CASE REPORT

TJG
The Turkish Journal of Gastroenterology

Splenomegaly as the first manifestation of pancreatic adenosquamous carcinoma: A case report

Ke CHEN, Xiao-Wu XU, Kun XIE, Yu-Cheng ZHOU, Yi-Ping MOU

Department of General Surgery, Sie Run Run Shaw Hospital, Hangzhou Zhejiang Province, China

Adenosquamous carcinoma of the pancreas directly invading surrounding organs is rare. Here, we describe a case of pancreatic adenosquamous carcinoma directly invading the spleen and colon in a 44-year-old man. Imaging examinations revealed a huge heterogeneous mass in the enlarged spleen and a colonic lump, but showed no obvious space-occupying lesion in the pancreas. An exploratory laparotomy revealed that the enlarged spleen, pancreatic tail, and splenic flexure of the colon were firmly attached to one another. Splenectomy combined with resection of the distal pancreas and splenic flexure of the colon was performed. In the distal pancreatectomy specimen, a 0.8-cm solid mass was present in the tail. The tumor contained definite components of both adenocarcinoma and squamous cell carcinoma. The patient died of cachexia five months after admission. This case is unique in that the metastatic tumor involving the spleen was considerably larger than the primary tumor itself.

Key words: Adenosquamous carcinoma of the pancreas, splenic invasion, colonic invasion

Splenomegali ile prezente olan pankreatik adenoskuamöz karsinom; olgu sunumu

Çevre dokuları invaze eden pankreasın adenoskuamöz karsinomu nadir görülür. Burada, 44 yaşındaki erkek hastada dalak ve kolonu invaze eden pankreas kökenli pankreasın adenoskuamöz karsinomu vakası sunulmuştur. Görüntüleme yöntemleri ile büyümüş dalakta dev heterojen kitle ve kolonda kitle tespit edilmiş ancak pankreasta yer kaplayan lezyon görülmemiştir. Tanısal laparatomide dalağın, pankreas kuyruğunun ve kolonun birbirine yapıştığı tespit edilmiştir. Splenektomi ile beraber, pankreasın kuyruğu ve kolonun splenik fleksura bölgesi de eksize edilmiştir. Distal pankreatektomi örneğinde 0.8 cm boyunda solid kitle tespit edilmiştir. Tümörün adenokarsinoma ve skuamöz karsinoma özelliklerini bir arada taşığı görülmüştür. Başvurudan 5 ay sonra hasta kaşeksiden ex olmuştur. Bu vaka dalağı tutan metastatik tümörün orjinindekinden daha büyük olması nedeni ile özeldir.

Anahtar kelimeler: Pankreasın adenoskuamöz karsinomu, dalak invazyonu, kolon invazyonu

INTRODUCTION

Adenosquamous carcinoma (ASC) of the pancreas is a rare pancreatic neoplasm characterized by cellular mixture of both adenomatous and squamous subtypes in the same tumor. It accounts for only about 0.9% to 4.5% of all pancreatic malignancies, but is more aggressive than other forms of adenocarcinoma and associated with a poorer prognosis (1-3). Currently, the histogenesis of pancreatic ASC is still unclear and the most appropriate form of therapy has yet to be established. ASC of the pancreas directly invading surrounding organs is unusual, and splenomegaly as the clinical manifestation of direct spread of pancreatic ASC to the spleen is extremely rare (4). Here, we describe a very rare case of pancreatic ASC directly invading the spleen and colon, with left upper abdominal

Address for correspondence: Yi-Ping MOU
Sie Run Run Shaw Hospital, Department of General Surgery,
Hangzhou Zhejiang Province, China
E-mail: mouyiping@126.com

Manuscript received: 05.11.2011 **Accepted:** 13.03.2012

Turk J Gastroenterol 2012; 23 (6): 799-803
doi: 10.4318/tjg.2012.0504

pain and splenomegaly as the first clinical signs of the metastatic spread.

