

Dermatopathic lymphadenopathy in a patient with adult onset Still's disease

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ABSTRACT

Adult onset Still's disease (AOSD) is a systemic inflammatory disorder of unknown cause characterized by high fever accompanied by systemic manifestations. Since AOSD consists of heterogeneous symptoms and has no definite diagnostic tool, the diagnosis is based upon exclusive criteria. Dermatopathic lymphadenopathy (DL) is characterized by a localized paracortical proliferation of histiocytes and deposition of melanin in the lymph nodes. DL is not only a reactive hyperplasia of the lymph nodes, but has also been reported to be associated with hematological malignancies such as cutaneous T cell lymphoma (CTCL) and Hodgkin's lymphoma. It is therefore important to evaluate CTCL or Hodgkin's lymphoma in a patient with DL, in order to both rule out hematological malignancy and diagnose AOSD. In this report, we first describe a 37-year-old patient with AOSD whose biopsy of lymph node was proved to be DL.

Introduction

Adult onset Still's disease (AOSD) is a systemic inflammatory disorder of unknown cause characterized by high fever with leukocytosis accompanied by systemic manifestations such as arthralgia, skin rash, lymphadenopathy, hepatosplenomegaly (1). Since AOSD consists of heterogeneous symptoms and has no definite diagnostic tool, the diagnosis is based upon exclusive criteria.

Dermatopathic lymphadenopathy (DL) is characterized by a localized paracortical proliferation of histiocytes and deposition of melanin in the lymph nodes. DL is not only a reactive hyperplasia of the lymph nodes, but has also been reported to be associated with hematological malignancies such as cutaneous T cell lymphoma (CTCL) and Hodgkin's lymphoma (2). It is therefore important to evaluate CTCL or Hodgkin's lymphoma in a patient with DL, in order to both rule out hematological malignancy and diagnose AOSD.

Case report

A 37-year-old woman was referred to our hospital, February 2004, for a high

spiking fever, sore throat, arthralgia, a red-pinkish maculopapular rash on the anterior chest wall and lower extremities, and enlarged lymph nodes. Physical examination revealed palpable lymph nodes on cervical, axillar, and inguinal areas, mild splenomegaly, a slightly injected throat, and arthritis affecting the shoulders, wrists, knees, and ankles. Her body temperature was 39°C.

Laboratory findings showed a hemoglobin level of 10.7 g/dL, a white blood cell (WBC) count of 13,390/mm³, a platelet count of 217,000/mm³, an erythrocyte sedimentation rate (ESR) of 41 mm/h, and C-reactive protein (CRP) concentration of 18.1 mg/dL. Aspartate transaminase (AST) and alanine transaminase (ALT) levels were 66 IU/L and 55 IU/L respectively. Lactate dehydrogenase (LDH) and ferritin levels were elevated at 1,035 IU/L and 12,141 ng/mL respectively. Rheumatoid factor, antinuclear antibody, C-ANCA, and P-ANCA were negative. Blood cultures and serological tests for bacteria, viruses and parasites were negative. Moreover, therapeutic challenge with antibiotics was not successful. EKG and chest x-ray were normal. Computed tomography (CT) scans showed enlargement of lymph nodes at the bilateral neck, bilateral axillary, bilateral supraclavicular fossa, bilateral mediastinum and hilum, gastrohepatic ligament, portocaval space and both iliac chains, and mild hepatosplenomegaly without typical pathologic finding (Fig. 1). Whole body F18-fluorodeoxyglucose Positron Emission Tomography (FDG-PET) revealed increased FDG uptake in the lymph nodes at the supraclavicular fossae, axillae, upper abdomen, and groins. Diffusely increased FDG uptake was also observed in the spleen and bone marrow.

