

## Pancreatic Panniculitis as a First Sign of Liver Carcinoma

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Sir,

Pancreatic panniculitis (PP) is a rare disease that is caused by the massive release of pancreatic enzymes into the bloodstream and results in cytosteatonecrosis of the hypodermis. PP is clinically characterized by painful or asymptomatic nodules of the legs that closely resemble erythema nodosum or infectious panniculitis (1). The nodules may sometimes spontaneously ulcerate and drain brownish gelatinous sterile material. From a histopathologic point of view, PP is a mainly lobular panniculitis with intense, characteristic necrosis of adipocytes. We report on a case of PP with a dramatic presentation of massive cancer of the liver.

### CASE REPORT

An otherwise healthy 58-year-old man developed erythematous subcutaneous nodules on both legs (Fig. 1). None of the nodules showed an ulcerative evolution or fistulization. The nodules were tender and painful. During hospitalization, laboratory examination showed increased hepatic enzymes (aspartate amino transferase 65 U/l [normal values 0–37],

amino alanine transferase 196 U/l [normal values 0–40], gamma glutamyl transpeptidase 430 U/l [normal values 11–50]) and above all an increase in pancreatic amylase (11346 U/l [normal values 10–220 U/l]) and isoamylase (8620 U/l, [normal value 10–115 U/l]). An insuline-dependent diabetes was also diagnosed (glycosuria 599 mg/dl [normal values 0–15 mg/dl]). The



Fig. 1. Multiple erythematous nodules on both the legs.

patient denied alcohol abuse and any previous abdominal symptoms.

Liver ultrasonography showed the presence of numerous hypoechoic nodules, 5 mm–6 cm in diameter, which were biopsied. Histologic examination revealed hepatocellular carcinoma with a trabecular structure and acinar aspects. A total body CT scan confirmed structural alterations of the liver but did not reveal any pancreatic focal lesions.

A biopsy of a nodule of the leg showed the typical pattern of hypodermic steatonecrosis with areas of lobular fat necrosis. Anucleate, necrotic adipocytes with a ghostlike appearance were present. A month later, the patient developed acute, severe and painful arthritis of the ankles, knees and hands. Culture from synovial liquid was negative. The patient was treated with low-dose steroids and antibiotics but with only a slight improvement of the lesions.

As the primary hepatic tumour was in an advanced stage and virtually unresponsive to chemotherapy, after consultation with the oncologist, the patient himself decided not to undergo further treatment. He died 4 months later of complications.

## DISCUSSION

PP is caused by liquefactive fat necrosis caused by pancreatic enzymes (amylase, trypsin, lipase) in the subcutis (1–3).

The pancreatic diseases most frequently associated with PP are acute or chronic pancreatitis, pancreatic carcinoma, lithiasis of the pancreatic duct, abdominal traumatic or ischaemic events and even malformations (3–6). Moreover, there have also been cases where high levels of pancreatic lipase were detected but no pancreatic disease was recognized (7).

PP may be found at the time of diagnosis of a pancreatic disease, or later. However, according to Hughes et al. (4) and Dahl et al. (5), cutaneous lesions preceded the diagnosis of pancreatic involvement in 40% and 45% of cases, respectively. In our case, the panniculitis was the presenting feature of a primitive liver tumour; in fact the patient had been completely symptomless until that moment.

Although the most striking peripheral manifestation of pancreatic disease is subcutaneous fat necrosis, monoarticular or oligoarticular arthritic symptoms have been reported in 56% of the patients of Dahl's series and in rare cases have preceded the other

symptoms of the disease (8). These arthritic manifestations are not a primary inflammatory process of the articular synovial tissues, but are caused by focal necrosis of the periarticular fat (9, 10). The intramedullary fat, the omentum and the peritoneum may also be affected.

When a panniculitis closely resembling erythema nodosum develops in association with intestinal symptoms, arthritis or polyserositis, a diagnosis of PP must be taken into consideration and a cutaneous biopsy carried out. The characteristic pathological findings resulting from the biopsy lead to identification of the disease and suggest the most appropriate clinical examinations, after which a treatment can be chosen.

To the best of our knowledge, this is the first case in which PP was due to a primitive liver cancer. Although the total body CT scan did not reveal any pancreatic lesions, we hypothesize that a reactive inflammatory process and/or pancreatic compression may have led to the massive release of pancreatic enzymes.

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