A clustered dense body in a patient with splenic lymphoma with villous lymphocytes

We report a case of splenic B-cell lymphoma with villous lymphocytes (SLVL), in which clustered lysosomal granules, indicative of T-cells, were observed by electron microscopy.

The patient is a 76-year old man who was admitted to hospital because of lymphocytosis and anemia. On physical examination, splenomegaly was found without lymphadenopathy or hepatomegaly. Ultrasonic imaging and computed tomography confirmed the splenomegaly and absence of involvement of other organs. $^{67}$Ga uptake was only found in the spleen. Complete blood counts were as follows: platelets $184 \times 10^9$/L, leukocytes $13.0 \times 10^9$/L, including 8% segmented neutrophils, 2% eosinophils, 89% lymphocytes and 1% monocytes. The reticulocyte count was elevated up to 82.5‰ and hemoglobin concentration was 6.0 g/dL. As for blood chemistry, lactate dehydrogenase (LDH) level was increased while the haptoglobin level decreased. The direct Coombs' test was positive. These data suggested that this patient had autoimmune hemolytic anemia. The other results of blood chemistry test were within normal ranges.

Microscopic blood smear examination revealed that 89% of lymphocytes had a villous structure on the cell surface (Figure 1). A tartrate resistant acid phosphatase (TRAP) assay gave a negative result, which ruled out the possibility of hairy cell leukemia. These lymphocytes with similar morphologic characteristics existed as a major population (68.5%) in the bone marrow. Serum IgM was increased (3,540 mg/dL) and monoclonality of the $\lambda$ chain was demonstrated by immuno-electrophoresis. Serum IgG and IgA values were normal to slightly decreased.

Immunophenotyping showed the peripheral blood lymphocytes to be CD3-, CD5-, CD10-, CD11c-, CD19+, CD20+, CD21-, CD22-, CD23+, CD25+, CD38-, CD56-, sIgMbright and sIgDdim. The lambda chain was dominantly expressed, indicating the clonal nature of the B-lymphocytes. These results do not coincide with typical chronic lymphocytic leukemia, in most cases of which CD5 and CD23 are intensely positive and cell surface immunoglobulins IgM and IgD are weakly positive. From these data, a diagnosis of SLVL was made.

Electron microscopic examination demonstrated a cluster of lysosomal granules in a population of blood lymphocytes, which has been termed clustered dense body (CDB) and shown to be highly indicative of T-lymphocytes (Figure 2). CDB was found in 31% of tumor cells examined. Despite the results of laboratory tests, indicating a B-cell origin, the electron microscopic examination thus showed that the neoplastic cells have a T-cell nature as well and suggested that the tumor may have arisen from lymphoid stem cells or show aberrant expression of lineage markers, a phenomenon known as lineage infidelity in leukemia cells. Although it remains to be determined whether CDB is exclusively present in T-cells, the present observation indicates that detailed electron microscopic examination could provide further insight into the cell origin of lymphoid malignancies, including SLVL.

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Resolution of cyclosporine-induced gingival hyperplasia resistant to azithromycin by switching to tacrolimus

Cyclosporine (CsA)-induced gingival hyperplasia (CIGH) is a common side effect of CsA. A 54-year old woman was diagnosed as having severe aplastic anemia with trilineage cytopenia. Since she had no HLA-matched relatives, she was treated with immunosuppression including anti-lymphocyte globulin, methylprednisolone, recombinant human granulocyte colony-stimulating factor and CsA (oral dose of 3.5 mg/kg/12 h). Six weeks after the beginning of the treatment the patient presented with oral discomfort and frequent gum bleeding. At that time, a physical examination showed severe gingival hyperplasia (Figure 1a). Based on a recent paper that shows the efficacy of azithromycin in the treatment of CIGH, two courses of this macrolide antibiotic (500 mg/24 h on day 1 followed by 250 mg/24 h on days 2-5) were administered, in spite of which the CIGH progressed.1 CsA was discontinued and oral tacrolimus (FK-506) at 3 mg/12 h was started, resulting in complete remission of the CIGH and the associated symptomatology within the next weeks (Figure 1b). Withdrawal of CsA and replacement with FK-506 may be a good approach in cases of CIGH resistant to azithromycin.

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