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Relevance of CD79a expression for T-cell lineage attribution in CD7+/CD3- acute lymphoblastic leukemia

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We report two cases of a very early CD7+/CD3- T-cell acute lymphoblastic leukaemia (T-ALL) with the co-expression of the CD79a molecule. This association has never been described in very early T-ALL cases, and may reflect the immaturity of the haemopoietic precursor targeted by the leukaemic noxae. Moreover, co-expression of CD79a allows to exclude the myeloid lineage and, therefore, may be regarded as a useful marker for establishing T-cell lineage even in very immature forms.
The CD79 molecule is composed of two polypeptide chains, named mb-1 (CD79a) and B29 (CD79b). On B-cell membrane CD79 is physically associated with immunoglobulin. Being expressed early during B-cell development, almost all B-precursor lymphoblastic neoplasms are positive when tested with anti-CD79a antibodies. Thus, these antibodies have become of great value for the identification of B-cell malignancies.[1] Aberrant expression of CD79a has been reported in 10-30% of CD3+ T-cell acute lymphoblastic leukaemias (T-ALLs).[2,3] On the contrary, with the use of recent anti-CD79a monoclonal antibodies, aberrant expression of CD79a has never been observed in acute myeloid leukaemia.[4] These observations suggest that CD79a might be useful for T-lineage attribution, especially in cases lacking a clear T-cell immunophenotypic pattern, as usually occurs in the very immature CD7+/CD3- T-ALLs.[5,6] These suggestions are further supported by the present two cases.
A 30-year old women (case #1) and a 59-year old man (case #2) were admitted to our hospital because of leukocytosis and anaemia. Platelet count was normal in both cases. Blood chemistry parameters were all within the normal range. Physical examination revealed a moderate enlargement of the spleen. In both cases, bone marrow aspirate showed subtotal bone marrow infiltration by L2 morphology blasts. Immunophenotypic analysis was performed by FAC-scan on bone marrow samples using a broad panel of monoclonal antibodies, including, inter alia, anti-cytoplasmic and cell surface TCR e chain (CD3), anti-CD2, CD5, CD117 and CD19. Bone marrow leukaemia infiltration was confirmed by bone marrow biopsy. Immunohistochemical analysis was performed on paraffin sections from bone marrow biopsy using anti-CD20, anti-CD79a, anti-PAX5, anti-CD68 (PG-M1), anti-CD7 and anti-CD3 antibodies.[7]
The immunophenotype analysis of leukaemia cells in our patients did not allow a definite lineage attribution of leukaemia. In both cases, in fact, cells were CD34, TdT, CD7, HLA-DR, and CD79a positive. In addition, co-expression of the myeloid-associated antigens CD33 and CD13 was observed in case #1 and case #2, respectively. In case #2, expression of the CD117 and of the T-cell-associated antigen CD2 was also detected. All the other T-, B- an myeloid-cell markers were negative. Immunohistochemical analysis on bone marrow biopsy confirmed the co-expression of CD7 and CD79a on leukaemia blasts in absence of CD3 antigen. The possible T-cell origin of the leukaemia cells was suggested by the pattern of CD7 expression (high-intensity) and, in case 2, by CD2 co-expression together with the negativity for B-cell, NK and myeloid markers, including the absence of the BSAP/PAX-5 gene product, the cytoplasmic myeloperoxidase (MPO) protein and of the CD56 molecule. Furthermore, negativity for all the other features distinguishing more mature T-cell ALL,

and positivity for the CD7, CD34 and CD117, together with the co-expression of myeloid-associated antigens, suggested a possible origin from a very immature T-cell oriented haemopoietic precursor. These suggestions were subsequently confirmed in case 1 by PCR analysis that documented the TCRdelta Dd2-Jd1 rearrangement while the TCRalphabeta and TCRgamma genes were germ line. The Dd2-Jd1 junction is indeed both a strong T-lineage predictor,[8] being very rarely observed in either B-precursor ALL, NK or myeloid acute leukaemia, and a marker of immaturity, being the first TCR rearrangement to be detected during T-cell development.[9,10] In case #2, origin of the leukaemic cells should be even more immature as suggested by the TCRdelta germ line gene configuration found at Southern Blot analysis.

Both patients received an intensive induction and consolidation treatment including high dose cytosine-arabinoside, achieving complete haematological and even molecular (case #1) remission of the disease (14+ months, case 1; 8+ months, case #2). Although related to two cases only, these results appear to be interesting, if compared with the generally reported unfavourable prognosis of early CD7+ T-ALL with conventional chemotherapy. Kurtzberg et al.[11] in a series of 9 patients with CD7+ undifferentiated leukaemia observed no response even to conventional induction chemotherapy.

In conclusion, our data represent the first evidence of an aberrant expression of the CD79a molecule in a CD7+/CD3- very early T-ALL. The following findings are with underlying: 1) expression of CD79a in T-ALL may reflect the immaturity of the haemopoietic precursor targeted by the leukaemic noxae; 2) in cases in which the immunophenotype fails to attribute a clear cell lineage origin, co-expression of CD79a allows to exclude the myeloid lineage and, therefore, may be regarded as a useful marker for establishing T-cell lineage even in very immature form and in the absence of genotypic analysis. Future large studies are warranted to assess the biologic and clinical significance of CD79a co-expression in T-ALL patients.

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