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CASE REPORT

Pancreatic panniculitis as the first manifestation of the pancreatic involvement during the course of a gastric adenocarcinoma

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Abstract Pancreatic panniculitis (PP) is a rare disease presenting during the course of pancreatic diseases such as acute and chronic pancreatitis, pancreatic carcinoma. There are also a few reports of PP associated with other carcinomas. We present a 69-year-old male patient of gastric carcinoma with PP. The literature is reviewed, clinical and histological features of the case are discussed. This is the first case of PP in a gastric carcinoma patient reported in literature. As a conclusion, PP can be the first manifestation of a pancreatic metastasis of any carcinoma.

Keywords Pancreatic panniculitis · Gastric adenocarcinoma · Metastasis · Lipase

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Introduction

Pancreatic panniculitis (PP) is a rare disease, caused by high amounts of pancreatic enzymes in the blood that results in necrosis of the subcutaneous tissue. PP is clinically characterized by painful or asymptomatic nodules on the legs that mostly resemble erythema nodosum or infectious panniculitis [1, 2]. We report an extensive case of PP with high levels of lipase diagnosed in the course of gastric adenocarcinoma which was unresponsive to any treatment modality due to the late stage of the disease.

Case

A 69-year-old male patient with diabetes/hypertension and familial Mediterranean fever presented with painful red nodules on both of his legs. These nodules appeared first 2 months ago short after a gastrointestinal bleeding. Significant weight loss and anemia were the other signs detected at that time. The patient's ECOG performance status was 2. His CEA level was 1.5 ng/ml (<3); Hgb 7 g/dl, and Hct 23%.

Abdominal CT revealed prominent increase in gastric wall thickness. The increase in spleen dimensions and the heterogeneity of spleen parenchyme was highly suggestive for metastasis. An MRI was done for verification. According to MRI, the lesion in stomach was evaluated as tumoral lesion and the lesion in spleen was evaluated as hemorrhage.

An endoscopic examination was performed and with the biopsy taken, the diagnosis of gastric signet ring cell adenocarcinoma was established. Then a laparotomy was planned both for evaluation of active hemorrhage and operability of the patient. Together with the tumor in the

stomach, massive metastatic lymph nodes in peritoneum and peritoneal involvement were seen. Both the spleen and the pancreas were enlarged, hard in consistency, and fixed to the posterior abdominal wall. Therefore, during the operation the case was accepted as inoperable. A biopsy from the infiltrated lymph nodes revealed the same features of gastric adenocarcinoma.

After the laparotomy, his cutaneous lesions began to scatter throughout buttocks and gluteus. At the time of dermatologic examination, there were numerous red or purple-brown, painful subcutaneous nodules, with the size of 2–5 cm in diameter (Fig. 1). Some of the lesions were indurated and hard, whereas the others were fluctuating (Fig. 2). During a deep punch biopsy, brownish-yellow discharge was also observed through the punch hole. The histopathologic examination revealed extensive enzymatic fat necrosis within the subcutaneous fat tissue, mainly in the lobules (Fig. 3). Necrotic areas were composed of amorphous granular debris, showing an eosinophilic rim. Basophilia due to calcification was evident in most of the areas (Fig. 4). Around and in-between the necrotic areas, there was a heavy neutrophilic infiltrate, together with many macrophages with foamy cytoplasm. Occasional multinucleated cells were seen (Fig. 5). Accordingly, these lesions were diagnosed as PP.

Blood pancreatic enzymes were as follows: amylase 9 U/l (normal range: 13–53 U/l), alpha-1 antitrypsin 310 mg/dl (normal range: 92–200 mg/dl), and lipase 41405 U/l (normal range: 13–60 U/l). Culture of the discharge from the lesions were negative both for routine and acid fast bacteria.

