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CASE REPORT

Extramedullary Plasmacytoma of the Pancreas Complicated with Left-Sided Portal Hypertension—a Case Report and Literature Review

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Introduction

Plasma cell neoplasms (PCNs) are clonal diseases of terminally differentiated B cells, which secrete a typical monoclonal immunoglobulin called M-protein or paraprotein. They account for approximately 1% of malignant and 10–15% of hematopoietic tumors [1]. PCN can occur as a single lesion (so-called solitary plasmacytoma) or as a multiple lesion (multiple myeloma). Solitary plasmacytomas account for only about 5% of PCNs and present mostly as a single bone lesion (solitary bone plasmacytoma), less commonly as a soft tissue mass (primary extramedullary plasmacytoma (EMP)) [2, 3]. EMPs therefore represent approximately 3% of all PCNs [4].

Almost 80–90% of extramedullary plasmacytomas occur in the head or neck, primarily in the upper respiratory tract. Less than 10% of EMPs affect the gastrointestinal tract (mostly the liver and the stomach) [4, 5]. It is very rare for a plasmacytoma to affect the pancreas: they account for fewer than 0.1% of all pancreatic tumors. Pancreatic involvement is usually the result of a secondary lesion by a known multiple myeloma. In other words, cases of solitary primary pancreatic plasmacytoma are extremely rare worldwide [1].

The first published case of a pancreatic plasmacytoma was in 1947; since then, only 50 cases have been reported in the literature worldwide, most of them as a secondary involvement of the pancreas by a multiple myeloma [1].

Primary extramedullary plasmacytoma mostly affects men (its men to women ratio is 3:1) in the fifth and sixth decades of life. A monoclonal paraprotein is detected in the serum or urine of fewer than 25% of patients. The risk of distant relapse and developing a multiple myeloma is only 30%. The patients' prognosis is generally very good—statistically, 70% of patients survive 10 years when early treatment is administered [3].

The diagnostic criteria for solitary extramedullary plasmacytoma described by the International Myeloma Working Group in 2009 are 1. no M-protein in serum or/and in urine; 2. extramedullary tumor of clonal plasma cells; 3. normal bone marrow; 4. normal skeletal survey; and 5. no related organ or tissue impairment [6].

Typical clinical signs of a pancreatic plasmacytoma are abdominal pain and obstructive jaundice [7]. The presence of a pancreatic mass, usually in the head of the pancreas, is confirmed by a CT scan or MRI. The CT features are not specific; in a few cases, the tumor has been described as multilobular homogenous solid tumor, hypodense to the pancreatic tissue [4, 12]. Endosonography (EUS) with fine-needle biopsy is currently the method most commonly used to confirm the diagnosis and has very good sensitivity and specificity [15, 16]. On EUS, the reported plasmacytomas usually appear as predominantly hypoechogenic heterogeneous masses [4].

Radiotherapy and surgery are the most common treatment methods. Radiotherapy alone is often chosen in cases of extramedullary plasmacytoma of the head and neck; for EMP in other locations, surgical removal is recommended,

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sometimes with adjuvant radiotherapy. Adjuvant chemotherapy should be considered in refractory or relapsed disease, or in patients with tumors > 5 cm [3].

Left-sided portal hypertension (left-sided, sinistral, segmental portal hypertension (LSPH)) is a rare cause of bleeding in the upper gastrointestinal tract. The pathogenetic basis of the syndrome is the obstruction/thrombosis of the portal or splenic vein. This is most commonly caused by a pathological process in the pancreas; primary pathology in the spleen is a very rare cause of LSPH. The typical clinical picture for LSPH is bleeding from isolated gastric varices in the upper gastrointestinal tract in conjunction with splenomegaly, but in the absence of liver pathology. An abdominal CT with contrast medium is used for diagnosis. The therapeutic approach is determined by the primary pathological process. The treatment of choice is splenectomy or splenic artery embolization, ideally in conjunction with surgical treatment of the underlying disease [8, 9]. The patient's prognosis is strongly determined by the etiology of the LSPH [10].

