Revista Española de Enfermedades Digestivas
THE SPANISH JOURNAL OF GASTROENTEROLOGY

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DOI: 10.17235/reed.2018.5203/2017
Link: PubMed (Epub ahead of print)

Please cite this article as:
de Frutos Rosa Diego, Espinosa Taranilla Laura, González de Canales de Simón Pilar, Vélez Velázquez María Dolores, Guirado Koch Cristina. Pancreatic panniculitis as a presentation symptom of acinar cell carcinoma. Rev Esp Enferm Dig 2018. doi: 10.17235/reed.2018.5203/2017.

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NC 5203 inglés

Pancreatic panniculitis as a presentation symptom of acinar cell carcinoma

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Received: 04/08/2017

Accepted: 25/01/2018

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Key words: Panniculitis. Pancreas. Acinar cell carcinoma.

ABSTRACT

Pancreatic panniculitis is a rare skin manifestation associated with pancreatic conditions. This condition has similar characteristics to those of other panniculitis types and its course parallels the triggering condition and may occasionally precede it. We report the case of a female patient with asymptomatic pancreatic panniculitis; the etiologic study identified a pancreatic acinar cell carcinoma with liver metastases.

INTRODUCTION

Pancreatic panniculitis (PP) or enzymatic subcutaneous fat necrosis is a rare clinical manifestation that is usually associated with pancreatic conditions. PP manifests with painful erythematous, which are nodular lesions identical to those of other panniculitides and therefore require a differential diagnosis. Skin biopsy is the gold standard for diagnosis with quasi-pathognomonic findings such as lobular involvement,

the presence of ghost cells and saponification. The clinical significance is due to the fact that skin manifestations precede pancreatic involvement in almost half of cases. Thus subsequent diagnostic tests are focused on pancreatic conditions. We report the case of a 50-year-old female patient who presented with PP in the context of a pancreatic acinar cell carcinoma (PACC) with distant metastases.

CASE REPORT

A 50-year-old woman with an unremarkable medical and family history, except for smoking, presented to the Emergency Room with generalized joint pain and painful skin lesions in her lower extremities over the last one and a half months. The patient was assessed by Dermatology and multiple tender nodules of up to 25 mm in diameter were found with no deep adhesions and poorly delimited borders in the pretibial, malleolar and crural regions. There was some spread across the dorsal area. Due to the non-specific nature of the lesions, a biopsy was performed. The histopathological analysis of the sample identified lobular panniculitis with extensive enzymatic fat necrosis and dystrophic calcification foci, which prompted a diagnosis of PP. The patient was then referred for evaluation to the Department of Digestive Diseases. The patient remained otherwise asymptomatic, without abdominal pain, anorexia, asthenia or weight loss. Lab tests identified lipase levels at 24,360 IU/l (normal range, 6-51 IU/l), amylase at 11 IU/l (normal range, 39-118 IU/l) and C-reactive protein (CRP) at 91.6 mg/l. There were no other abnormal values in the chemistry panel, including CEA and CA 19-9. In view of these findings, an abdominal-pelvic computed tomography (CT) scan was performed that revealed ten solid space-occupying lesions (SOLs) in the liver. The largest one was 87 x 73 mm in size with central hypodense bands and peripheral uptake, as well as nonspecific thickening in the pancreatic uncinate process with an identical dynamic behavior when compared to the rest of the gland. The CT findings prompted an upper digestive echoendoscopy and a magnetic resonance imaging (MRI) scan with a liver-specific contrast medium (Primovist©).

The MRI scan identified liver lesions that were consistent with a secondary or metastatic origin. A 35 x 25 mm hypervascular lesion that was suggestive of malignancy was identified at the uncinate process. Echoendoscopy confirmed the

presence of a 30 x 20 mm lesion on the uncinate process. The lesions were punctured under EUS guidance using a 22G Cook© cytology needle in three passes and an in-room pathologist obtained samples for cytohistology. An immunohistochemical analysis of the material revealed neoplastic cells that were positive for AE1/AE3 and CK 18 and negative for chromogranin, synaptophysin, CD56, CD57, NSE, beta-catenin, and alpha-fetoprotein. Neoplastic cells had PAS-DIASTASE-positive granules inside the cytoplasm. These cytologic findings were consistent with PACC.

