lethargy, weakness and melena. The patient smoked 1 pack of cigarettes per day and had social alcohol consumption for the past 40 years. He had never been hospitalized for any medical or surgical condition. Two weeks prior to this admittance to our institute, he was sent to a district hospital for severe anemia and low blood pressure. After resuscitation, he received panendoscopy there and was found to have multiple purple duodenal polypoid tumors. For persistent severe anemia, he was referred to our hospital. Physical examination revealed an ill-appearing man with pale conjunctivae. Initial laboratory investigation showed a hemoglobin level of 8.6 g/dL with a normal mean corpuscular volume. Serum levels of tumor markers including carcinoembryonic antigen, carbohydrate antigen (CA19-9) and  $\alpha$ -fetoprotein were normal. Chest X-ray disclosed mild bilateral lower lung field infiltration. Panendoscopy was repeated

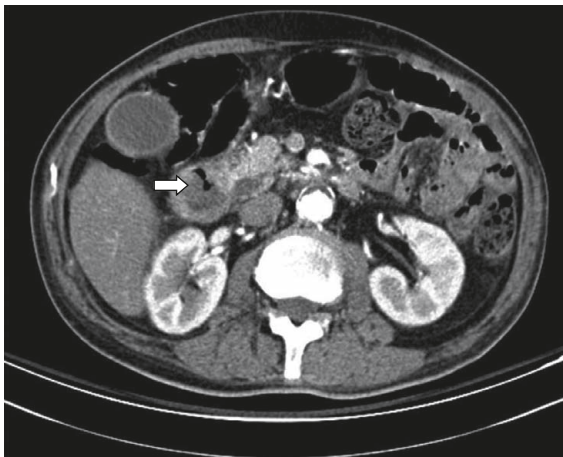
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**Figure 1.** Endoscopy shows multiple red-purple polypoid tumors (arrows) measuring 2–3 cm scattered in the duodenum.



**Figure 3.** Multiple red-purple polypoid tumors (arrows) measuring 2–3 cm scattered in the duodenum seen during the Whipple procedure.



**Figure 2.** Post-contrast abdominal computed tomography shows duodenal diverticulitis and 1 suspicious tumor (arrow).

(Figure 1), revealing a long segment and huge ulcerative lesion with friable mucosa and easy-contact bleeding at the proximal second portion of the duodenum and more than 5 red-purple polyps scattered in the duodenum, though sparing the papilla. Biopsy was obtained. Abdominal computed tomography showed no other intra-abdominal lesions except suspicious duodenal diverticulitis and a 2-cm intraluminal tumor (Figure 2). Initial biopsy report was poorly differentiated adenocarcinoma.

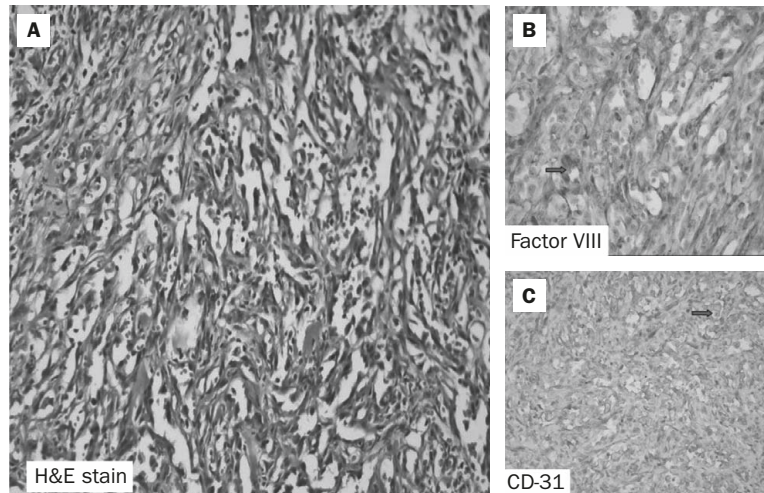
The patient underwent the Whipple procedure (pancreaticoduodenectomy). Before the operation, his hemoglobin level was 8.0 g/dL (after transfusion resuscitation at the other hospital), and he also received packed red blood cell (RBC) transfusion of 4 units the day before the operation. The procedures were conducted smoothly, with blood loss of about 1,000 mL, and the patient's blood pressure was stable throughout

the operation. However, he had blood transfusion with packed RBC 6 units, whole blood 4 units and fresh frozen plasma 4 units. Occasional poor oxygenation was reported by the anesthesiologist. In the postoperative recovery room, the patient showed tachypnea, needed high inspired-oxygen (FiO<sub>2</sub>) up to 60%, and could only achieve PaO<sub>2</sub> 71 mmHg. Central venous pressure measured 9 mmHg. Chest X-ray showed bilateral diffuse alveolar infiltration. Due to the development of acute respiratory distress syndrome, the patient was transferred to the intensive care unit. He died 18 days after the operation. Autopsy was not performed.

Grossly, there were multiple dark-red grape-like tumors, 2–3 cm in diameter each, in the duodenum (Figure 3). Microscopically, the tumors were characterized by sheets of polygonal cells and many spaces suggestive of vascular differentiation (Figure 4). Peripancreatic lymph node examination showed positive metastatic foci. Immunohistochemical studies were done on formalin-fixed, paraffin-embedded tissues. Staining with keratin and epithelial membrane antigen were negative. Positive immunohistochemical staining for vimentin, factor VIII-related antigen and CD31 (Figure 4) confirmed the angioformative nature of the tumor.