CASE REPORT

A 44-year-old man was referred to our hospital with a one-month history of left upper quadrant abdominal pain. He was previously in good health. He had noted a weight loss of 2 kg over the past three months. His hematologic values, serum biochemical data, and urinalysis were within normal limits, with the exception of a mildly elevated concentration of carbohydrate antigen (CA)19-9 (326.1 ng/ml). A computed tomography (CT) scan of the abdomen revealed a huge hypodense mass measuring 10x8x6 cm in the enlarged spleen (Figure 1). Color Doppler ultrasound revealed that the lesion had a heterogeneous internal pattern (Figure 2). The splenic vein and splenic artery were only slightly compressed. Colonoscopy revealed a colonic lump about 70 cm from the anus, which showed a circumferential growth pattern (Figure 3). Further endoscopic procedures failed due to the stenosis of the intestinal canal caused by the tumor. Histological examination of the specimen from the lesion showed adenocarcinoma. There were no obvious abnormalities detected by other examinations, such as gastroscopy and pectoral CT. These findings were initially considered to represent a primary malignant process arising from the splenic flexure of the colon, with extension to the spleen.

An exploratory laparotomy was then performed. Intraoperative findings revealed a giant tumor in the enlarged spleen, approximately 10 cm in diameter. The tail of the pancreas and the splenic

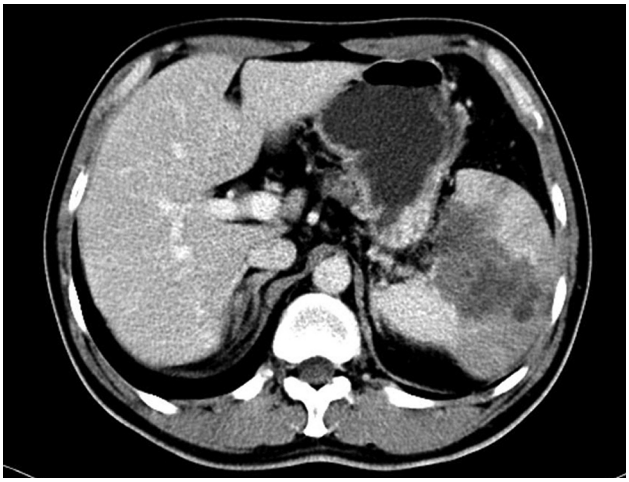

Figure 1. A contrast-enhanced CT scan of the abdomen showing a large heterogeneous mass within the enlarged spleen.

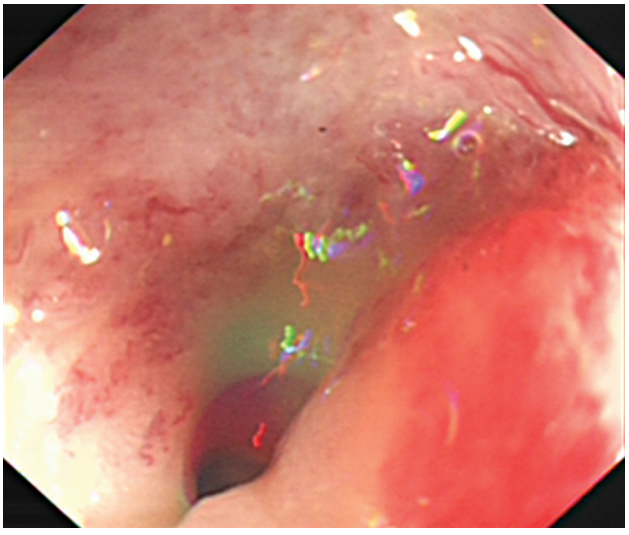

Figure 3. Colonoscopy revealing a lump showing a circumferential growth in the colon, about 70 cm away from the anus.

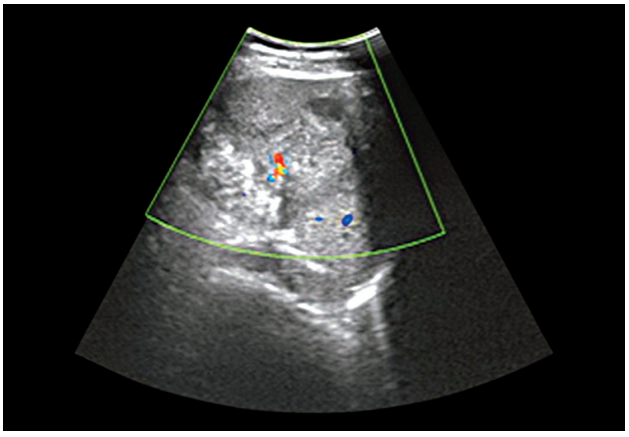

Figure 2. Transabdominal ultrasound showing a heterogeneous and vascularized mass with a predominantly solid component.