After establishing a definitive diagnosis of stage-IV PACC with liver metastases, the case was presented to the multidisciplinary committee of abdominal tumors. Palliative-intent chemotherapy (Abraxane®-gemcitabine scheme) was initiated due to the advanced stage of disease. Following treatment onset, the patient experienced a torpid clinical course with progressive general impairment and eventually died a few months after diagnosis.

DISCUSSION

PP or enzymatic subcutaneous fat necrosis was first described by Chiari in 1883 in patients with acute pancreatitis (1). This is an uncommon clinical manifestation which occurs in around 2-3% of patients (2) and affects individuals with pancreatic diseases. Although cases have been reported where no underlying pancreatic illness was identified (3). It usually develops between the fourth and sixth decades of life, with a higher prevalence in males (5:1) (2).

As with other panniculitides, this condition manifests with multiple nodular, erythematous, warm, painful skin lesions, predominantly in the lower limbs. These lesions typically tend to develop ulcers that produce an oil-like exudate. They may be accompanied by systemic manifestations such as fever, abdominal pain and inflammatory polyarthropathy, which constitute the so-called PPP syndrome (panniculitis, pancreatitis, polyarthritis) and, to a lesser extent, with ascites or pleural effusion. Fat tissue necrosis may involve other sites, including bone marrow fat (associated with osteolytic lesions), intrahepatic fat, intestinal fat and central nervous system fat. The association of subcutaneous nodules, polyarthritis and eosinophilia is known as Schmid's triad and has a poorer prognosis (4).

Its clinical course parallels that of the underlying condition and has been reported in association with both benign (most commonly acute pancreatitis) and malignant diseases. The physio-pathogenesis of the condition is poorly understood. The best established hypothesis relates this to an increased release of pancreatic enzymes into the blood stream, which would result in subcutaneous fat necrosis and secondary inflammation. However, serum levels of these enzymes do not directly correlate with clinical findings, although higher levels do seem to be associated with malignancy. Along these lines, a cut-off for serum lipase at 4,414 U/l is thought to discriminate between inflammatory and neoplastic conditions (S 73.0%, Sp 82.1%) (1). Similarly, local immune complex-mediated vascular endothelial damage and venous stasis have also been proposed as cofactors for the development of clinical manifestations (2).

The condition is histologically characterized by the development of subcutaneous fat tissue necrosis due to digestion by pancreatic enzymes, lipase, amylase and trypsin. Lipase has the strongest association with the condition and has been attributed the typical findings, such as neutral fat hydrolysis, which releases glycerol and free fatty acids, which in turn give rise to necrosis and inflammation. Lobular involvement with predominantly neutrophilic infiltration and the presence of foamy histiocytes and multinucleated giant cells is characteristic of the condition. Fat necrosis areas may be seen with adipose degeneration, liquefaction, microcyst formation, bleeding foci and the presence of so-called “ghost cells”. These are usually anucleate necrotic adipocytes, which are highly suggestive, albeit not pathognomonic, of the condition (4). Other characteristics include the development of calcification sites and the presence of a laminar-deposited basophilic material that results from adipocyte saponification by calcium salts.

The clinical significance of this condition derives from the fact that skin lesions often precede the clinical manifestations of pancreatic involvement in up to 45% of cases, as in the present case report. There is no specific therapy for the condition. Basically, the underlying disease is treated with the addition of analgesic measures for skin lesions. Some studies suggest using somatostatin analogues such as octreotide to relieve symptoms due to their role as pancreatic secretion inhibitors. Although experience with these drugs is limited (5).

With regard to our case report, PACC represents 1%-2% of all primary pancreatic tumors. Concomitant PP has been reported in 16% of cases, which represents 85% of all neoplasm-associated panniculitides (4). This is a functioning exocrine tumor, therefore it may occasionally manifest in a paraneoplastic manner with lipase hypersecretion. The incidence peaks during the sixth decade of life with a higher prevalence in males (2:1) (6) and nonspecific symptoms including abdominal pain and nausea, etc. This type of cancer is mainly sporadic in nature but has also been reported in the context of Lynch syndrome and familial adenomatous polyposis. Predominantly occurring in the head of the pancreas, these tumors are usually large at diagnosis and up to 50% already exhibit distant spread (7). Histologically, they are characterized by the presence of eosinophilic acinar cells with PAS-positive cytoplasmic granules (pancreatic enzyme content). From an immunohistochemical perspective, they are characterized by positive CK8, CK18, CAM 5.2 and AE1/AE3 staining, whereas CK7, CK19 and CK20 staining is negative. These tumors are very aggressive with a 5-year overall survival rate lower than 10%[7].