Despite systemic steroids, antibiotics and chemotherapy regimen for gastric adenocarcinoma (FOLFOX; oxaliplatin 85 mg/m^2 on day 1, folinic acid 200 mg/m^2 on day 1, 5-fluorouracil 400 mg/m^2 IV bolus on day 1, and 5-fluorouracil 2400 mg/m^2 for 46 h continuos infusion) patient's

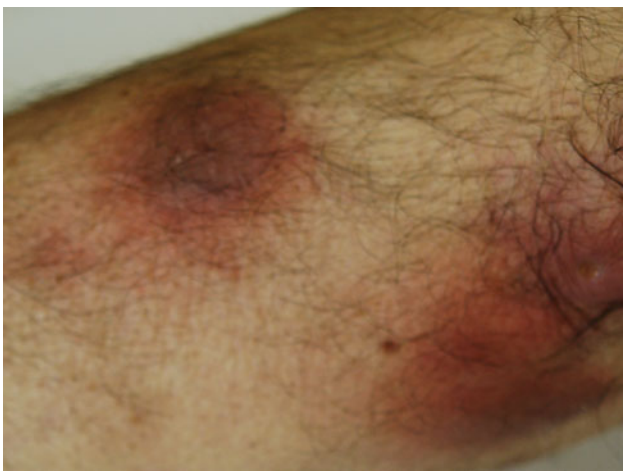

Fig. 1 Subcutaneous nodules

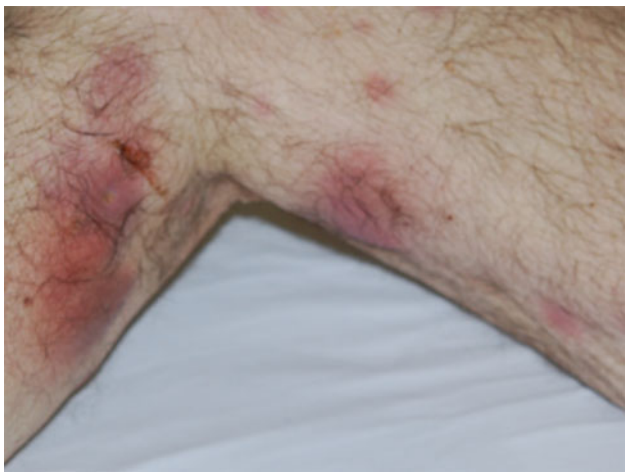

Fig. 2 Some of the nodules were indurated and some were fluctuating

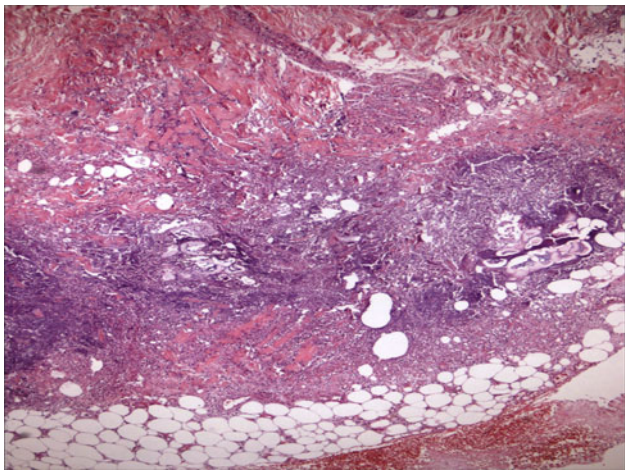

Fig. 3 PP: extensive enzymatic fat necrosis in the subcutaneous fat tissue (HE ×40)

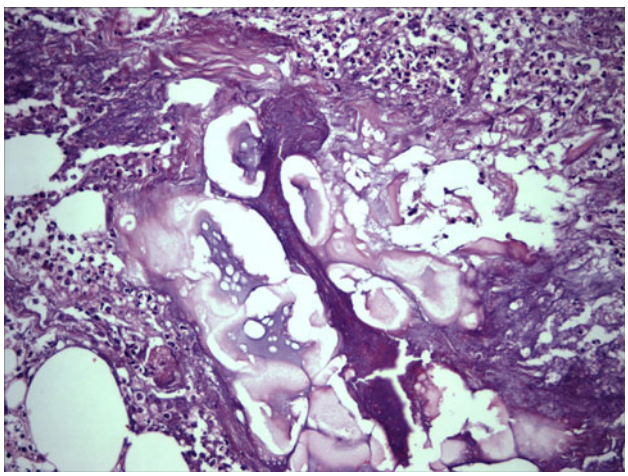

Fig. 4 The zone of calcification and fat necrosis with neutrophils around them (HE ×200)

