

A Case of Subcutaneous fat Necrosis Associated with Pancreatitis

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We report a case of subcutaneous fat necrosis associated with pancreatitis that may be the first case in Korean literature as far as we know. The patient was a 41-year-old man who presented erythema nodosum-like erythematous subcutaneous nodules on both lower extremities.

Histopathologic findings showed subcutaneous focal fat necrosis and ghost-like cells. Granular basophilic material was deposited in and around the necrotic fat cells and stained positively with von Kossa stain.

The lesions subsided gradually without any specific treatment, as the underlying pancreatitis was ameliorated. (*Ann Dermatol* 8:(1)38-42, 1996).

Key Words : Subcutaneous fat necrosis. Pancreatitis

Subcutaneous fat necrosis, a type of panniculitis associated with pancreatic disease, is a rare entity that was first described in 1883 by Chiari¹, but has not yet been reported in Korean literature.

The clinical differential diagnoses include a wide range of panniculitis and collagen vascular disease. In general, the diagnosis of subcutaneous fat necrosis is suggested by the presence of pancreatic disease and is confirmed by the characteristic histopathologic findings of biopsy specimens.

We experienced a case of subcutaneous fat necrosis associated with pancreatitis and intend our report to be a source of fundamental information for any further advanced study.

REPORT OF A CASE

A 41-year-old man consulted our department for his skin lesions which consisted of multiple, variable sized (few millimeters to 1 cm), tender,

erythematous subcutaneous nodules on both lower extremities which developed 2-3 days after admission due to acute pancreatitis (Fig. 1). The patient had a medical history of alcoholism and smoking for about 20 years. His vital signs were stable except for a mild fever. A skin biopsy was taken from a nodule on the shin and stained with H & E (Fig. 2). The epidermis appeared normal. In the dermis, there was a moderate perivascular lymphohistiocytic infiltration and also signs of periappendageal and perifollicular infiltration of lymphocytes and eosinophils. The characteristic histopathologic changes were fat necrosis and fine granular basophilic material deposition within and around the necrotic fat cells in the subcutaneous tissue. There were "ghost like" fat cells with thick shadowy walls and no nuclei (Fig. 3). Von Kossa stain for calcium was positive in the area of fine granular basophilic material.

On admission, there were leukocytosis (18,000/mm³) without eosinophilia, elevated ESR (28 mm/hr) and blood urea nitrogen (41 mg/dl), normal liver function test and electrolytes except for hypocalcemia (7.5 mg/dl). The serum amylase elevated markedly to 6560 U/L, but serum lipase changes were not so remarkable (0.2 to 1.44 U/L ;

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Fig. 1. Multiple, tender, erythematous subcutaneous nodules are noted on both lower extremities especially on the extensor surface.

Fig. 2. The epidermis appear normal but perivascular and periappendeal inflammatory infiltrates are shown in the dermis. Focal fat necrosis and fine granular basophilic material deposition are observed in the subcutis (H & E, $\times 40$).

Fig. 3. Ghost-like fat cells with thick shadowy walls and no nuclei are well noted in and around the necrotic area (H & E, $\times 100$).

Fig. 4. Pancreatic pseudocyst (arrow heads) with calcifications (arrow) is shown by abdominal CT scan.

normal range 0-1 U/L). C-reactive protein and RA factor were positive but negative for ANA, VDRL, and viral hepatitis markers. The chest PA view showed left pleural effusion and right lung consolidation. Massive ascites and fluid-debris levels with stippled calcifications on the inferior and posterior to the pancreatic head portion with pancreatic pseudocyst was revealed throughout the

abdominal CT scan (Fig. 4), and on ERCP (endoscopic retrograde cholangiopancreatography), there was pancreas divisum (Fig. 5), that would contribute to pancreatitis. In peritoneal and mesenteric biopsy with repeated abdominal paracentesis, no evidence of malignancy was detected. The skin lesions subsided gradually several (4 to 5) days after the skin biopsy without any specific therapy, as

the underlying pancreatitis was ameliorated. Serum amylase levels correlated roughly with clinical recovery (Fig. 6). We could find no other cutaneous complications except for residual mild hyperpigmentation.