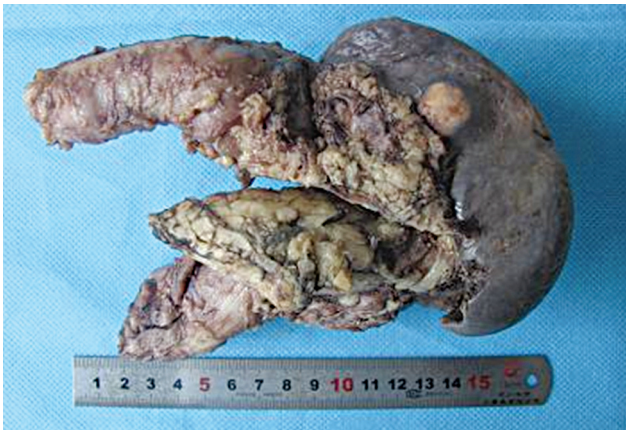

Figure 4. A resected giant tumor from the enlarged spleen, approximately 10 cm in diameter.

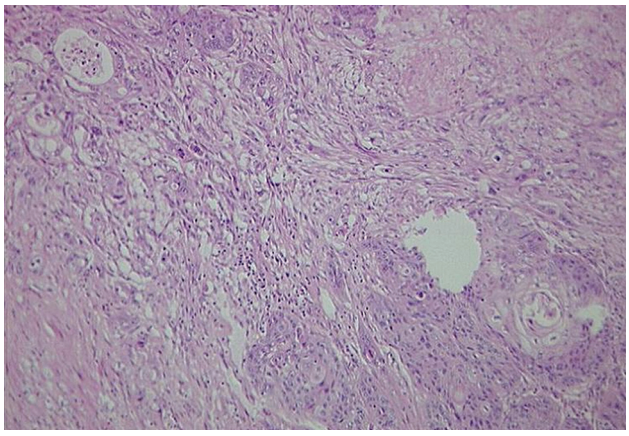

Figure 5. A hematoxylin&eosin-stained tissue section showing the tumor composed of both adenocarcinoma and squamous components (H&E stain, x100).

flexure of the colon were firmly attached to the mass (Figure 4). There was no evidence of ascites, peritoneal dissemination, or liver metastases. The texture of the pancreas was soft, and no obvious space-occupying lesion was found in the pancreas. The splenic hilar lymph nodes were swollen. The stomach, left kidney, and diaphragm were all intact. The origin of the mass could not be defined. Splenectomy combined with resection of the distal pancreas and splenic flexure of the colon was performed. Meanwhile, biopsies were taken from the colon and left renal capsule. Frozen section examination was performed and no cancer cells were found in either of the tissues. A handsewn side-to-side anastomosis was then performed. Total intraoperative blood loss was 200 ml.

Macroscopically, the splenic tumor was a solid mass of elastic consistency, with a relatively smooth surface. Sections through the splenic parenchyma revealed that the tumor was solitary, homogeneous, and yellowish-white in color. There were ulcerative lesions in the colon. In the distal pancreatectomy specimen, a 0.8-cm solid mass was present in the tail. Microscopically, the tumor contained definite components of both adenocarcinoma and squamous cell carcinoma, and a gradual transition was recognized between the two (Figure 5). It extended into the peripancreatic soft tissue, and was present throughout the colon wall. Sections of the spleen showed focal groups of atypical glands with hyperchromatic nuclei and increased mitotic activity. These histological features were consistent with an adenocarcinoma. Immunohistochemical staining of spleen sections with the DAKO EnVision™ System (Dako, Glostrup, Denmark) demonstrated a strong positivity for CK7 and CK19, which was consistent with the primary tumor. Immunohistochemistry also demonstrated that tumor cells were partially positive for CK, weakly positive for NSE, and negative for CK20, CDX-2, Syn and CgA. Additionally, there was perineural and lymphovascular invasion, with five of the 18 lymph nodes positive for metastatic adenocarcinoma.

The postoperative course was uneventful, and the patient developed no clinically significant complications postoperatively. Flatus was passed on the third postoperative day. Liquid diet was started on postoperative day 4, followed by a soft diet on postoperative day 6. Left pleural effusion persisted for one week after the operation, and the patient was finally discharged on postoperative day 12. After one month, the patient's serum CA19-9 level had dropped to 279.1 ng/ml. The patient was treated with adjuvant chemotherapy, which was discontinued after two sessions due to intolerable side effects. The patient's general condition deteriorated gradually, and he died of cachexia five months after admission.