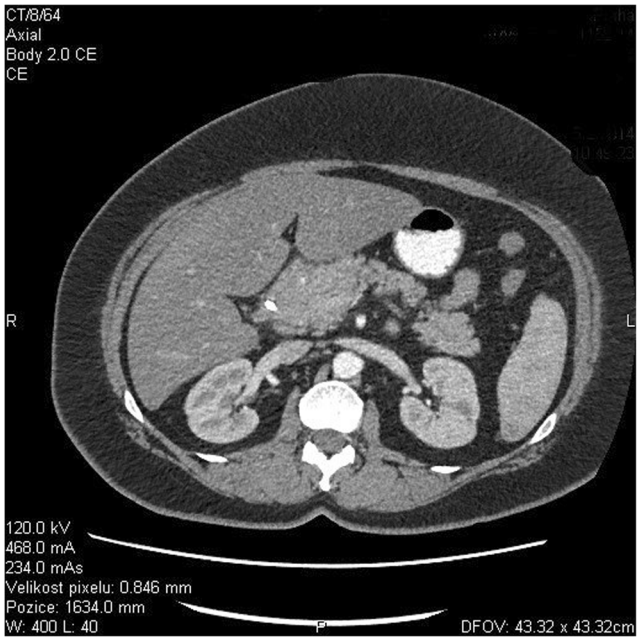

Fig. 1 CT image of the tumor (February 2014)

Course of the Case

A 52-year-old obese patient, hypertonic and diabetic on PAD for 2 years, was reviewed in the Department of Internal Medicine at the 1st Medical Faculty of Charles University and Central Military Hospital in Prague in February 2014 for obstructive jaundice, abdominal pain, and a weight loss of 5 kg in 3 months. Laboratory tests with elevation of cholestatic liver function tests (LFTs) were performed, followed by an abdominal ultrasonography and CT of the abdomen, which described a homogeneously tumorous pancreatic head enlargement to 50 mm, with the invasion of the common hepatic artery, portal vein, vena lienalis, and superior mesenteric vein (Fig. 1). ERCP was performed and a plastic biliary stent was introduced as a common bile duct stricture was found.

When admitted to our clinic, the patient was described as obese, with a palpable mass in the epigastric area, mild laboratory cholestasis without hyperbilirubinemia, and normal Ca 19-9 24.5 kU/l (reference interval 0–34). The indicated endosonographic examination revealed a bulky tumor of the pancreatic head with angioinvasion; after use of a contrast agent, there was visible hypoenhancement of three fourths of the tumor, suggesting a high proportion of connective tissue in the tumor, which is typical of malignant tumors (Fig. 2). Cytology was repeated again, and a total of three times round-cell cellularization prevailed with considerable flood lymphocytes in the cytological sample. Tumor cells were not found, and the findings were interpreted as chronic pancreatitis. We abandoned the originally intended percutaneous electroporation and chemotherapy (considered for locally advanced inoperable cancer without metastatic disease). The patient was then transferred to outpatient care and was without difficulties for half a year.

In August 2014, the patient was once again admitted to our internal department for progressive lumbosacral spinal pain, weight loss of 5 kg per month, repeated vomiting, and diarrhea. A CT of the abdomen showed moderate-sized tumor progression with expansion of the pancreatic head and new development of portal collaterals. Large esophageal varices and D1 duodenal stenosis were endoscopically identified. A jejunal enteral tube was introduced, and the patient was treated for presumed exacerbation of chronic pancreatitis of uncertain etiology (alcohol abuse and autoimmune markers were negative). Hospitalization complications also included acute cholangitis due to dysfunctional biliary drainage, which was replaced by ERCP. At the same time, hematemesis first appeared, for which sclerotization of the large esophageal varices was performed, and subsequent pharmacological treatment with terlipressin was administered. The patient was released to home care on enteral nutrition.

Another hospital stay was scheduled for late October 2014; in the meantime, the patient was on enteral nutrition and weight-stable without significant difficulties. Soon after readmission to hospital, the patient suffered repeated massive hematemesis with melena; the bleeding esophageal varices were re-treated using endoscopic sclerotization, and when another massive relapse with the appearance of hemorrhagic shock occurred, we introduced a Sengstaken-Blakemore probe as a rescue therapy. Even after extraction of the probe (24 h later) and despite ongoing pharmacotherapy for portal hypertension (terlipressin, somatostatin) plus adequate substitution of blood loss for 2 weeks, the patient once again suffered massive gastrointestinal bleeding. We therefore

