CD30 expression by peripheral blood monocytes and hepatic macrophages in a child with miliary tuberculosis

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Abstract

The peripheral blood of a 3 month old boy with disseminated tuberculosis showed CD30 positive monocytes on flow cytometric analysis. His liver contained CD30 positive staining macrophages and giant cells. CD30 is an activation antigen which has not been previously found on peripheral blood monocytes.

Case report

A 3 month old boy presented with a six week history of persistent cough and pallor. On examination he was tachypnoeic and had gross firm hepatosplenomegaly. A chest x ray picture showed widespread, coarse, reticulo-nodular shadowing. A full blood count showed a normochromic, normocytic anaemia with a haemoglobin of 8.1 g/l and a white cell count of $18 \times 10^9/l$, including 10% monocytes. Bone marrow aspirates and biopsy specimens yielded normal results. The diagnosis of disseminated tuberculosis was established by the liver biopsy specimen showing widespread caseating granulomas, and containing acid and alcohol fast bacilli. *Mycobacterium* species were later grown in culture from gastric aspirates and urine specimens. He showed a good clinical response to standard treatment for tuberculosis.

Using a panel of monoclonal antibodies, flow cytometric analysis of whole blood was performed at diagnosis, and then five days and six weeks after starting treatment. The initial forward versus side scatter plot (fig 1A) appeared typical for lymphocytes and polymorphs, but the monocytic population comprised larger cells than normal. On selective gating these cells showed the following immunophenotype: CD45⁺ > 99%, CD14⁺ 98%, CD30⁺ 87%, HLADR⁺ > 99%, CD16⁺ 35%, CD4⁺ 50%, CD8⁺ < 1%, CD3⁺ < 1%, CD56⁺ < 1%. Thus all of the cells in this discrete population were CD45⁺, CD14⁺ monocytes and 87% displayed CD30 (fig 1B). As far as we are aware, this finding has not been previously described in peripheral blood. Repeat testing at five days showed that this population was still present, but that it contained fewer cells, with some having apparently moved over to merge with normal sized monocytes. This was confirmed by the finding of cells with a similar phenotype among both populations. Five weeks after treatment, no CD30⁺ cells were found.

Routine histological examination of the percutaneous liver biopsy specimen showed that the hepatic architecture had been preserved.

Numerous granulomas were present throughout the parenchyma and in portal tracts. These contained Langhans' giant cells and several showed central caseating necrosis. Acid and alcohol fast bacilli could be identified using the Ziehl Neelsen stain. Bile ductular proliferation was seen at the limiting plate of some portal tracts, possibly as a result of local biliary obstruction by granulomas. Immunostaining of 3 µm dewaxed sections with the anti-CD30 antibody, Ber-H2, using an indirect immunoperoxidase method with nickel/cobalt enhanced 3,3'-diaminobenzidine as chromogen, showed diffuse cytoplasmic staining of Langhans' giant cells and some epithelioid cells. Weak staining was also seen on proliferating bile ductules but not hepatocytes and Kupffer cells (fig 2).

Figure 1 (A) Forward (size) versus side (granularity) light scatter plot (after red cell lysis of whole blood using commercial lysing solution) at diagnosis, showing normal position of lymphocytes (R1) and displacement of monocytes from usual position at R3 to R2. (B) Two-colour fluorescence analysis of cells gated in R2, demonstrating dual staining of CD14 and CD30 in 87% of cells.

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Figure 2 CD30 immunoreactivity in a multinucleate giant cell (arrow) and in an adjacent proliferating bile ductule (BD) (Ber-H2; indirect immunoperoxidase with Ni/Co enhancement. Staining within macrophages and giant cells was cytoplasmic with accentuation at the cell membranes (arrowheads).

Comment

CD30 is recognised by the monoclonal antibodies Ki-1¹ and Ber-H2.² Its expression has been analysed in a wide range of both normal and neoplastic tissues in an attempt to resolve the question of the origin and lineage of Hodgkin's and Reed-Sternberg cells. The diagnostic importance and tissue distribution of CD30 has recently been reviewed by Pallesen.³ Normal cells in which CD30 expression has been described include activated T lymphocytes, plasma cells, follicular dendritic cells and exocrine pancreatic cells. Malignant cells expressing CD30 are seen in Hodgkin's and non-Hodgkin's lymphomas, interdigitating cell sarcoma, embryonal carcinoma and a variety of other solid tumours and cell lines. CD30 is

currently thought to be an activation marker because normal peripheral blood B and T lymphocytes have been induced to express CD30 in association with CD25 after exposure to phytohaemagglutinin, HTLV I and II, Epstein-Barr virus and *Staphylococcus aureus*.⁴ Similarly, cells of macrophage lineage may be induced to express CD30 in vitro.⁵ No definite CD30 staining of monocytes and macrophages in vivo has hitherto been reported.

This case also shows that monocyte derived epithelioid and giant cells in granulomas may express CD30. The relevance of CD30 positivity of proliferating bile ductules remains to be determined. Immunolabelling of malignant epithelial cells has previously been regarded as representing a cross reaction with an epitope of an unrelated antigen.³ Nevertheless, the possibility that CD30 expression is a feature of liver cells undergoing ductular metaplasia merits further study.

CD30 expression was first described in Hodgkin's disease, a lymphoma associated with complex immunopathological phenomena. Many of the histological changes are related to reactive changes occurring in the node and may be analogous to the systemic reactions to tuberculous infection. In both cases T lymphocyte and macrophage cooperation, with associated cytokine release and recruitment of effector cells, are implicated in tissue damage and granuloma formation. The finding of monocytes and liver macrophage derived cells expressing CD30 in this patient suggests that this antigen reflects an as yet undefined functional capacity of a given cell, rather than its lineage.

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