Cytophagic Histiocytic Panniculitis
-A Case Report and Review of the Literature

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Recently, we evaluated a 4-year-old boy with fever, abdominal pain and multiple reddish blue subcutaneous nodules of the low back and the extremities, especially of the lower legs for 10 days. Laboratory studies showed leukocytosis, thrombocytopenia and liver dysfunction. The bone marrow aspiration excluded a proliferative disease of the haematopoietic or lymphatic system. Serological tests excluded virus infections. In the histopathologic examination of skin biopsy, there was an intense inflammatory infiltration of the adipose tissue and proliferation of histiocytes with haemophagocytosis. The eruption resolved within 3 to 4 weeks using the corticosteroid therapy. The symptoms and examinations of this patient were consistent with cytophagic histiocytic panniculitis. This case had a short and benign course. We report here a case presentation and a review of the literatures. (Dermatol Sinica 25: 53-58, 2007)

Key words: Cytophagic histiocytic panniculitis, Histiocytic cytophagic panniculitis, Weber-Christian syndrome

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INTRODUCTION

The main clinical features of cytophagic histiocytic panniculitis are inflammatory panniculitis, fever, pancytopenia and haemorrhagic diathesis. The course is usually fatal. Histopathology of the lesions shows a proliferation of benign-looking histiocytes with haemophagocytosis.

We report a 4-year-old boy with subcutaneous nodules. Although the clinical evidence was not quite compelling and the disease did not progress to a fatal systemic panniculitis, the diagnosis was confirmed by the histologic analysis of the skin lesions showing rather characteristic appearance of cytophagic histiocytic panniculitis.

We suggest that if the cases of cytophagic histiocytic panniculitis are limited to the skin and subcutaneous tissue without severe liver dysfunction or depletion of coagulation factors, their diseases may have a more benign course and result in remission using appropriate corticosteroid therapy.

CASE REPORT

A four-year-old boy was admitted to Kaohsiung Medical University Hospital in June 2006 with fever, intermittent abdominal pain, general malaise and cutaneous lesions for about 10 days. There were multiple reddish blue subcutaneous nodules of the low back and the extremities (Fig. 1). These lesions were relapsing and hyperemic with tenderness. There was no history to arthritis, arthralgia, viral disease, drug allergy and the family history was unremarkable.

On physical examination, the boy had fever and multiple reddish blue subcutaneous nodules of the low back and extremities, especially the lower legs. Lymphadenopathy of bilateral sides of the neck was also noticed. Laboratory investigations showed leukocytosis (WBC 26.8 x 1000/µL), microcytic anemia (Hgb 9.7 g/dl, MCV 58.3 µL), thrombocytopenia (PLT 16 x 1000/µL), elevated erythrocyte sedimentation rate (41 mm/hr), mild abnormal liver function (AST 49 IU/L, ALT 21 IU/L) and a normal renal function (BUN 5.2 mg/dl, creatine 0.43 mg/dl). Urinalysis and stool exam revealed normal. Immunoglobulin levels of IgA, IgG, IgE and IgM were within the normal range. Antinuclear antibodies showed negative. The C3 and C4 levels were within the normal range. Investigations for viral hepatitis (A, B, C), Epstein-Barr virus, cytomegalovirus (CMV), human immunodeficiency virus (HIV), herpes simplex virus, varicella zoster virus, tuberculin skin test and blood cultures were all negative. Tissue culture of the skin and subcutaneous tissue revealed no evidence of the infection of bacteria, mycobacterium or fungus.

The chest radiograph and the abdominal ultrasound were both normal. Bone marrow evaluation revealed a hypocellular marrow without any haemophagocytosis.

We performed an incisional skin biopsy of one of the skin lesions on his left lower leg. Under the microscope, the epidermis was intact without erosion or ulceration. There was prominent infiltration of the dermis and subcutis (Fig. 2). Medium power view showed inflammation and hemorrhagic necrosis of the septal and lobular adipose tissue (Fig. 3). The blood vessel walls were not involved. High power view revealed several cytophagic histiocytes engulf-
ing lymphocytes and erythrocytes to form so-called "bean bag cells" (Fig. 4). The immunohistochemical study showed a strong expression of CD68 by the benign histiocytes, several of which were large and cytophagic, admixed with numerous CD3+ T lymphocytes in the subcutaneous infiltrate.

Therefore, the histopathological pattern and immunohistochemical study were both compatible with the diagnosis of cytophagic histiocytic panniculitis.

The child was subsequently treated with oral prednisolone (30 mg) for 6 days followed by tapered dosage for 2 weeks. Under this treatment, the fever and skin lesions subsided gradually (Fig. 5). Other clinical symptoms also improved. The patient is now free of symptoms after his illness.

