Subcutaneous Panniculitis-like T-cell Lymphoma: Successful Initial Treatment with Prednisolone and Cyclosporin A

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Abstract

A case of subcutaneous panniculitis-like T-cell lymphoma (SPTCL) is reported. A 27-year-old man presented with fever and abdominal swelling. His laboratory examination revealed pancytopenia and liver dysfunction. The diagnosis of SPTCL was made by biopsy based on thickened subcutaneous tissue. In addition, bone marrow specimen showed a hemophagocytosis syndrome (HPS). Methylprednisolone pulse therapy was initiated followed by prednisolone (60 mg/day) and cyclosporin A (150 mg/day). He responded to the treatment and remained asymptomatic for at least for 6 months. Our results suggest that a trial of cyclosporin A is warranted in patients with SPTCL complicated by HPS.

Key words: subcutaneous panniculitis-like T-cell lymphoma, hemophagocytosis, cyclosporin A, Weber-Christian disease

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Introduction

Subcutaneous panniculitis-like T-cell lymphoma (SPTCL) is a rare form of non-Hodgkin lymphoma infiltrating into subcutaneous tissue. Systemic symptoms are variable and some patients present with hemophagocytic syndrome (HPS) with pancytopenia, fever, and hepatosplenomegaly. The treatment strategy for SPTCL is not standardized, and this disorder has a high mortality rate despite the use of aggressive chemotherapy. Recently, several patients with SPTCL were reported to respond dramatically to cyclosporin A treatment (1). We have successfully used prednisolone and cyclosporin A to treat a patient with SPTCL. This report provides review of our case and discusses the rational for using cyclosporin A.

Case Report

A previously healthy 27-year-old Indonesian man visited a family physician complaining of abdominal swelling and low-grade fever. He had a 2-month history of an abdominal pain, general fatigue, low-grade fever and lower limb edema. His initial laboratory exam revealed elevated transaminases (aspartate aminotransferase (AST) 111 IU/l, alanine aminotransferase (ALT) 66 IU/l) and high lactate dehydrogenase (LDH) level (1,615 IU/l). At this time, liver tumor was suspected and he was referred and admitted to our hospital for further evaluation and treatment.

On physical examination, he presented with a conjunctive anemia, eyelid edema, and lower limb edema with a massive tumor detected in his right infracostal region. The laboratory examination showed a pancytopenia (WBC count 1.4×10⁹/l, hemoglobin 10 g/dl, platelets 124×10⁹/l), mildly elevated transaminases (AST 161 IU/l, ALT 83 IU/l), high LDH (1,793 IU/l), and high ferritin (6,029 ng/ml) level. An abdominal ultrasound and abdominal computed tomography (CT) (Fig. 1) revealed noticeable thickening of subcutaneous tissue compatible with the region of massive tumor in the right infracostal region. The laboratory examination showed a pancytopenia (WBC count 1.4×10⁹/l, hemoglobin 10 g/dl, platelets 124×10⁹/l), mildly elevated transaminases (AST 161 IU/l, ALT 83 IU/l), high LDH (1,793 IU/l), and high ferritin (6,029 ng/ml) level. An abdominal ultrasound and abdominal computed tomography (CT) (Fig. 1) revealed noticeable thickening of subcutaneous tissue compatible with the region of massive tumor in the right infracostal region in addition to hepatosplenomegaly. Based on these results, we diagnosed him with panniculitis accompanied by hemophagocytic syndrome (HPS). The patient was infected with Epstein-Barr virus (EBV) in the past; Results of serological tests for EBV-related antibodies were as follow: titers of IgG antibody to viral capsid antigen (VCA); 40, IgM-VCA; 10>, and EB nuclear antigen.

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For further evaluation, bone marrow biopsy and skin punch biopsy were performed on day 3 of admission. Bone marrow specimen (Fig. 2) showed hemophagocytosis of red blood cells and neutrophils by histiocytes. Histopathology of the skin biopsy specimens was consistent with panniculitis; it showed infiltration of neutrophils and lymphocytes in subcutaneous fat tissue but no evident atypical lymphoid cells were present. These examinations were consistent with the initial diagnosis.

Within 3 days, pancytopenia has exacerbated (WBC count 0.83×10^9/l; hemoglobin 9.9 g/dl; platelets 97×10^9/l) with up to 40°C fever. To control the HPS, methylprednisolone pulse therapy (1 g/day intravenously) was introduced for 3 consecutive days. On the next day, he became afebrile and by day 6 his WBC count started to increase.

For additional studies, an incisional skin biopsy was repeated; infiltrating atypical lymphocytes were small and karyorrhexis was observed with proliferation of histiocytes (Fig. 3). Immunofluorescent staining (Fig. 4) showed CD3 (+), CD4 (-), CD8 (+), CD30 (-), and CD56 (-) lymphocytes with expression of cytotoxic molecules including granzyme B positive, perforin negative, and T-cell intracellular antigen, which was concordant with SPTCL. In situ hybridization of EBV was negative. By this time the remaining laboratory examination at admission was available and showed interleukin-2 receptor (IL 2-R) to be 5,460 U/ml.