DISCUSSION

According to the World Health Organization (WHO), ASC is characterized by the presence of variable proportions of mucin-producing glandular elements and squamous components. In addition, the squamous component should account for at least 30% of the tumor tissue (5). Currently, the pathogenesis of pancreatic ASC remains unknown since the pancreas does not normally contain any squamous cell elements (6). As squamous cell carcinoma grows faster and exhibits more aggressive behavior than adenocarcinoma (7,8), pancreatic ASC has a worse prognosis, as compared to the more common ductal pancreatic cancer (DPC). The median overall survival ranges between three to six months among patients with advanced pancreatic ASC and about 24 months among patients with resectable cancer (9).

In most cases, the clinical, radiological and macroscopic aspects of a pancreatic ASC closely mimic those of a common DPC (2,10). Common clinical manifestations include abdominal pain, weight loss, and jaundice. In addition, pancreatic ASC is associated with no specific serum data, including tumor markers such as carcinoembryonic antigen, CA19-9, and squamous cell carcinoma antigen (11,12). Currently, the accurate diagnosis of pan-

creatic carcinoma is usually possible before treatment, due to the improvement in imaging techniques. In our case, however, the major symptom was left upper abdominal pain, possibly caused by splenomegaly. Abdominal CT revealed a tumor in the spleen. In contrast, the lesion in the pancreas was not significant. These data are consistent with the findings of a previous study reporting a case of pancreatic ASC that presented as splenic rupture (13), suggesting that spleen invasion may be the first sign of disease in some cases of pancreatic ASC, as the secondary tumor may be considerably larger than the primary tumor itself. Such an unusual tumor growth pattern is worth attention, for it could result in the misdiagnosis of primary tumor sites.

Another interesting point of our case is the direct splenic and colonic invasion. Direct invasion of the spleen is considered a rare event in the course of malignant solid tumors, but occasionally occurs with tumors originating from surrounding organs, such as the pancreas (14), stomach (15), liver (16), colon (17), and retroperitoneum (18). There have been at least two cases reported in the literature previously of direct invasion of pancreatic ASC to the spleen (13,19). In our case, the enlarged spleen and pancreas tail were firmly attached to each other due to extensive adhesions resulting from the direct spread of the cancer. The spleen may be directly invaded from the subperitoneal space through the splenic hilum (13). In addition to the spleen, the colon was also invaded in our case. Colonoscopy revealed a colonic lump showing a circumferential growth pattern. Interestingly, a previous study demonstrated that pancreatic ASC simultaneously invaded the spleen, left adrenal gland, left kidney, and transverse colon (19). These data indicate that in extremely few cases, when the colon has been infiltrated by adenocarcinoma originating from surrounding organs, an infiltrative tumor might form in the colonic wall, and endoscopists may misidentify this secondary tumor as a primary colon adenocarcinoma.

In most cases, when the spleen has been infiltrated, the primary tumor usually has already formed to a relatively large size, and often has involved the surrounding organs; therefore, it is not difficult to make an exact diagnosis of the primary tumor. In our case, however, the patient's pancreas seemed completely normal, and the primary tumor was so small that it could not be defined until after microscopic examination of the resected spleen. Our findings, together with previous observations that pancreatic APC tends to directly invade surrounding organs (19), indicate a significant propensity for pancreatic ASC to invade surrounding tissues as a localized lesion. Even in the early stage, wide spread to surrounding organs could have occurred.

In our case, surgical treatment seemed to be a valid treatment strategy for the following reasons. First, our initial diagnosis was a primary malignancy arising from the splenic flexure of the colon, with extension to the spleen; furthermore, there was no evidence of multivisceral metastasis. Surgical resection is the only treatment known to provide long-term survival in patients with stage IV disease (20). In addition, many of these patients require colonic cancer resection to treat life-threatening symptoms of hemorrhage and/or obstruction (20). Second, surgical treatment is indicated when the lesion is solitary, as splenectomy significantly increases the odds of long-term survival (21). Third, the patient's major symptoms, possibly caused by splenomegaly, could be relieved by splenectomy. Finally, there is a risk of spontaneous splenic rupture secondary to tumor invasion (13,14,22). Unfortunately, the operation did not contribute to long-term survival in our case.

In conclusion, we present a case of ASC of the pancreas directly invading the spleen and colon. Our case is unique in that the metastatic tumor to the spleen was considerably larger than the primary tumor itself, and further, splenomegaly was the first clinical sign of metastatic spread, which may have caused the misdiagnosis of primary tumor sites. This case illustrates an atypical presentation for pancreatic ASC and demonstrates some of the challenges in its diagnosis.