DISCUSSION

Cytophagic histiocytic panniculitis (CHP) is a histiocytic disorder described in 1980 by Winkelmann and Bowie. It is a heterogeneous disorder that presents with subcutaneous panniculitis with or without hemophagocytic syndrome (HPS). Many cases of HPS with CHP are being classified and considered as a natural disease progression of subcutaneous panniculitic T-cell lymphoma (SPTL).
CHP is frequently a fatal systemic disease characterized by recurrent, widely distributed, painful subcutaneous nodules associated with malaise and fever.\(^1\)\(^{-4}\) Patients usually die with a hemorrhagic death due to disseminated intravascular coagulopathy.\(^1\)\(^{-10}\) Rarely, in some patients, the disease seems to localize at the skin and follows a more benign course.\(^3\)\(^{-4}\)\(^,\)\(^11\)

In review of the previous reports, various medications have been tried to treat CHP. These drugs include nonsteroidal anti-inflammatory drugs (NSAIDs), arsphenamine, antibiotics, sulfonamides, antimalarial agents, amphotericin B, corticosteroids, thalidomide, and immunosuppressive agents such as cyclosporine. However, if the disease was systemic and fulminant, not a specific therapy could produce a favorable outcome.\(^12\)\(^,\)\(^13\)

It has been reported that the term CHP is undesirable for 2 reasons. First, as in most presumed histiocytic neoplasms in general, the actual tumor cells in CHP have been shown to pursue a lineage of differentiation that is not within the phagocyte-macrophage (histiocytic) system. Second, this condition is, in most cases, at least a “smoldering” lymphoid malignancy rather than an inflammatory disease, as its current designation suggests. As Wick and Patterson suggested, it would be more appropriate to use the term panniculitis-like subcutaneous lymphoma with cytophagocytosis to describe the process in question. In the same report, they also suggested that if the dermatologist and the dermatopathologist elect to retain the original designation of cytophagic panniculitis, explanatory notes on the expected biology of this disease should be included in diagnostic and clinical patient records.\(^14\)

In systemic reviews of CHP in children since 1990 (when the first cases were reported),\(^15\) most of cases showed fever, generalized lymphadenopathy, hepatosplenomegaly, pancytopenia and subcutaneous cytophagic panniculitis.\(^1\)\(^,\)\(^4\)\(^,\)\(^6\) Their diseases usually followed a long chronic fatal course and the patients died of complications of a terminal hemophagocytic syndrome.\(^11\) Bone marrow failure, disseminated intravascular coagulation and systemic infections including opportunistic bacterial and fungal infections are important causes of death.\(^16\)\(^,\)\(^17\)

Although usually fatal, prolonged survivals have been recorded in CHP. Barron et al. reported the first patient with CHP who did not experience a fatal outcome. He stated that early diagnosis and early aggressive chemotherapy resulted in complete clinical remission.\(^18\) White et al. documented a survival time of 15 years in one patient.\(^19\) Inatomi et al. presented an 8-year-old girl with erythema on the legs and intermittent high fever. Lobular panniculitis and beanbag cells were seen histologically. However, she showed no evidence of liver dysfunction or coagulation disorders and responded well to oral corticosteroids therapy.\(^20\) Suchitra et al. reported a 7.5-year-old boy having chronic febrile, recurrent crops of painful subcutaneous nodules on lower extremities and cytophagic histiocytic activity in the skin and bone marrow. The disease progressed to abnormal liver function and hemorrhagic diathesis even under the treatment of corticosteroid. However, after cyclosporin A was administered, he gradually recovered within 6 months.\(^21\) Cheah et al. described two cases of CHP with a slow but progressive improvement. Both patients responded well to cytotoxic therapy. One presented with exudative ascites reflecting an inflammatory process in the peritoneal cavity possibly due to mesenteric panniculitis. The other developed pleural effusion, arthralgia and edema.\(^22\) In conclusion, those experiencing a benign course differ from the fatal cases on the basis of duration, clinical and laboratory features, degree of cytophagia in the subcutaneous fat, and presence of cytophagia in extracutaneous organs.

The observations from our patient suggest that if the cases of CHP are limited to the skin and subcutaneous tissue without the development of severe liver dysfunction, cytophagia in
extracutaneous organs and intravascular coagulo-
apathy, the disease may have a benign course and recovers rapidly using appropriate therapy.

CHP must be distinguished from other conditions in which erythrophagocytosis or hemophagocytosis may be a feature. These diseases include subcutaneous T-cell panniculitic lymphoma, angiocentric lymphoma and cutaneous Rosai Dorfman disease.

In subcutaneous T-cell panniculitic lymphoma, the lymphocytes show cytological atypia with karyorrhexis and mitotic activity. Angiocentric T-cell lymphoma is characterized by an angioinvasive and frequently angiodestructive atypical lymphoid infiltrate usually accompanied by widespread coagulative necrosis. In cutaneous Rosai Dorfman disease, the infiltrate is usually centered on the dermis. Lymphophagocytosis is often marked but erythrophagocytosis is not usually present.

The skin biopsy specimen of our case revealed benign subcutaneous panniculitis with hemophagocytic histiocytes. No cytological atypia, angioinvasive or angiodestructive atypical lymphoid infiltrate was noticed. The infiltrate extended from the upper dermis to the subcutaneous tissue.

The clinical pattern of multiple painful bright red to bluish subcutaneous nodules involving extremities might appear in polyarteritis nodosa and other vasculitides. The histological feature of large areas of hemorrhagic necrosis in our patient might also be observed in polyarteritis nodosa. However, polyarteritis nodosa is characterized by necrotizing vasculitis of small- and medium-sized muscular arteries, which was not seen in our patient. Clinically and pathologically, the patient’s illness is most consistent with CHP.

The experience with this patient shows the need for accurate histologic characterization as the essential first step in the diagnosis and management of any form of panniculitis. Although CHP is uncommon in children, it must be considered in patients with panniculitis, pancytopenia and coagulation disturbances. Most importantly, our case shows that CHP does not always portend a grave prognosis. Without systemic involvement, CHP confining to the skin usually follows a benign clinical course.

REFERENCES