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Weber-Christian disease and pituitary dysfunction in a patient with polymyositis

Sirs,

In August 1998, a 48-year-old Chinese male was diagnosed as having polymyositis with myalgia, proximal muscle weakness, elevated muscle enzymes and electromyogram showing slow waves. He was treated with prednisone and azathioprine and became symptom-free until a fever with cough occurred in September 2001. He was given empirical antibiotic treatment and made an uneventful recovery.

In November 2001, the patient developed excessive, symmetrical painful dark erythematous nodules ranging from 1 to 5 cm^2 on his limbs, fever and chills, myalgia, arthralgia and abdominal distention. Physical examination revealed an expressionless facial appearance. Blood analysis showed neutrophilia (7.2 x 10^9/L), erythrocyte sedimentation rate 115 mm/hour, C-reactive protein 11.17 mg/dl (normal range 0-16), creatinine phosphokinase 331 u/L (20-174), lactate dehydrogenase 376 u/L (109-245), serum amylase 120 u/L (0-95), urine amylase 260 u/L(0-490), free T3 1.50 mol/L(2.30-6.36), T4 4.22 pmol/L (8.36-29.6), thyroid-stimulating hormone 0.25 mIU/L (0.4-4.0), adrenocorticotropic hormone < 1 pg/ml (0-46), morning and afternoon serum cortisol (8:00 and 14:00) 38.8 ng/ml (68.9-223.9) and 157.9 ng/ml (19.4-115) respectively, and testosterone 5.2 nmol/L (7.3-52.3). MRI showed no pituitary gland compression. Search for an underlying malignancy was negative. Biopsy of the subcutaneous nodules suggested active panniculitis (Fig. 1). No bacterial pathogens were isolated from the patient's blood, sputum or skin biopsy.

The patient was diagnosed as having Weber-Christian disease with pituitary necrosis and dysfunction, recent chest infection and underlying polymyositis. He was treated with prednisolone 40-20 mg/d for 3 months to no avail. Intravenous immunoglobulin G 10 g/day over 5 days was given, but the response was unsatisfactory with relapse of fever. Three pulses of low-dose iv cyclophosphamide (0.4 g/10-21 day) also failed to control the condition. Leflunomide (20 mg/day) (1) was added to his drug regimen and he made a full recovery after 2 months. Our patient fulfilled all of the following 3 criteria for Weber-Christian disease: (1) fever, arthralgia, myalgia and relapsing painful subcutaneous nodules; (2) scar lipoatrophy of the nodules; (3) pathological evidence with characteristic panniculitis (2, 3). The diagnosis of hypopituitarism was based on his abnormal facial appearance and the low serum levels of thyroxin, adrenocortisol, testosterone and pituitary hormones.

Pathologically Weber-Christian disease may be divided into three stages: early stage: inflammatory nodosa with neutrophil infiltration and fat cell degeneration; middle stage: histiocyte phagocytosis of necrotic fat cells and foam cells, and mononuclear cell infiltration; late stage: fibrosis and atrophy (3). Fat necrosis is a particular clinical manifestation of Weber-Christian disease which may involve all organs (4). We believe that our patient's hypopituitary state was secondary to fat necrosis of the pituitary gland. This extremely rare complication has been reported previously (5).

The cause of Weber-Christian disease is unknown but etiological factors include fat metabolic disorders, infection, autoimmunity, and drugs. In our patient, most of the known secondary causes of Weber-Christian disease were excluded. Potentially, however, the patient had contracted bronchopneumonia 2 months earlier and his condition could perhaps be linked to this or to his underlying polymyositis (6).

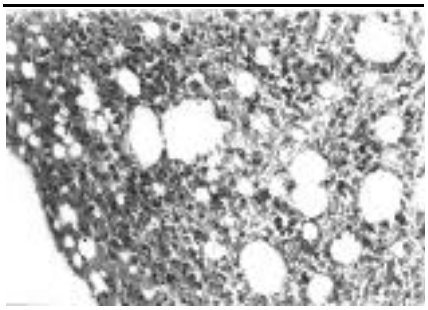

Fig. 1. Pathological section of subcutaneous nodule showing obvious fat denaturalization and necrosis in fat tissue, with intense histiocyte (mainly macrophage) infiltration and some lymphocyte infiltration (x200).

The conventional treatment for Weber-Christian disease includes the use of steroid and immunosuppressive agents such as cyclophosphamide, azathioprine and cyclosporine A (7), but when our patient did not respond to these we added leflunomide, an inhibitor of pyrimidine synthesis in activated immune cells (1). This is the first report of the successful use of cyclophosphamide and leflunomide combination treatment for Weber-Christian disease.

In conclusion, we have reported the case of a patient with Weber-Christian disease complicated by hypopituitarism. The Weber-Christian disease was probably secondary to a recent infection, although a possible casual relationship with polymyositis cannot be ruled out. This is the first time that such a combination of syndromes has been reported. Additionally, we show that leflunomide may be considered in the treatment of Weber-Christian disease.

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