Fig. 5. Typical finding of pancreas divisum is well shown by ERCP.

* : common bile duct.

arrow head : duct of Santorini

arrow : duct of Wirsung

DISCUSSION

Subcutaneous fat necrosis associated with pancreatic disease is a very rare entity. It is not difficult to misdiagnose when multiple tender erythematous nodules initially appear on the legs if there is no information about pancreatitis. The entities most often considered in the differential diagnosis include a wide range of panniculitis : erythema nodosum, Weber-Christian disease, lupus profundus, and collagen vascular disease : polyarteritis nodosa, hypersensitivity vasculitis, Wegener's granulomatosis, systemic lupus erythematosus, and others : subacute bacterial endocarditis, gout, thrombophlebitis, Whipple's disease, cutaneous lymphoma². The eruptions resolve with hyperpigmentation and occasional scarring. This entity occurs more commonly in the male patient. Pancreatitis caused by chronic alcoholism associated most commonly with this entity; other causes include cholelithiasis, trauma, and rupture of a pancreatic pseudocyst³. Other cases associated with pancreatic adenocarcinoma and acinar cell carcinoma usually have a metastatic disease and a poor prognosis⁴. Our case showed skin lesions confined to the lower extremities which resolved with mild hyperpigmentation without scarring. We could find no evidence of malignancy and the clinical course was relatively favorable.

Arthropathy, synovitis, painful osteolytic bone lesions with medullary necrosis, and polyserositis are known as extracutaneous findings^{3,5}. Joint

Fig. 6. The skin lesion lasted from the 4th admission day to the 11th day. The change of serum amylase level correlated roughly with the recovery from pancreatitis.

manifestations most commonly involve the ankles and have great diagnostic importance^{5,6}, but our patient complained only of mild arthralgia on the knee and ankle joints.

The diagnosis of subcutaneous fat necrosis is confirmed by the characteristic histopathologic findings of the biopsy specimens that include foci of fat necrosis with ghost-like fat cell with thick shadowy walls and no nuclei⁷. Areas of fat necrosis are surrounded by polymorphous inflammatory infiltrates including neutrophils, histiocytes, foamy cells, foreign body giant cells, and lymphocytes. Granular basophilic material in and around the fat cells stains positively with von Kossa.

Berman et al⁸ performed in vitro study where they incubated normal subcutaneous fat with either human pancreatic amylase or lipase, but there were no significant changes such as fat cell necrosis or saponification. Well-documented cases of fat necrosis also have been described in the presence of normal serum lipase levels^{2,9}. Wilson et al¹⁰ examined serum lipolytic enzyme levels serially on a patient with arthropathy and subcutaneous nodules associated with pancreatitis, and found there were persistent elevation of phospholipase A, trypsin, and lipase in serum. The lipids content in the aspiration of a subcutaneous nodule and synovial fluids were predominantly nonesterified fatty acid.

The pathogenesis is poorly understood and may be related to the release of enzymes from the pancreas into the circulation after a complex interaction between trypsin, lecithinase, phospholipase A, and free fatty acids allows the pancreatic lipase to absorb and enter the fat cells^{8,10}. Lipase-mediated fat degradation results in the liberation of free fatty acids that combine with calcium to form calcium soaps¹¹. In addition, Rubinstein et al¹² proposed an association between disseminated fat necrosis and α 1-antitrypsin deficiency that might contribute to the low incidence of this syndrome. In our case, serum amylase levels elevated markedly but serum lipase level changes were subtle. Unfortunately, we did not conduct an in vitro study as noted above. Such a future study needs to be related with the pathogenesis of enzymatic fat necrosis.

Various treatment modalities include lipase inhibitors, parenteral corticosteroids, NSAID, and immunosuppressants' agents, but they have not been effective in treating the cutaneous lesions^{5,13-15}. Medical and surgical treatments of the underlying

pancreatic disease are the primary therapeutic approaches. Bed rest, leg elevation, compression stockings, and pain control may be of benefit for symptom relief^{5,16}. In our patient, the skin lesions subsided gradually without any specific treatment, as the pancreatitis was ameliorated.

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