To exclude other diseases mimicking AOSD, biopsies of skin, lymph node and bone marrow were performed. Skin biopsy on the back showed superficial neutrophilic and eosinophilic dermatosis with diffuse basal vacuolization, acanthosis, and focal parakeratosis. These findings were consistent with connective tissue disease associated with vasculitis or drug eruption,

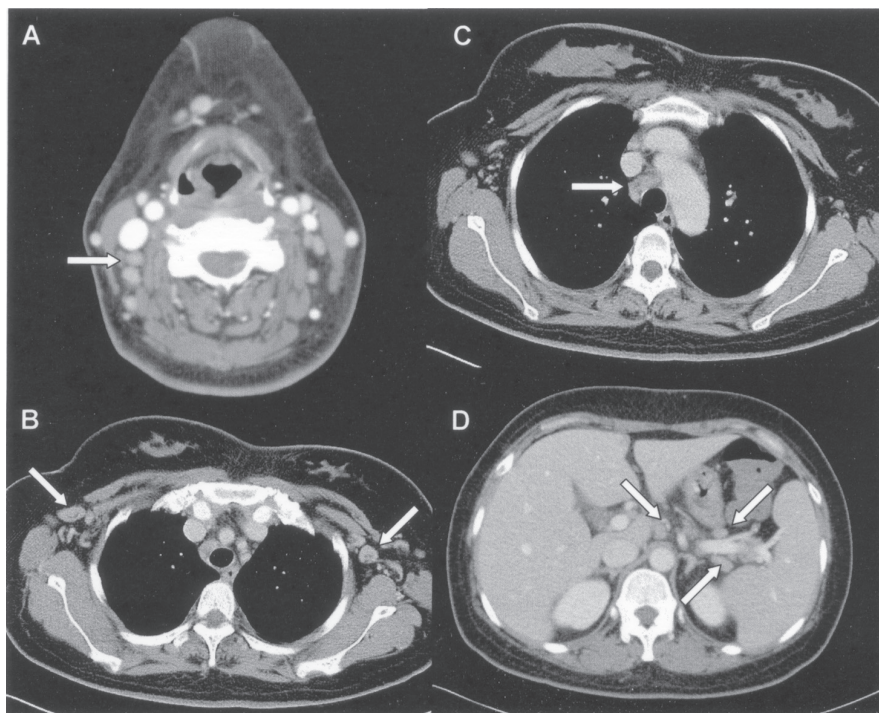


Fig. 1. Computed tomography (CT) scans showed multiple enlargement of lymph nodes at the neck (A), mediastinum and hilum (B), bilateral axillary (C), and in the abdomen (D).