REFERENCES

1. Ishikawa O, Matsui Y, Aoki I, et al. Adenosquamous carcinoma of the pancreas: a clinicopathologic study and report of three cases. Cancer 1980; 46: 1192-6.
2. Madura JA, Jarman BT, Doherty MG, et al. Adenosquamous carcinoma of the pancreas. Arch Surg 1999; 134: 599-603.
3. Okabayashi T, Hanazaki K. Surgical outcome of adenosquamous carcinoma of the pancreas. World J Gastroenterol 2008; 14: 6765-70.
4. Klein B, Stein M, Kuten A, et al. Splenomegaly and solitary spleen metastasis in solid tumors. Cancer 1987; 60: 100-2.

5. Klöppel G, Hruban RH, Longnecker DS, et al. Tumours of the exocrine pancreas. In: Hamilton SR, Aaltonen LA, editors. World Health Organization classification of tumours. Pathology and genetics of tumours of the digestive system. Lyon: WHO, 2000; 219-51.
6. Cihak RW, Kawashima T, Steer A. Adenoacanthoma (adenosquamous carcinoma) of the pancreas. Cancer 1972; 29: 1133-40.
7. O'Connor JK, Sause WT, Hazard LJ, et al. Survival after attempted surgical resection and intraoperative radiation therapy for pancreatic and periampullary adenocarcinoma. Int J Radiat Oncol Biol Phys 2005; 63: 1060-6.
8. Iemura A, Yano H, Mizoguchi A, et al. A cholangiocellular carcinoma nude mouse strain showing histologic alteration from adenocarcinoma to squamous cell carcinoma. Cancer 1992; 70: 415-22.
9. Katz MH, Wang H, Fleming JB, et al. Long-term survival after multidisciplinary management of resected pancreatic adenocarcinoma. Ann Surg Oncol 2009; 16: 836-47.
10. Kardon DE, Thompson LD, Przygodzki RM, et al. Adenosquamous carcinoma of the pancreas: a clinicopathologic series of 25 cases. Mod Pathol 2001; 14: 443-51.
11. Makiyama K, Takuma K, Zea-Iriarte WL, et al. Adenosquamous carcinoma of the pancreas. J Gastroenterol 1995; 30: 798-802.
12. Yamaue H, Tanimura H, Onishi H, et al. Adenosquamous carcinoma of the pancreas: successful treatment with extended radical surgery, intraoperative radiation therapy, and locoregional chemotherapy. Int J Pancreatol 2001; 29: 53-8.
13. Asai K, Watanabe M, Matsukiyo H, et al. Pancreatic adenosquamous carcinoma presenting as splenic rupture: report of a case. Surg Today 2011; 41: 872-6.
14. Smith WM, Lucas JG, Frankel WL. Splenic rupture: a rare presentation of pancreatic carcinoma. Arch Pathol Lab Med 2004; 128: 1146-50.
15. Biswas M, Rahi R, Tiwary SK, et al. Leiomyosarcoma of stomach: a case report. Kathmandu Univ Med J 2006; 4: 510-2.
16. Yan ML, Wang YD, Lai ZD, et al. Pedunculated hepatocellular carcinoma and splenic metastasis. World J Gastroenterol 2009; 15: 5239-41.
17. Pisanu A, Ravarino A, Nieddu R, et al. Synchronous isolated splenic metastasis from colon carcinoma and concomitant splenic abscess: a case report and review of the literature. World J Gastroenterol 2007; 13: 5516-20.
18. Oliphant M, Berne AS, Meyers MA. Direct spread of subperitoneal disease into solid organs: radiologic diagnosis. Abdom Imaging 1995; 20: 141-7.
19. Onoda N, Kang SM, Sugano S, et al. Mucoepidermoid carcinoma of the pancreas: report of a case. Surg Today 1995; 25: 843-7.
20. Okuno K. Surgical treatment for digestive cancer. Current issues - colon cancer. Dig Surg 2007; 24: 108-14.
21. Izuishi K, Sano T, Usuki H, et al. Isolated splenic metastasis of ovarian cancer 20 years after operation: a case report and literature review. Tumori 2010; 96: 784-6.
22. Hoar FJ, Chan SY, Stonelake PS, et al. Splenic rupture as a consequence of dual malignant pathology: a case report. J Clin Pathol 2003; 56: 709-10.