## Discussion

Angiosarcomas occur very rarely in the gastrointestinal tract.<sup>1</sup> From October 1990 to December 2006, there were a total of 15 cases of angiosarcoma diagnosed in our institute; 8 of them occurred on the scalp, 2 in the liver, 1 in the bone, 1 in the breast, 1 in



**Figure 4.** (A) Anastomosing vascular channels are lined by spindle and large plump polygonal cells with eosinophilic cytoplasm and hyperchromatic nuclei (hematoxylin & eosin [H&E]; original magnification, 100 $\times$ ). Positive immunostaining of: (B) cytoplasm for factor VIII-related antigen (original magnification, 200 $\times$ ), and (C) cell membrane for CD-31 (original magnification, 100 $\times$ ).

the torso, and 1 in the pericardium. The present case was the first one that was found in the duodenum.

The majority of malignant small bowel tumors are symptomatic, though some may remain asymptomatic and are diagnosed incidentally. The most common initial symptoms include abdominal pain, bowel obstruction, gastrointestinal hemorrhage, and perforation. In comparison, patients with angiosarcoma arising from the gastrointestinal tract mostly present with symptoms related to gastrointestinal bleeding.<sup>6,7</sup> Diagnostic methods include endoscopy, barium studies, computed tomography, and technetium-99m-labeled RBC scan.

Many angiosarcomas have a dimorphic pattern that includes vasoformative as well as solid elements. The vasoformative structures can range from well-formed vessels, easily recognized as vascular spaces, to slit-like poorly developed anastomosing vascular channels. Not uncommonly, these tumors have a solid growth pattern that may consist of spindle-shaped cells or large polygonal epithelioid-type cells. Therefore, the histologic features can sometimes be confused with other neoplasms, such as poorly differentiated carcinoma, malignant melanoma, mesothelioma, or sarcoma, and often require an extensive immunohistochemical workup for proper classification. Factor VIII-related antigen, a component of the factor VIII complex, which is synthesized by endothelial cells, can be demonstrated within the endothelial cells of angiosarcomas by immunoperoxidase staining, and this has been traditionally considered a valuable diagnostic tool for the diagnosis of angiosarcoma. Other typical immunohistologic findings include positivity for vimentin and endothelial markers (e.g. UEA-I, CD31, CD34) and negativity for

the epithelial marker keratin and epithelial membrane antigen.<sup>6,8</sup> In our case, the initial small biopsy specimen had epithelioid cytology mimicking poorly differentiated carcinoma. Based on its location, it was then reported as poorly differentiated adenocarcinoma and no further immunohistochemical workup was carried out until the whole specimen was obtained after operation. Thus, the diagnosis should be kept in mind, especially when clues to angioformative morphology such as focal clefting are noted, and followed with a well-directed immunohistochemical workup.

The prognosis of angiosarcoma is generally poor. In a review of the English literature, 19 cases of angiosarcoma involving the gastrointestinal tract were reported.<sup>6</sup> Seven of the cases were associated with a history of pelvic/abdominal radiation for gynecologic malignancies. One case developed secondary gastrointestinal involvement from an angiosarcoma arising in the fibrous capsule of a gauze sponge left behind from a gynecologic operation 25 years earlier. Ten cases involved the small bowel, 7 involved the colon, 1 involved the ileocecal area and small bowel, and 1 involved the stomach. Most cases had a rapidly progressive course, with a median survival time of 2 months, and complete surgical resection was the only factor that correlated with disease-free survival. When searching for published Asian experiences, we found 1 case in Korean of primary angiosarcoma of the ileum, presenting as recurrent gastrointestinal bleeding and ileoileal intussusception.<sup>9</sup> Two cases with post-irradiation angiosarcoma were reported in Taiwan. One patient had cervical cancer and had received radiotherapy 8 years prior to the diagnosis of small bowel

angiosarcoma leading to small bowel perforation,<sup>10</sup> and the other patient had angiosarcoma of the terminal ileum developing 39 months after radiotherapy for recurrent squamous cell carcinoma of the uterine cervix.<sup>11</sup> Our patient did not have identifiable precipitating factors for this rare type of malignancy; there was no history of radiation exposure and no intra-abdominal foreign body found at operation. A case of Kaposi's sarcoma coexisting with angiosarcoma was recently reported.<sup>12</sup> However, we did not check the HIV antibody status in this patient. Our patient underwent curative surgery, but died of acute respiratory distress syndrome, in which multiple blood transfusion and suspected transfusion-related acute lung injury may have been the cause. This was the most significant event in this patient, though certainly there were other possibilities for acute lung injury.<sup>13,14</sup>

In conclusion, angiosarcomas are rare malignant neoplasms that can be primary to the gastrointestinal tract, any part of which can be involved. They often present with gastrointestinal bleeding and anemia and are refractory to conventional therapies, with death often resulting from uncontrollable hemorrhage. Early diagnosis and early surgical intervention may give the patient the best chance of long-term survival.

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