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Early Onset of Daunomycin Cardiotoxicity in a Case of Acute Myelogeneous Leukemia Associated with Sweet's Syndrome

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ABSTRACT

A patient of acute leukemia with Sweet's syndrome who developed heart failure after receiving 107 mg/m^2 daunorubicin was reported. There seemed to be genetic factors of individuals in inducing anthracycline cardiotoxicity. Further study on genetic analysis of such a disease will be necessary for clarification of the genetic factors susceptible to anthracyclines.

Cardiotoxicity is a well-known side effect of the cytotoxic anthracyclines, such as doxorubicin and daunorubicin[4], but it is relatively unknown on the early onset of anthracycline cardiotoxicity, which was recently reported by Bristow et al[1]. This case report describes a patient of acute leukemia with Sweet's syndrome who developed heart failure after receiving 107 mg/m^2 daunorubicin.

CASE REPORT

A 52-year-old man was admitted to the hospital with a 2-week history of painful skin eruptions on the right elbow, hip, forearm and scalp that had been accompanied by malaise and fever for 1 week. His temperature was 38.9°C. The only other abnormal findings were a hemoglobin level of 10.6 g/dl and an erythrocyte sedimentation rate of 134 mm in the first hour. A skin biopsy specimen showed intense perivascular neutrophilic infiltration in the dermis, consistent with Sweet's syndrome. Betamethasone therapy was initiated with an oral dose of 2 mg daily. The patient became afebrile, and within 2 weeks the skin lesions had become less erythematous and most had cleared.

Because of persisting mild anemia and leukocytosis and the gradual appearance of abnormal immature cells in the peripheral blood, a bone marrow examination was done. It revealed that 51% of the cells were blast forms and 17% were promyelocytes and myelocytes with abnormal maturation. Peroxidase staining of the leukemic cells gave a positive reactions, and the leukocyte alkaline phosphatase score was low. The findings were consistent with acute myelogeneous leukemia (M2 by the French-American-British classification). Chromosome analysis of the leukemic cells showed interstitial deletion of chromosome 9, with the karyotype 46, XY, del(9) (pter→q21::q31→pter). The HLA (human leukocyte antigen) phenotype was HLA-A2, w24;B7, w60;Cw2, -;DR1, 7JW2. The patient was treated according to the BH-AC•DMP protocol (N^4-behenoyl-l-β-D-arabinofuranosylcytosine(BH-AC), daunorubicin, 6-mercaptopurine and prednisolone). He had no history or symptoms referable to the cardiorespiratory system. After the first course of BH-AC•DMP chemotherapy (Fig. 1), he suddenly developed dyspnea. The total dose of daunorubicin was 160 mg, or 107 mg/m^2. Physical examination revealed a blood pressure of 54/30 mmHg, edema and disturbance of consciousness. Electrocardiograms showed diminution of QRS amplitude and flat or negative T wave (Fig. 2). A chest

X-ray showed an enlarged heart and developing pulmonary edema. Supportive therapy for the heart (GIK therapy(3), CoQ_{10} and vitamin E) was carried out with a slow improvement in the patient's clinical states. However, the ECG abnormalities continued for more than two months. Complete remission occurred a few months later, following treatment with BH-AC•MP chemotherapy excluding daunorubicin and blood transfusion (Fig. 1). Since then, BH-AC•MP therapy was carried out as the consolidation and maintenance therapy for leukemia, however, no evidence of heart failure, ECG changes and abnormalities of chest X-P have been observed until at present time. Therefore it was confirmed to be a heart failure induced by daunorubicin.

In addition, during the remission status, the lymphocyte subpopulations in the peripheral blood were analysed by a fluorescence-activated cell sorter (FACS Ⅳ) utilizing monoclonal antibodies. (Fig. 3). Increment of $T4^+$ (helper/inducer T) cells and decrease of the $T8^+$ (suppressor/ cytotoxic T) cells and $B1^+$ cells were remarkable. The imbalance of $T4^+$ and $T8^+$ subsets of T lymphocyte may be a cause of Sweet's syndrome in inducing an autoimmune injury of the skin.

