

## Case 2: Pancreatic Panniculitis

by Dr. M.H. Ho

Date:	11 March 1998
Venue:	Yaumatei Skin Center
Organizer:	Social Hygiene Service, DH; Clinico-pathological Seminar

### CASE SUMMARY

#### History

LSC was a 91-year old lady and was first presented to the Medical Unit of Queen Mary Hospital. For three months she had been suffering from painful nodules on both legs and arthralgia. Dermatological opinion was consulted. She was seen by a private dermatologist before hospitalization, and was treated as nodular vasculitis with non-steroidal anti-inflammatory drugs and cephalexin without much improvement. Her past health was unremarkable. There was no past history of pulmonary tuberculosis.

#### Physical examination

There were multiple, tender, erythematous subcutaneous nodules on both calves and shins (Figure 1). Left knee swelling was noted.

#### Differential diagnoses

The differential diagnoses included erythema induratum, erythema nodosum, and other panniculitis.

#### Investigations

Complete blood picture showed normochromic, normocytic anaemia with Hb 10g/dl. ESR was 70 mm/hr. Liver function test showed elevated ductal enzymes; alkaline phosphatase 386 U/L (normal: 55-160), gamma glutamyl transferase 221 U/L (normal: 8-57) and alanine amino transferase 34 U/L (normal: 5-31); aspartic amino transferase 74 U/L (normal 14-36); albumin 27 g/L (normal: 44-56). The serum amylase was normal. Fasting lipid profile was within normal limit. CEA,  $\alpha$ FP



**Figure 1: Erythematous subcutaneous nodule on right leg**

were normal. CA19.9, a tumour marker specific for pancreatic carcinoma, was 46 U/ml (normal: 0-37). According to opinion of the gastroenterologist, the result was non-specific. In carcinoma of pancreas, the CA 19.9 level should be highly elevated, at least 100 U/ml.

Chest X-ray was normal. Abdominal X-ray did not show any pancreatic calcification.

Aspiration of the left knee was performed. The synovial fluid was very turbid with a total cell count of 15000 x 10<sup>6</sup>/l. The cells composed of neutrophil 69%, lymphocyte 1% and mononuclear cell 30%. There were positive birefringent crystals consistent with calcium pyrophosphate. Gram stain was negative. The culture did not grow any organism.

Skin biopsy was performed on the right calf. It showed extensive lobular fat necrosis in the subcutis. Ghost fat cells and basophilic amorphous calcification were observed. The inflammatory infiltration consisted of lymphocytes, histiocytes, neutrophils and a significant number of eosinophils. There was no evidence of vasculitis. Immunofluorescent studies were negative. The diagnosis was lobular panniculitis and fat necrosis. The pattern was compatible with pancreatic panniculitis.

Ultrasonic examination of the abdomen showed that the liver was slightly enlarged. Multiple echogenic nodules were seen in both lobes of liver, compatible with multiple liver metastases. Biliary tree was not dilated. Gallbladder was unremarkable with no stone inside. Portal vein was patent with normal flow direction. Spleen was not enlarged. Pancreas appeared normal in the head and body region. The tail of pancreas was obscured. No obvious pancreatic mass lesion was seen. Both kidneys were unremarkable. Multiple hypoechoic nodules were seen at the para-aortic region, consistent with multiple para-aortic lymphadenopathy. The impression was **multiple liver metastases and para-aortic lymphadenopathy**.

### Progress

The patient was transferred to convalescent hospital. She subsequently died several weeks later. Post-mortem examination was refused by her relatives.

## REVIEW ON PANCREATIC PANNICULITIS

Pancreatic panniculitis is a rare complication of pancreatic diseases in which necrosis of fat occurs in the skin and other distant foci. It was first described by Chiari in 1883.<sup>1</sup> Not until 1947 was it first reported in the English literature by Szymandic and Bluefarb. They described the pathognomonic histopathologic findings of focal subcutaneous fat necrosis and 'ghost-like' cells.<sup>2</sup> The association of panniculitis with underlying pancreatic pathologic conditions, either pancreatitis or pancreatic carcinoma, varies from 80% - 100%.<sup>1</sup> Other associations include islet cell carcinoma, abdominal trauma, pancreatic pseudocysts, and sulindac therapy.<sup>2</sup>

### Clinical features:<sup>1, 2, 4</sup>

There are tender, firm, erythematous subcutaneous nodules on the lower extremities. It can occur on thighs, buttocks, trunk, upper extremities and the scalp. They tend to appear in groups which become confluent and ulcerate, draining oily, odorless fluid. It is associated with polyarthropathy, usually involving the ankles. Polyserositis and intramedullary fat necrosis of bone can also happen. There may be peripheral eosinophilia. The serum amylase and/or lipase level are usually elevated.