To conclude, this is a rare case and there are no more than 150 similar cases reported in the literature, thus exemplifying how the finding of PP represents a rare clinical manifestation that should raise an alarm and prompt the search of a pancreatic trigger. Should the clinical evidence be present, a number of diagnostic tests should be performed, particularly imaging tests to identify the underlying etiology which often entails a neoplastic disease.

In our case, PP was seemingly associated with PACC, a particularly aggressive, rare neoplasm that is commonly associated with PP. This is possibly due to the paraneoplastic overproduction of pancreatic enzymes.

REFERENCES

1. Zundler S, Erber R, Agaimy A, et al. Pancreatic panniculitis in a patient with pancreatic-type acinar cell carcinoma of the liver. Case report and review of literature. BMC Cancer 2016;16:130. DOI: 10.1186/s12885-016-2184-6

2. Fernández-Jorge B, Verea-Hernando MM, Álvarez-Rodríguez R, et al. Presentación de un caso de paniculitis pancreática y revisión de la bibliografía. An Med

Interna 2006;23(9):431-4. DOI: 10.4321/S0212-71992006000900007

3. Aznar-Oroval E, Illueca-Ballester C, Sanmartín-Jiménez O, et al. Paniculitis pancreática como forma de presentación inicial de adenocarcinoma gástrico con metástasis hepáticas. Rev Esp Patol 2013;46(1):40-4. DOI: 10.1016/j.patol.2011.11.001

4. Ballester Sánchez R, De Unamuno Bustos B, Hernández Bel P, et al. Paniculitis pancreática. Revisión de 7 casos. Piel 2012;27(7):367-71. DOI: 10.1016/j.piel.2012.04.006

5. Jiang Zheng Z, Gong J, Ming Xiang G, et al. Pancreatic panniculitis associated with acinar cell carcinoma of the pancreas: a case report. Ann Dermatol 2011;23(2):225-8. DOI: 10.5021/ad.2011.23.2.225

6. La Rosa S, Sessa F, Capella C. Acinar cell carcinoma of the pancreas: overview of clinicopathologic features and insights into the molecular pathology. Front Med 2015;2:41. DOI: 10.3389/fmed.2015.00041

7. Chaudhary P. Acinar cell carcinoma of the pancreas: a literature review and update. Indian J Surg 2015;77(3):226-31. DOI: 10.1007/s12262-014-1049-y

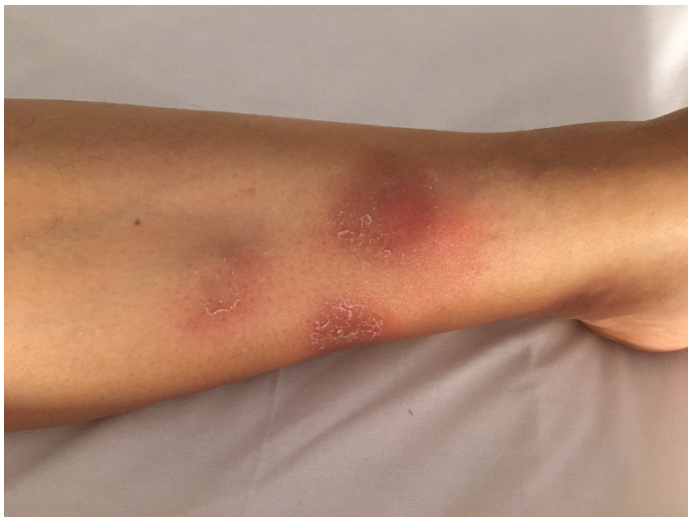

Fig. 1. Nodular skin lesions on the left lower limb.

