

Inflamed Bipedal Nodules with a Distant Occult Cause

A 76-year-old Chinese male presented with red and tender rashes associated with progressive swelling over both lower limbs for 2 weeks. Concurrently, he had fever and non-bloody diarrhoea. There was no abdominal pain, joint pain, loss of appetite or weight. He was otherwise systemically well. His past medical history was significant for diabetes mellitus, hypertension and hyperlipidaemia. Long-term medications included glipizide, metformin, enalapril, nifedipine and simvastatin. There were no new medications commenced 6 months prior to the onset of his rashes.

On examination, there were warm tender erythematous nodules over both anterior shins, posterior aspect of calves and thighs (Figs. 1A and 1B). Pitting oedema up to the level of the knees was present. Cardiovascular, respiratory and abdominal examination was unremarkable.

Histological examination of a skin biopsy from the left thigh showed fat necrosis with “ghost-like” cells, characterised by anucleated adipocytes with a partially digested cell membrane (Fig. 2). This was also accompanied by basophilic deposits of saponified fat (Fig. 3).

What is the diagnosis for these cutaneous lesions?

- A. Erythema nodosum
- B. Erythema induratum
- C. Lupus profundus
- D. Subcutaneous panniculitis-like T cell lymphoma (SPTCL)
- E. Pancreatic panniculitis

Discussion

The serum amylase was 767 U/L (normal 36-128 U/L) and serum lipase was >400 U/L (normal 5-50 U/L). The leukocytes was mildly elevated at 9.5 ($3.6-9.3 \times 10^9/L$), c-reactive protein was 112 mg/L (0-5), pro-calcitonin was 0.33 ug/L (0-0.05) and adjusted calcium was 2.44 mmol/L (2.15-2.58). His liver function test was as follows: alkaline phosphatase 527 U/L (38-126), gamma-glutamyl transpeptidase 492 U/L (7-50), alanine aminotransferase 67 U/L (17-63), aspartate aminotransferase 62 U/L (15-41), bilirubin 17 $\mu\text{mol/L}$ (7-31) and albumin 25 g/L (35-48). Magnetic resonance imaging (MRI) of the pancreas revealed

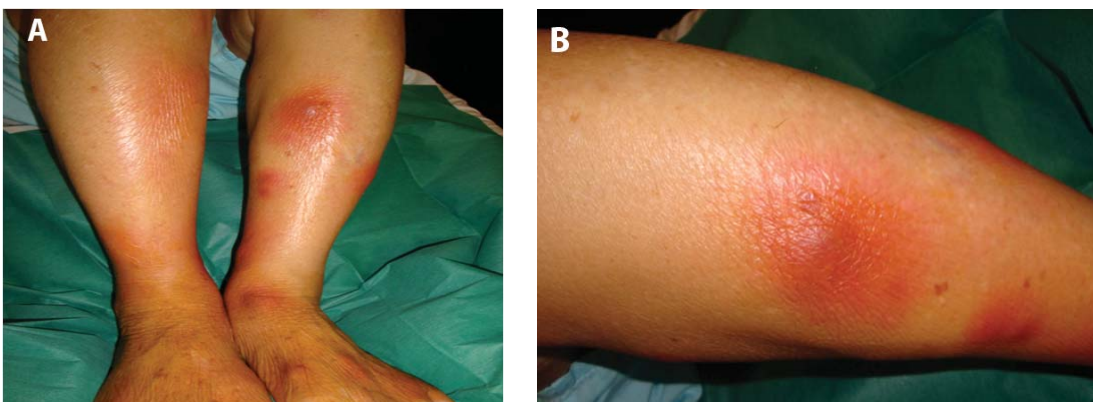


Fig. 1. Images showing the nodules in the patient. In A), inflamed subcutaneous nodules on a background of lower limb oedema are seen. In B), a closer look of the multiple tender erythematous nodules over the patient's left anterior shin.

Answer: E

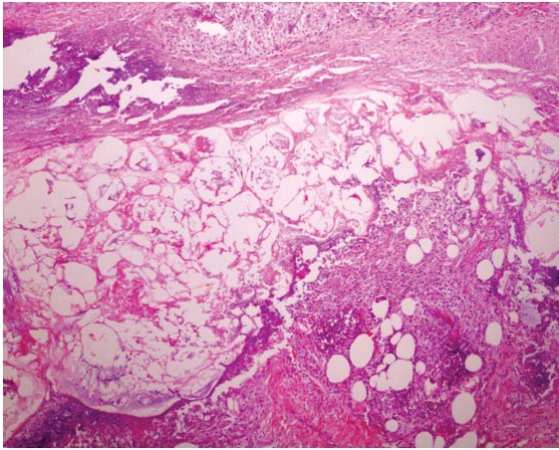


Fig. 2. Adipocytes within fat lobules with fat necrosis and retention of ghost outline. There is an infiltrate of neutrophils admixed with eosinophils and histiocytes within the fat septae, associated with surrounding necrotic adipocytes. (Haematoxylin and eosin, x 200).

