Lobular panniculitis: A manifestation of pancreatic tumor with fatal outcome

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INTRODUCTION

Lobular panniculitis is a skin condition that may be the first sign of underlying pancreatic disease. Though rare, the condition has been sufficiently well defined and pathognomonic, thus making differentiation from idiopathic lobular panniculitis quite possible. A 77-year-old woman was in apparently good general health condition when developed skin lesions in a form of erythematous painful fluctuant nodules localized predominantly on the breast, but also present on the arms, thighs, and trunk. Her serum and urinary amylase levels were respectively 3 and 8 fold higher than normal. On histology, skin biopsy showed acute lobular panniculitis with large foci of adipocyte necrosis. Examination of the breast excluded any specific process other than nodular subcutaneous inflammation, but revealed a tumor of the pancreatic head. The nodules spontaneously ulcerated exuding an oily thick brownish material. Her condition deteriorated, and she became progressively debilitated. The patient died before operation, within the next 3 weeks. Subcutaneous fat necrosis was the first manifestation of an otherwise occult pancreatic disease with fatal outcome.

KEY WORDS: Lobular Panniculitis; Fat Necrosis; Pancreatic Neoplasms; Fatal Outcome; Tumor Markers, Biological

CASE REPORT

A 77-year-old non-atopic woman was admitted to the Clinic of Dermatovenereologic Diseases in Novi Sad, with a 4-month long history of painful disseminated skin nodules predominantly localized on the breast and thighs. Any specific process of the breast was previously excluded at the Institute of Oncology in Sremska Kamenica. The histology of an excised nodule showed the features consistent with erythema nodosum. On admission, the patient was in a good general health condition. Multiple, widespread, ill-defined erythematous and red-brownish edematous fluctuant nodules 1-3 cm in diameter were present on the arms, thighs, buttocks, and lower legs. A disproportionate number of lesions were concentrated on the left breast. Within the next few days, crops of new lesions developed. Some of the lesions extruded a thick, yellow-brownish oily material from the extensive ulcerations. The fistulated nodule on the right buttock resolved, leaving a central atrophic depression with multiple scars.

Laboratory investigations revealed the following abnormal tests: decreased white blood cell count 2.31 x 10⁹/L with 19.1% monocytes, increased lactate dehydrogenase 768 IU/L (normal range 230-460 IU/L), increased alanine aminotransferase 53 J/L (normally < 37 J/L), increased aspartate aminotransferase 110 J/L (normally < 37 J/L), increased gamma glutamyl transpeptidase 93 U/L (normally < 37 U/L), increased serum amylase 281 U/L (normally < 82 U/L), and increased urinary amylase 8390 U/L (normally <1000 U/L). The following serum levels of tumor markers were normal: CEA - carcinoembryonic antigens 2.42 mg/L (normally < 2.5 mg/L), AFP - alpha fetoprotein antigens 5.4 ng/ml (normally < 6 ng/ml), CA 15-3 carbohydrate antigen 21.7 U/ml (normally < 53.0 U/ml), CA 125 carbohydrate antigen 20.8 U/ml (normally < 21.0 U/ml). The serum level of tumor marker CA 19-9 carbohydrate antigen was increased 53.6 U/ml (normally <33.0 U/ml).

A biopsy of thigh necrotic nodule revealed lobular panniculitis with the characteristic picture seen in pancreatic fat necrosis. Focal areas of the subcutaneous fat necrosis were prominent, and surrounded by dense and diffuse lobular collections of polymorphonuclear leukocytes, lymphocytes, plasmocytes, and lipid-laden macrophages. Anucleated adipocytes surrounded by a thickened shadowy cell membrane resulting in a “ghost-like” appearance were grouped in small clusters at the center of the fat lobule (Figure 1). Microcysts surrounded by microvacuolated lipophages were also visible.
Abdominal ultrasound showed dilated ductus choledochus and the main pancreatic ductus of diameters 15 and 10 mm respectively, and an enlarged head and processus uncinatus of the pancreas, which on computed tomography (CT) showed a well defined hypodense polycystic expansive formation with dimensions of 25x50 mm, primary suggesting polycystic mucinous tumor of the pancreas (Figure 2).

Based on CT findings, it was only a duodenal diverticulum to be distinguished in differential diagnosis. Thus, barium supported gastroduodenal radiography was performed. Instead of diverticulum, an extraluminal compression of the proximal part of descendent duodenum was detected. A diagnosis of pancreatic panniculitis due to pancreatic tumor was considered.

Initially, the treatment was primarily supportive. Although a slight improvement in her laboratory values was detected, during this therapy the patient developed abdominal pain, fever, and arthralgias, not responsive to support measures, thus requiring continuous sedation. The nodules failed to respond clinically, and older nodules spontaneously ulcerated, draining an oily thick brown material (Figure 3). Her condition deteriorated, and she became progressively debilitated. The patient died before operation, 1 month after the diagnosis was made. Autopsy was not conducted respecting the patient’s family decision.