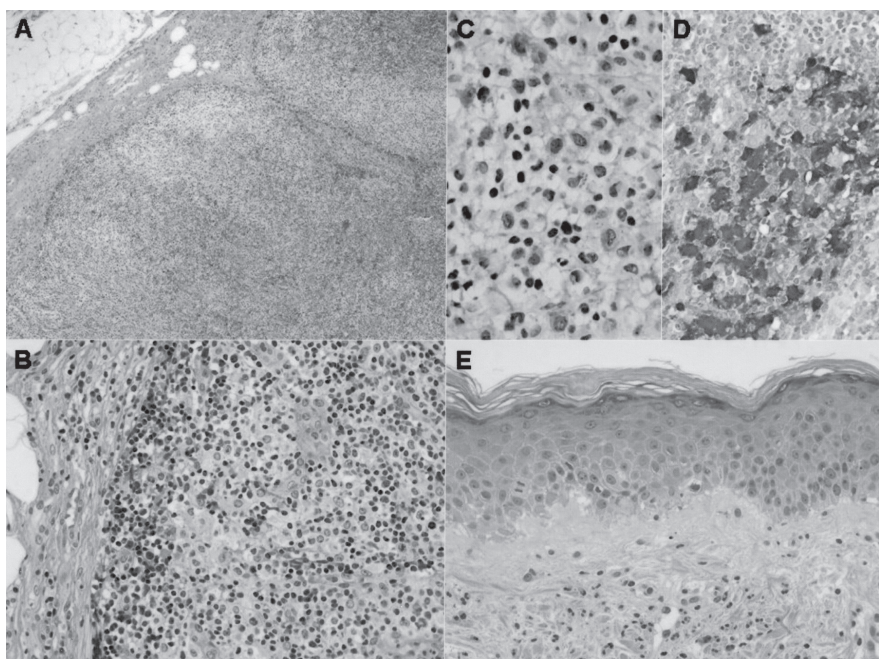


Fig. 2. Pathologic findings of the right neck lymph node and the back skin lesion. (A) Large, confluent, palely stained areas of histiocytic aggregates are seen in the lymph node cortex (original magnification $\times 40$, Hematoxylin-Eosin). (B) The histiocytes show abundant pink cytoplasm and small centrally located nuclei (original magnification $\times 100$, Hematoxylin-Eosin). (C) and (D) The histiocytes show cytoplasmic staining for CD1a and S-100 protein on immunohistochemical analysis. (E) Skin biopsy reveals superficial neutrophilic and eosinophilic dermatosis with diffuse basal vacuolization (original magnification $\times 200$, Hematoxylin-Eosin).

but there was no evidence of either of these. Biopsy of right neck lymph node revealed large, confluent, palely stained areas of histiocytic aggregates in the

lymph node cortex. The histiocytes contained abundant pink cytoplasm with small centrally located nuclei, and immunohistochemical analysis revealed

cytoplasmic staining for CD1a and S-100 protein (Fig. 2). These findings were consistent with DL. Bone marrow biopsy showed a nearly normal M/E ratio, full maturation of myeloids with shift to left, and abundant megakaryocytes with 50-60% cellularity.

There was no evidence of hematological malignancy that can be associated with DL. The patient fulfilled the criteria for AOSD proposed by Yamaguchi (1). She was diagnosed as AOSD and treatment with high dose prednisolone (1 mg/kg) was started. Her symptoms and laboratory findings improved gradually. However, after 9 days of treatment with prednisolone, her ferritin level had increased again to 13,134 ng/ml: this was thought to reflect aggravation of the disease and treatment with cyclosporine-A (2 mg/kg) was added. After this, the patient no longer complained of her previous symptoms, and laboratory results including ferritin, were improved. She has been under observation in an outpatient office with tapering of prednisolone and cyclosporine-A without development of hematological malignancy since May 2006.

Discussion

AOSD is a chronic systemic inflammatory disorder of unknown etiology, characterized by various non-specific manifestations that also occur in patients with hematological malignancies (1, 3-6). In addition, lymphadenopathy in AOSD has been shown to present a wide spectrum of histopathological features from simply reactive hyperplasia to atypical paracortical hyperplasia mimicking various lymphomas. Investigation of the lymph node pathology in AOSD is therefore critical in order to exclude other malignancies (7).

DL has been reported to be associated with hematological malignancies such as CTCL and Hodgkin's lymphoma (2). CTCL encompasses a group of neoplasms characterized by epidermotropic, or skin-homing T cells. The diagnosis of CTCL is difficult due to its numerous and often non-specific manifestations, and the equivocal pathological findings early in its course. The interval between the onset of skin lesion

and the definitive diagnosis of CTCL ranges from 4 to 10 years, with a mean of 6 years (8). Thereafter, repetitive biopsies of skin lesions over many years may be required to exclude CTCL in AOSD patients with DL.

Although there was no definite evidence accounting for the link between DL and AOSD, the evidences that DL can be induced by chronic dermatitis and anti-TNF-alpha therapy can improve the clinical course of AOSD suggest that the overflow of pro-inflammatory cytokines in AOSD may induce the development of DL as a reactive lymphadenopathy (9). However, the mechanism still remains unclear.

This report describes the first case of DL in AOSD. There has been no evi-

dence of hematological malignancy in this patient till now, however, close follow-up will be needed to exclude the malignancy.

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