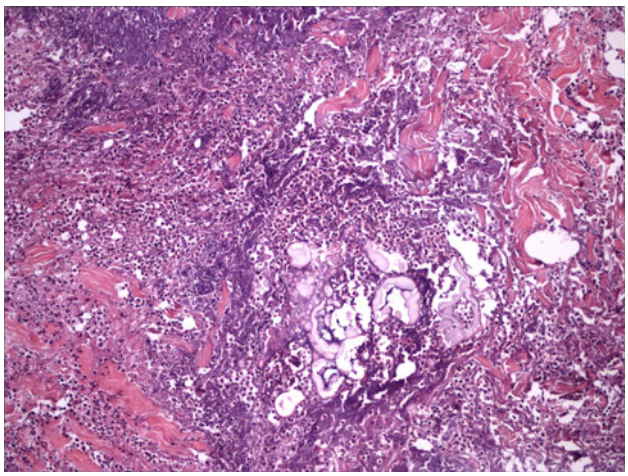

Fig. 5 Due to the calcification of the necrotic fat cells, granular basophilic material, intermingled with neutrophils are detected (HE ×100)

lipase level never fell below 22000 U/l and skin lesions continued to spread to upper extremities and torso and even head and neck. The pain of the lesions could only be controlled with increasing amount of morphine with every new lesion. The patient died in 6 weeks due to a multi-organ failure.

Discussion

Disseminated liquefactive fat necrosis is a rare phenomenon which rarely occurs during the course of pancreatic diseases [3]. In a series of 863 patients with various pancreatic diseases, only one case of panniculitis was seen [4]. The condition occurs a few weeks or months before or during the course of an underlying disease [1, 2]. Most cases are related with acute or chronic pancreatitis or pancreatic carcinoma, mostly of acinar type [1–3]. There are also sporadic case reports in which the condition occured during the course of other diseases such as pancreatic pseudocysts, pancreatic fistulas, congenital anomalies of pancreas (pancreas divisum), HIV infection [1–3]. There are also solitary reports of patients with systemic lupus erythematosus [5], nephrotic syndrome [6], liver carcinoma [7], and adenocarcinoma of unknown origin [8]. Our case presented with the signs and symptoms of gastric adenocarcinoma and at the time of diagnosis the tumor had already spread to the whole abdomen and peritoneum. Together with the initial symptoms of the tumor, subcutaneous nodules were detected during dermatologic examination and were diagnosed as PP according to histologic features. Although pancreas was found to be hard in consistency during the operation, pancreatic involvement was not clear-cut at that time. After the diagnosis of PP, the blood pancreas enzymes were evaluated and enormously high lipase level was assessed. All these findings were interpreted as the pancreatic involvement of the tumor.

The pathogenesis of PP is not well established but the elevation of one or more pancreatic enzymes such as lipase, amylase, and trypsin were well established in nearly all cases. It was also postulated that there must be some other co-factors besides high lipase levels since not every patient with high lipase or amylase level have PP [1]. Mullin et al. [4] noted that the necrosis in the adipose tissue should be related to the lytic effect of trypsin and lipase together. The role of immune complexes and inflammatory cytokines is also pointed out [1, 2]. There is no well-established treatment for PP. Surgery for the underlying cause, somatostatin analogues, steroids, and chemotherapy were all tried with some success. Our case was not eligible for surgery, could not tolerate the chemotherapy and did not respond to the steroid treatment. Morphine sulfate was the only medication that helped for his pain.

As in our case, PP may be the first manifestation of underlying pancreas metastases. In literature, PP was reported in the course of many other carcinomas, such as liver carcinoma, but to our knowledge, it is the first case of PP coming out during the course of gastric carcinoma.

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