DISCUSSION

The syndrome of pancreatic disease and lobular panniculitis is rare, and appears in approximately 0.1-2% of all patients with pancreatic diseases (4,5,6). We can also confirm this rarity, since our patient is the first well-documented case at the Clinic of Dermatovenereologic Diseases in Novi Sad during the past 20 years. Although, for many years this form of panniculitis was classified as a variant of idiopathic Weber-Christian disease, regarding the most striking peripheral manifestation of pancreatic disease, the subcutaneous fat necrosis, it is now sufficiently well defined to be distinguished from idiopathic lobular panniculitis (7,8). Pancreatic panniculitis, also named enzymatic panniculitis, has distinctive clinical and pathognomonic histopathologic findings that can be the presenting features of pancreatic disease, preceding its clinical symptoms in more than 40% cases by an average of 13 weeks (range 2-28 weeks) (1). Furthermore, at least 2% of all cases of acute pancreatitis are clinically silent (6). Thus, in our patient, skin lesions were quite distinct, suggesting the diagnosis of pancreatic disease even in the absence of abdominal symptoms. With the exception of α1-antitrypsin deficiency, the evolution of red painful nodules into sterile necrotic abscesses with spontaneous ulceration and drainage of the brownish oily material, which represents adipose tissue that has undergone liquefactive necrosis, could hardly be seen in association with other panniculitides (7,8).

The distal parts of the lower extremities are the most frequent locations of these lesions, although crops of nodules also appear on the arms, thighs, trunk, and at any other location. It is very peculiar concentration of lesions on and around the left breast, that was seen in our patient, although, subcutaneous nodules of pancreatic panniculitis in patients with pancreatic tumor tend to be more numerous, chronic, with ulceration, and involvement of cutaneous areas beyond the lower extremities (1). Nevertheless, when conducted a retrospective review of 11 patients with pancreatic panniculitis (6 with carcinoma and 5 with pancreatitis), Dahl et al, found only 1 patient with lesions on the chest, the patient was male and had pancreatic carcinoma (1).

In the past, the syndrome of pancreatic panniculitis was reported much more frequently among elderly males, but in a recent review, almost equal male to female ratio of 1.3:1 was reported (1). Our case supports this trend.
From a pathogenic point of view, it has been proposed that pancreatic enzymes, mostly amylase and lipase, that escape to the blood from the diseased pancreas are responsible for the subcutaneous fat necrosis in this panniculitis (8,9). Elevated serum and/or urinary amylase and/or lipase levels may serve as a helpful laboratory study to confirm diagnosis. This elevation was also documented in our case. However, pancreatic enzymes must not be the only etiologic factor, since there is a discrepancy between the relative frequency of pancreatic diseases with high serum levels of amylase and/or lipase, and the fact that pancreatic panniculitis is a rare disease. Moreover, there are well-documented cases of pancreatic panniculitis with normal serum levels of all pancreatic enzymes (10).

Since no other disease of the subcutaneous tissue histologically resembles pancreatic fat necrosis with a characteristic coagulative necrosis of the adipocytes, which leads to “ghost-like” cells, a deep skin biopsy is perhaps the most useful diagnostic test (11). Although pancreatic panniculitis shows the characteristic features of lobular panniculitis with extensive necrosis of the adipocytes, which we also detected in our patient, it is not surprising that the first histologic diagnosis was a sepal panniculitis of erythema nodosum. A similar case was reported by Durden et al. (12). Mostly, the histopathologic findings depend on the clinical stage and duration of the lesions (1,11). Thus, the earliest features of the septal panniculitis could result from the enzymatic damage of blood vessels within the sepal, which allow the crossing of pancreatic enzymes from the blood to the lobules (7,8). Moreover, we have demonstrated several different types of fat necrosis other than typically pancreatic, such as lipophagic and membranous, which in our patient was very extensive, producing microcysts, a late-stage necrosis of adipocytes (7).

In 80-100% of cases, the underlying pancreatic condition is either pancreatitis or pancreatic carcinoma. It has more frequently been described with acinar cell carcinoma, and less commonly with pancreatic islet cell carcinoma (1,8,13,14,15,16). Although acinous carcinoma accounts for only 10% of all pancreatic carcinomas, it accounts for more than 84% of all cases of pancreatic tumor panniculitis (14). Other less frequent pancreatic abnormalities include pancreas divisum, pancreatic cysts and pseudocysts, and vasculopancreatic fistulas (8,14). The underlying condition in our patient was a pancreatic tumor. In the absence of autopsy and histopathology of the tumor, any discussion about the nature of the tumor will be only speculative. Ca 19-9 is known as the most sensitive/ specific marker in the diagnosis of pancreatic cancer currently in use. Increased concentration Ca 19-9 > 37 U/ml is elevated in 87% of pancreatic cancer patients (17). The measurement of CA 19-9 assay values has been reported to be an aid in the management of patients with pancreatic or gastrointestinal cancer. Moreover, every elevation of CA 19-9, which has been observed in patients with metastases and in nonmalignant conditions, such as pancreatitis, hepatitis, cirrhosis, and nonmalignant gastrointestinal diseases has to be considered in conjunction with information available from clinical evaluation and other diagnostic procedures (18).

Treatment of pancreatic panniculitis is primarily directed to the underlying pancreatic disease. Although the treatment of subcutaneous fat necrosis and the associated underlying pancreatic disease is primarily supportive, in some cases as in our patient, surgical treatment is inevitable (14). Nevertheless, disseminated fat necrosis is a rare, but often, fatal complication of pancreatic disease. In a review of patients with pancreatic panniculitis done by Dahl et al., all patients with pancreatic carcinoma and 40% of the patients with pancreatitis died of their disease (1).