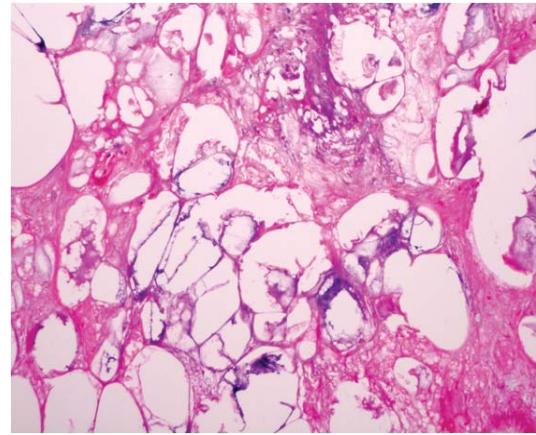


Fig. 3. Amorphous basophilic material due to deposition of calcium salts is present within ghost cells. (Haematoxylin and eosin, x 400).

a fluid-filled collection in the pancreatic head, reminiscent of a pseudocyst. The pancreatic head, body and tail appeared swollen with peripancreatic fat stranding. This was consistent with a diagnosis of acute on chronic pancreatitis complicated by a pseudocyst. Although there were no gallstones visualised in the common bile duct on imaging, gallstones with pericholecystic fluid were noted in the gallbladder, which may be the aetiology for his pancreatitis. Otherwise, he did not report any history of chronic alcohol ingestion. He was managed conservatively for his pancreatitis with intravenous antibiotics and supportive treatment after declining all further investigations. Fobancort, a potent topical corticosteroid cream containing betamethasone dipropionate 0.064% with fusidic acid 2% and local wound care were administered to some of the nodules that had begun to ulcerate. The nodules gradually healed within the next 3 months. A repeat MRI 6 months later showed resolution of the pancreatic pseudocyst with no relapse of his panniculitis.

Pancreatic panniculitis is rare, occurring in patients with acute or chronic pancreatitis or less commonly, pancreatic carcinoma (especially of the acinar type). In many cases, the cutaneous lesions are the initial presenting sign, preceding pancreatic disease by months.¹

Clinical presentation includes tender erythematous subcutaneous nodules typically on the lower limbs that may become fluctuant or ulcerated with an associated oily exudate. Systemic involvement can include visceral, periarticular and intraosseous fat necrosis. The condition can also comprise of an inflammatory polyarthritis, polyserositis, fever and abdominal pain. As in our patient,

signs of pancreatic disease upon presentation of panniculitis are not a prerequisite for its diagnosis.¹

It is believed that the release of pancreatic enzymes; such as amylase, lipase, phosphorylase and trypsin, play an important role in the pathogenesis of pancreatic panniculitis. Trypsin increases the permeability of blood vessels, allowing enzymes such as lipases to act on lipids in the adipocyte cell membrane and interior, leading to fat necrosis and inflammation. Another potential aetiology is blood vessel damage via inflammation or oedema during an infection, resulting in increased endothelial cell permeability.²

The diagnosis of pancreatic panniculitis is confirmed by the presence of pancreatic disease and typical histopathological findings. Histopathological features include a mostly lobular panniculitis without vasculitis. However, in the very early stage, a septal pattern has been described. Enzymatic damage allows pancreatic enzymes to cross from blood to fat lobules resulting in coagulative necrosis of the adipocytes and pathognomonic "ghost cells". These are anucleate necrotic cells with thick walls and fine basophilic granular material within their cytoplasm from dystrophic calcification.³ Treatment is primarily supportive and should be directed to the underlying pancreatic disease.

We describe a case of pancreatitis diagnosed through the presentation and histological analysis of panniculitic nodules on the legs. As demonstrated in this case, gastrointestinal symptoms may be absent or subtle, and an early diagnosis could be made through measurement of serum pancreatic enzymes levels.

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Harumi Ochi,¹ MBBS, Evelyn YX Tay,¹ MBBS, Joyce SS Lee,¹
MBBS, MRCP (UK), M Med (Int Med), Hong Liang Tey,^{1,2} MBBS, FRCP (Edin), FAMS

¹National Skin Centre, Singapore

²Lee Kong Chian School of Medicine, Nanyang Technological University, Singapore

Address for Correspondence: Dr Tey Hong Liang, National Skin Centre, 1
Mandalay Road, Singapore 308205.

Email: teyhongliang111@yahoo.com