Because there were several reports of patients with SPTCL who were successfully treated with cyclosporin A, oral prednisolone (60 mg/day) was administered in addition to cyclosporin A (150 mg/day) following steroid pulse ther-

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**Figure 1.** Abdominal CT: significant thickening of subcutaneous tissue compatible with region of huge tumor in the right infracostal region.

**Figure 2.** Histopathology of bone marrow specimen (HE stain, ×200): hemophagocytosis of red blood cells and neutrophils by histiocytes.

**Figure 3.** Histology of skin specimen (HE stain, ×200): infiltrating atypical lymphocytes were small and karyorrhexis was observed with proliferation of histiocytes.
Combination therapy of prednisolone and cyclosporin A not only improved HPS but also alleviated SPTCL, and the subcutaneous nodule diminished to 1 cm in diameter (Fig. 5). After 3 weeks of prednisolone therapy at a dose of 60 mg/day, the prednisolone dosage was gradually tapered off to 40 mg/day over 4 weeks. The abdominal CT scan confirmed improvement of subcutaneous tissue thickening. At the time of discharge, his laboratory data was as follow; WBC count 6.95×10^9/l; hemoglobin 13.2 g/dl; platelets 217×10^9/l; AST 14IU/l; ALT 19 IU/l; LDH 206 IU/l; ferritin 215 ng/ml; and IL2-R 493 U/ml. He returned to Indonesia for further treatment with prednisolone 40 mg/day and cyclosporin A 150 mg/day. Since leaving Japan, he has remained asymptomatic for 6 months.

**Discussion**

The distinctive clinicopathological features of a T-cell lymphoma involving the subcutaneous tissue were described in 1991 by Gonzalez et al (2). Immunophenotypic and genotypic findings confirmed the T-cell phenotype as well as monoclonality of this lesion. Thus, the T-cell origin of this lymphoma has been proved and in 1994, this disease was identified as a provisional entity in the Revised European-American classification of lymphoid neoplasms and named SPTCL (3). In the past, it is likely that many cases of SPTCL were reported as Weber-Christian disease or cytophagic histiocytic panniculitis.

HPS was originally described by Risdall et al as a response to viral infections (4). Following the original report, HPS has been reported with bacterial, fungal, and viral infections. HPS also occurs in association with malignant neoplasms, most often lymphoreticular neoplasms, which are usually of T-cell origin (5). The most consistent histopathologic feature in HPS is a proliferation of mature histiocytes that exhibit prominent erythrophagocytosis and cytophagocytosis. It has been reported that in HPS, the prominent phagocytic histiocytes are reactive and are stimulated by T cells (6). Furthermore, many of the findings in HPS may also be due directly or indirectly to cytokines produced by proliferating T-cell lymphocytes and reactive phagocytic histiocytes.

There is no objection that standard treatment strategy for malignant lymphoma includes aggressive chemotherapy. However, controlling HPS may become the key treatment for SPTCL; SPTCL has a high mortality rate despite the use of aggressive chemotherapy regimen, and in the majority of patients the mortality is a result of the complication of HPS and not to the lymphoma itself. As mentioned earlier, SPTCL is a T-cell origin and complicating HPS is due to...
the cytokines produced by proliferating T cells. The primary action of cyclosporin A is to block the expression of lymphokines produced by T cells, including interleukin (IL)-2, IL-3, IL4, interferon (IFN)-γ, and tissue necrosis factor (TNF)-α. Therefore, it is reasonable to consider that cyclosporin A is the drug of choice for the treatment of SPTCL complicated by HPS. In fact, there are several reports of patients with Weber-Christian disease (7), virus-associated hemophagocytic syndrome (8), cytophagic histiocytic panniculitis (9-11), or SPTCL (1), who were successfully treated with cyclosporin A.

It is not known yet whether subsequent chemotherapy is necessary after achieving remission by cyclosporin A. Shani-Adir et al reported a patient with SPTCL who dramatically responded to treatment with cyclosporin A alone and subsequent treatment with combination chemotherapy achieved complete remission that has been maintained for the past 18 months (1). On the other hand, Royle et al reported a case with cytophagic histiocytic panniculitis, who responded to treatment with cyclosporin A and prednisolone which maintained remission without chemotherapy for the past 2 years (9). More cases need to be compared to draw a conclusion on this issue. In the present case, the patient had a personal reason to receive further medical treatments back in his country, so we did not add subsequent chemotherapy.

In the literature, cyclosporin A was administered (with or without prednisolone) to four patients with SPTCL. In those patients, two did not have responses and the other two had brief partial responses (12-14). Recently, it has been reported that the presence of HPS and the expression of γδ T-cell receptors in tumor cells predict poor survival (15). The poor responses in these cases may be due to the differences in the T-cell receptor phenotype. For future investigation, it is conceivable to explore T-cell receptor phenotypes in relation to treatment strategy.

In summary, we report a case with SPTCL complicated by HPS who dramatically responded to treatment with prednisolone and cyclosporin A. Our results suggest that a trial of cyclosporin A is warranted at least in selected patients with SPTCL complicated by HPS.

References


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