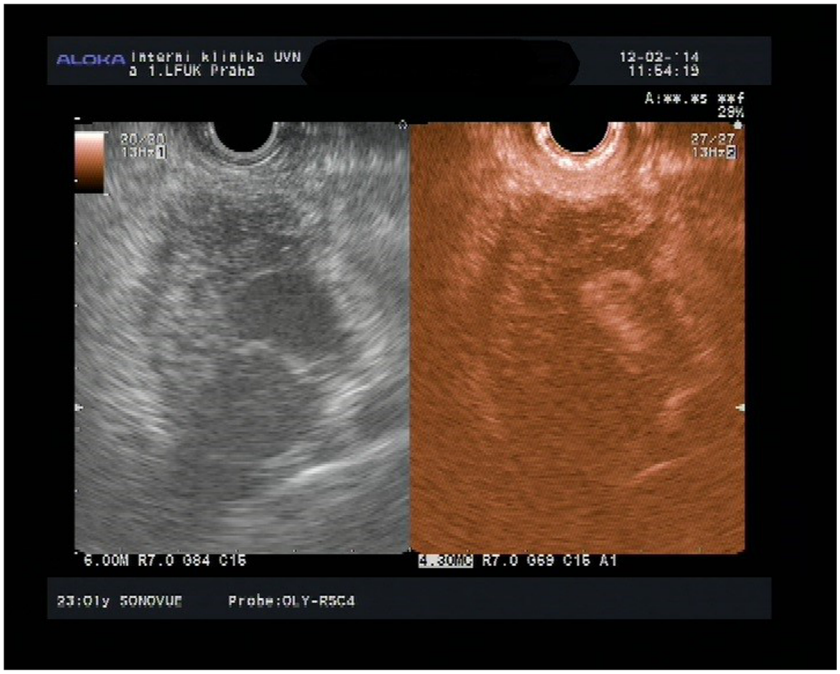

Fig. 2 Endosonography picture of the tumor (February 2014)

introduced a Danis stent into the esophagus. The stent was left in situ for 12 days without complication and subsequently extracted.

The severe left-sided portal hypertension was identified as intractable after repeated consultations with surgeons and the interventional radiologists. Repeat endoscopies portrayed an image of an infiltrated papilla of Vater, and biopsies were performed (Fig. 3). A repeat CT scan showed local progression of the pancreatic tumor with portal thrombosis. Repeated representative sampling of the papilla of Vater revealed dense plasmocellular infiltration with restriction of kappa immunoglobulin light chains, negative CD56, low proliferation determined by Ki67, and total absence of mature CD20-positive B lymphocytes. A superficially biopsied extranodal B cell lymphoma with a prominent plasmacytoid differentiation, or a plasmacytoma was considered in the differential diagnosis. After consultation with hematology, another examination was made. An X-ray of the skeleton was negative for bone involvement, and the paraproteins in the serum and urine were negative. A trepanobiopsy was made, which confirmed that the lymphoma had not infiltrated the bone marrow, and the flow cytometry of the bone marrow aspirate was negative.

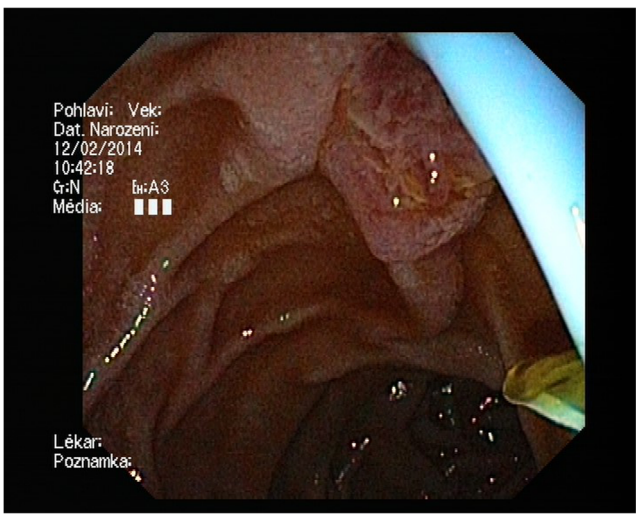

Fig. 3 The infiltrated papilla of Vater in October 2014

Given the severe overall clinical condition of the patient, with repeated hemorrhagic shock and massive bleeding from the esophageal varices, and portal hypertension making solutions involving closure of the portal vein impossible, we considered (in consultation with the surgeon, radiologist, and hematologist) that neither surgical treatment nor chemotherapy was indicated. The patient died on December 24, 2014, from the recurrent variceal bleeding and hemorrhagic shock. The autopsy confirmed infiltration of the pancreatic head by a tumor, without the involvement of the liver, spleen, or bone marrow. The diffuse tumor was formed of atypical plasmacytoid cells with a disperse admixture of large anaplastic cells, sometimes multinucleated (Fig. 4). Immunohistologically, there were positivities of CD45, CD138, CD79a, and MUM1 and a restriction of the kappa light chains (Fig. 5); proliferative activity assessed by Ki67 was between 10 and 20%, and CD20 and cytokeratins were negative. The diagnosis of an extramedullary anaplastic plasmacytoma of the pancreas was confirmed.