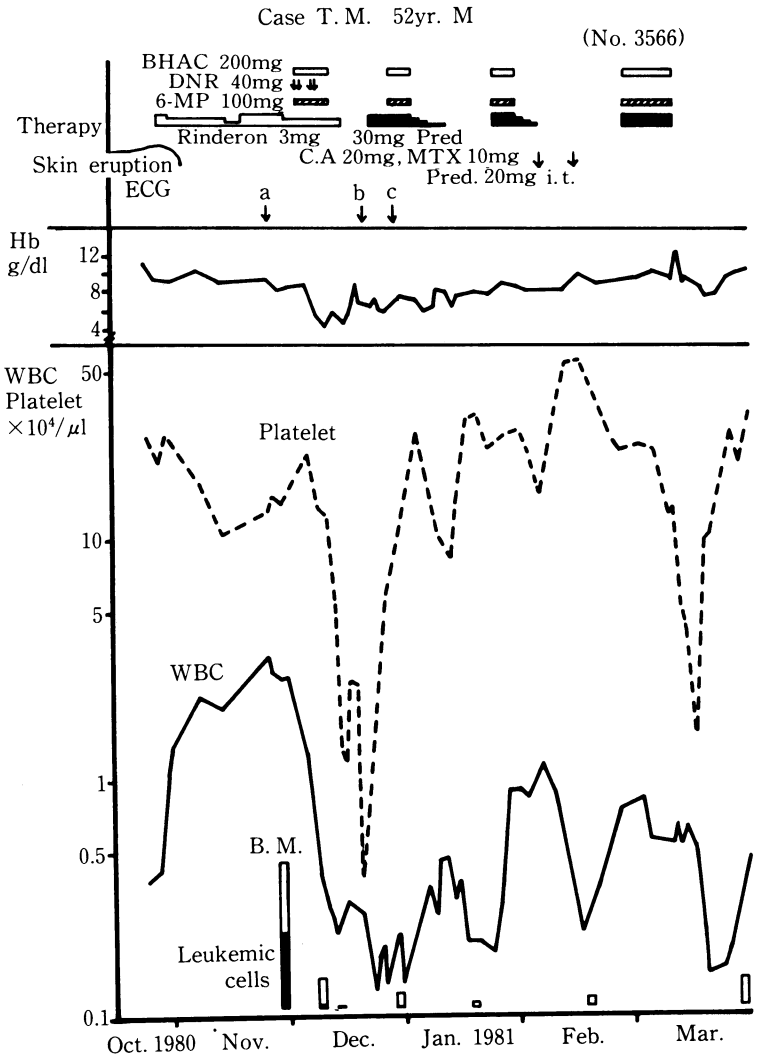

Fig. 1. Clinical course

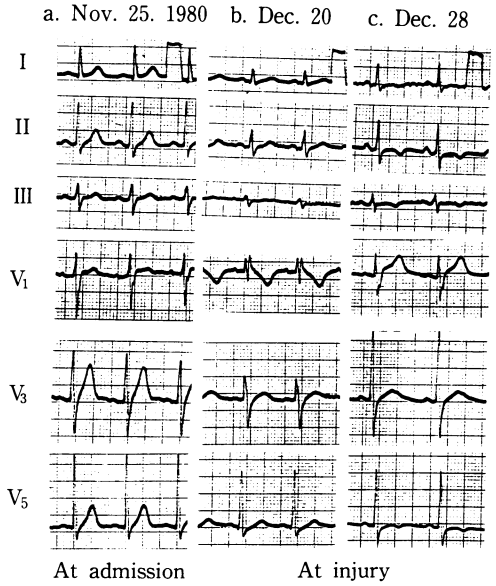

Fig. 2. Electrocardiographic changes on admission (a) and after Daunomycin infusion (b & c).

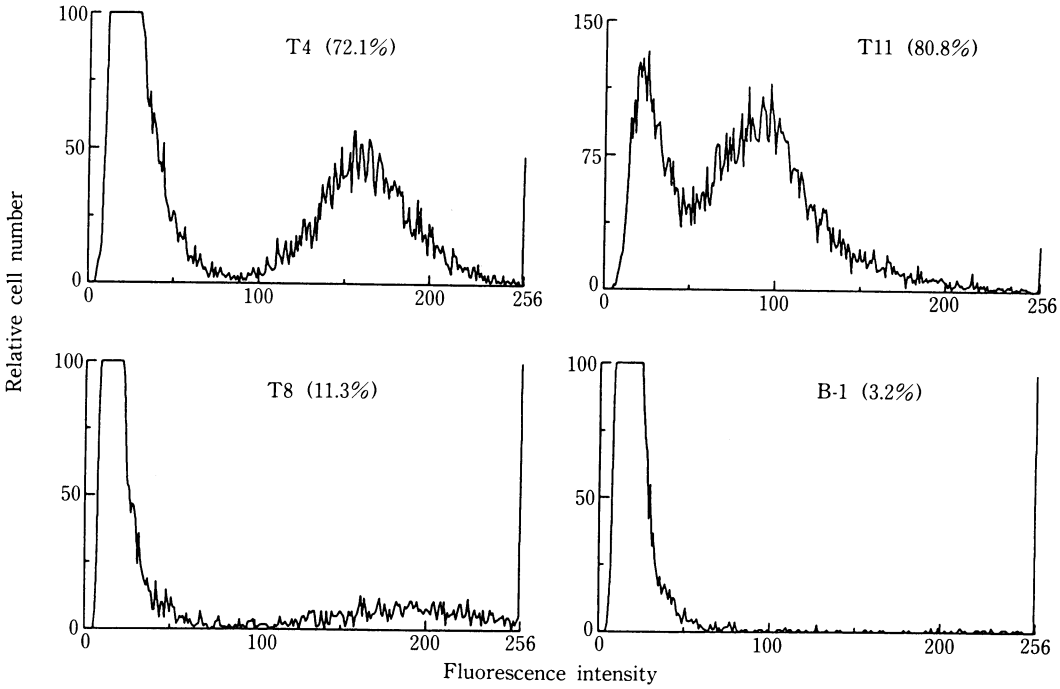

Fig. 3. Cell Sorter Analysis of the Lymphocyte Subpopulations in the Patient with Sweet's Syndrome

DISCUSSION

We suggested that anthracycline antibiotics may induce clinically significant cardiotoxicity. We may have to pay attention to not only chronic cardiomyopathy but also early cardiotoxicity induced by anthracyclines which are widely used in clinics. There seems to be a genetic factors of individuals in inducing anthracycline cardiotoxicity. To our knowledge, however, no evidence of genetic susceptibility to anthracyclines are reported. On the other hand, it is also strongly speculated that the association between Sweet's syndrome and leukemia suggests genetic factors[2].

This is the first report of anthracycline-induced cardiomyopathy developed in a patient of acute leukemia who associated with Sweet's syndrome. Further study on genetic analysis of such a disease will reveal the genetic factors susceptible to anthracyclines.

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