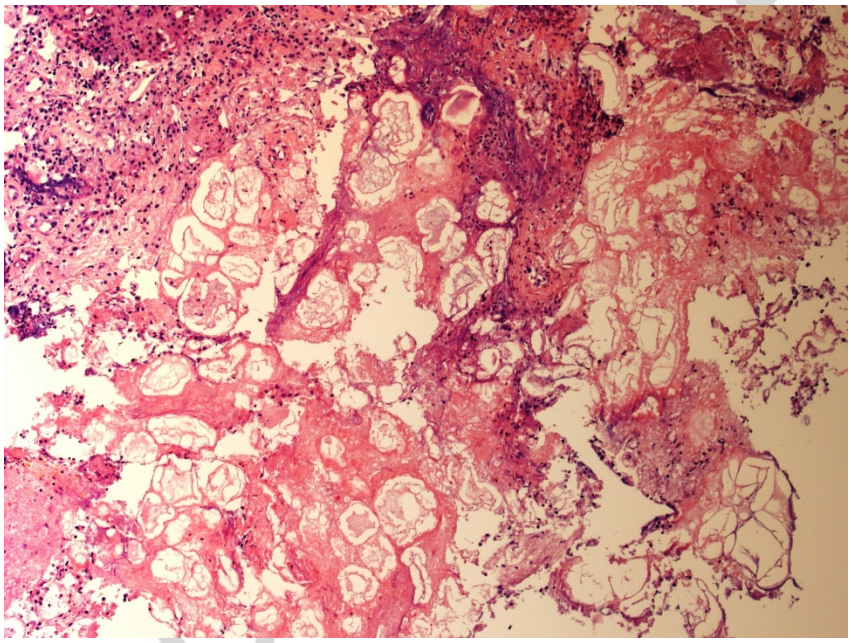

Fig. 2. Histological study of a skin biopsy sample (hematoxylin and eosin, x 10): lobular panniculitis with extensive enzymatic fat necrosis surrounded by areas with inflammatory infiltration and karyorrhexis.

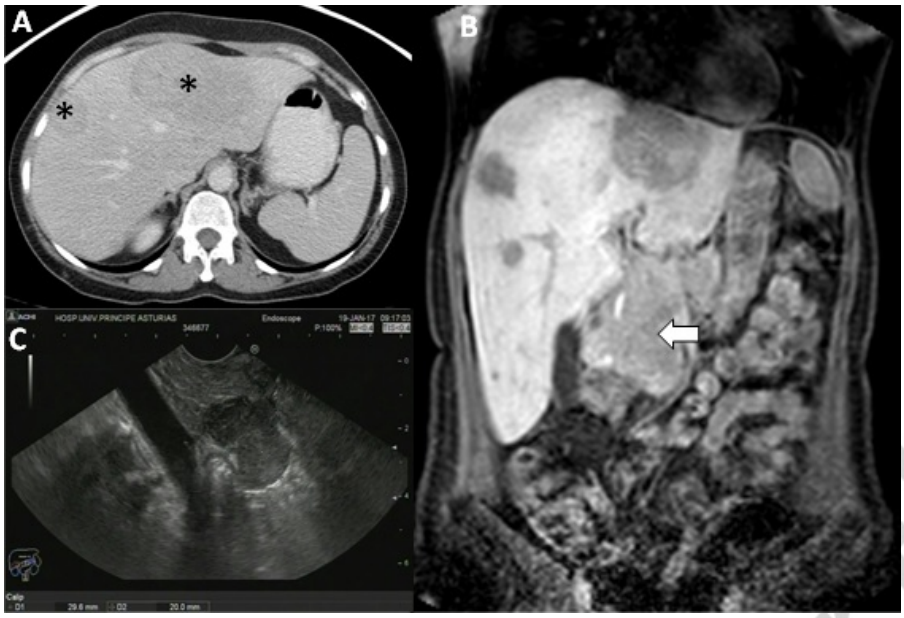

Fig. 3. A. CT section showing hypodense SOLs in the liver (asterisks). B. MRI with liver-specific contrast, late phase. Coronal reconstruction. A mass is visible in the uncinate process (arrow). C. Echoendoscopy image showing well-delimited hypoechoic SOL in the uncinate process.