The differential diagnoses should include all types of panniculitis such as erythema nodosum, erythema induratum, etc.

### Histology

The histologic features are pathognomonic. The characteristic findings include the following:<sup>1, 2</sup> focal subcutaneous fat necrosis; ghost-like cell (which is a residual cell membrane of adipocytes partially digested by pancreatic enzymes with no nucleus); finely granular dystrophic calcification caused by saponification of free fatty acids released by enzymatic hydrolysis of adipocyte triglyceride.

Dahl PR et al studied 11 patients with pancreatic panniculitis.<sup>1</sup> They found that the histologic findings varied with the clinical stage and duration of the lesions.

In acute lesion, it is characterised by acute lobular and septal panniculitis, focal fat necrosis, ghost-like cells. There are fine basophilic material within the cytoplasm of the necrotic cells at the periphery of the involved foci, representing saponified calcium. The necrotic areas are relatively free of inflammatory cells centrally but are surrounded by dense and diffuse collections of lymphocytes, macrophages, polymorphs and a variable number of eosinophils.

In chronic lesion, fat necrosis and ghost cells are less prominent. They are replaced by a granulomatous infiltrate consisting of Langhans giant cells, epithelioid macrophages and lymphocytes. Lipid laden macrophages are prominent. The septal and paraseptal areas are usually fibrotic.

### Pathogenesis

The mechanism of pathogenesis is poorly understood.

Pancreatic enzymes are postulated to play an important role. Pancreatic lipolytic enzymes, principally lipase, are released by the pancreas into the blood vessels or lymphatics and are subsequently activated at distant sites.<sup>2, 3, 4</sup> This is supported by the demonstration of positive intracellular staining of adipocytes with a monoclonal antibody to pancreatic lipase in a lesion of subcutaneous pancreatic fat necrosis.<sup>5</sup>

Some reports suggest that other factors are needed. An immune-complex mechanism is believed to be involved in the pathogenesis.<sup>5, 6, 7</sup>

In vitro study had been conducted to induce pancreatic panniculitis by incubating a piece of normal human breast skin in a medium containing serum human pancreatic lipase and amylase derived from a patient with fatal pancreatitis and pancreatic panniculitis. It failed to induce any subcutaneous fat necrosis. It was concluded that lipase and amylase alone were not sufficient to induce lipocyte necrosis.<sup>3</sup>

### Management

There is no specific treatment of pancreatic panniculitis. Supportive treatment is helpful. Treating

the underlying pancreatic diseases can sometimes lead to resolution of the lesions.<sup>1, 8</sup> Surgical removal of pancreatic pseudocyst or cholecystectomy in gallstone pancreatitis had resulted in complete resolution of the pancreatitis and panniculitis. Most cases require intravenous fluid and antibiotics as well as intensive monitoring. In cases of pancreatic carcinoma associated panniculitis, the tumour is usually not operable at presentation.

### **Learning points:**

*It is important to consider the possibility of pancreatic disease in a patient with panniculitis.*

### References

1. Dahl PR, Su WP, Cullimore KC, Dicken CH. Pancreatic panniculitis. *J Am Acad Dermatol* 1995; 33(3):413-7.
2. Ball NJ, Adams SP, Marx LH, Enta T. Possible origin of pancreatic fat necrosis as a septal panniculitis. *J Am Acad Dermatol*. 1996; 34(2 Pt2):362-4.
3. Berman B, Contreas C, Smith B, Leong S, Hornbeck L. Fatal pancreatitis presenting with subcutaneous fat necrosis. Evidence that lipase and amylase alone do not induce lipocyte necrosis. *J Am Acad Dermatol*. 1987; 17(2 Pt2):350-62.
4. Durden FM, Variyam E, Chren MM. Fat necrosis with features of erythema nodosum in a patient with metastatic pancreatic carcinoma. *Int J Dermatol*. 1996; 35(1):39-41.
5. Dhawan SS, Jimenez Acosta F, Popliti RJ, Barkin JS. Subcutaneous fat necrosis associated with pancreatitis: histochemical and electron microscopic findings. *Am J Gastroenterol*. 1990; 85(8):1025-8.
6. Potts DE, Mass MF, Iseman MD. Syndrome and pancreatic disease, subcutaneous fat necrosis and polyserositis: case report and review of literature. *Am J Med* 1975; 58:417-23.
7. Zellman GL. Pancreatic panniculitis (letter). *J Am Acad Dermatol*. 1996; 35(2 Pt1):282-3.
8. Lambiasi P, Seery JP, Taylor-Robinson SD, Thompson JN, Hughes JM, Walters JR. Resolution of panniculitis after placement of pancreatic duct stent in chronic pancreatitis. *Am J Gastroenterol*. 1996; 91(9):1835-7.