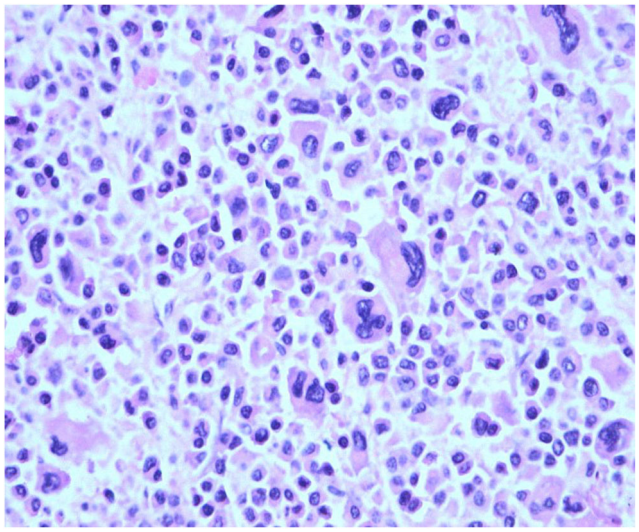

Fig. 4 Tumor of the pancreas at autopsy was composed of atypical plasmacytoid cells with an admixture of large anaplastic cells. H&E staining. Original magnification ×400

Discussion

Primary extramedullary plasmacytoma of the pancreas is a very rare disease, complicated by atypical clinical features and a difficult diagnosis. The patient's data, as well as clinical, laboratory, and imaging results, can mimic other diseases of the pancreas—acute pancreatitis, chronic pancreatitis, adenocarcinoma, lymphoma, or neuroendocrine tumor of the pancreas. To the best of our best knowledge, this case report is the first documented case of EMP in the Czech Republic. As our case study confirms, we must be aware of the possibility of EMP as a differential diagnosis in all cases of patients presenting with pancreatic tumor masses, who lack elevated oncomarkers or secondary liver metastases [11, 12]. Endosonography with biopsy should be considered crucial in determining a correct diagnosis, even though the picture of an irregular predominantly hypoechogenic heterogeneous mass is not specific [4, 15]. The published literature confirms that making the correct diagnosis in such cases simply on the basis of hematoxylin-eosin staining can be difficult or impossible, even for an experienced pathologist, as was also seen with our patient. Therefore, in cases when the result of the fine-needle aspiration is unclear, it may be necessary to make repeated biopsies and perform immunohistological analysis on the samples. An EUS-guided biopsy is assessed as safe worldwide with minimal complications, although these can include acute pancreatitis, bleeding due to pseudoaneurysm rupture, or acute portal vein obstruction [13–16]. Despite these potential complications, making the right diagnosis is essential for the patient, because treatment for EMP differs from that appropriate for other pancreatic neoplasms. Patient prognosis is better in the case of EMP than with other pancreatic neoplasms.

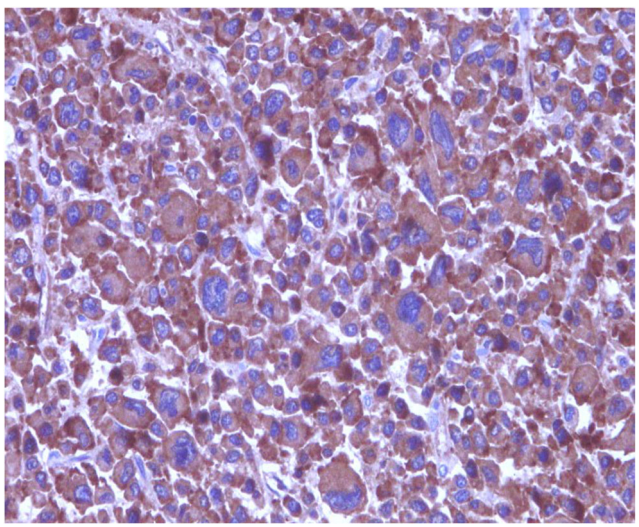

Fig. 5 The strong cytoplasmic positivity of kappa immunoglobulin light chains on tumor cells. Immunohistochemistry

Left-sided portal hypertension and massive gastrointestinal bleeding are rare complications of EMP [5]. However, it should be noted that these complications significantly increase the patient's morbidity and mortality. The most common cause of this complication is thrombotic occlusion of the portal vein [8–10]. Endoscopic and pharmacological treatment options are the same as for other variceal bleeding (sclerotherapy and variceal ligation, and administration of terlipressin and somatostatin). In our case, to address the re-development of hemorrhagic shock as a result of massive bleeding at a time when endoscopic hemostasis was impossible, we tried using an S-B probe and a Danis stent. The fact that hematemesis and severe shock were recurring more than once every 2 weeks during our patient's treatment was the deciding factor in our sensual agreement not to indicate an operation, radiotherapy, or even aggressive chemotherapy. In the late stages of the disease, this would not have yielded success in terms of the impact of severe portal hypertension, which became a fatal complication for our patient.

Compliance with Ethical Standards

Conflict of Interest The authors declare that there are no conflicts of interest.

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