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CORRESPONDENCE

Rapid Onset Anemia in Chronic Myeloid Leukemia Due to Red Cell Agglutination: A Rare Occurrence

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Dear Editor,

Anemia in a patient of chronic myeloid leukemia (CML) on therapy generally raises the suspicion of disease acceleration. We report a patient in whom a rapidly developing anemia turned out to be, as a simple low-power examination of the peripheral blood and bone marrow smear revealed, a result of blast crisis complicated most unexpectedly by prominent red cell agglutination (RCA), due possibly to cold agglutinins.

A 43 year old female with a 15 year history of Philadelphia positive CML in chronic phase presented with body ache, low grade fever, anemia and pedal edema. Her hemoglobin was 37 g/L, total leukocyte count 7.7 $\times$ 10^9/L, and platelets 72 $\times$ 10^9/L, a significant change from the corresponding figures a month back, of 146 g/L, 10.9 $\times$ 10^9 and 139 $\times$ 10^9/L.

The substantial drop in hemoglobin from 146 to 37 g/L over 1 month was found not to be due to acute blood loss. Peripheral blood smear showed leucoerythroblastic picture with 4% blasts and 2% basophils, and strikingly and unexpectedly, conspicuous agglutination of red cells (Fig. 1a). Serum LDH was high (408 U/L), direct Coombs test was positive and confirmed auto-immune hemolysis. Cold agglutinins could not be tested. Bone marrow aspirate showed a near total replacement by blasts, largely degenerated (Fig. 1b). Blasts were morphologically and immune-phenotypically lymphoid: CD45+, CD19+, CD79a+, CD10+, CD34−, MPO−, cCD3−. Dose of imatinib was increased to 600 mg and vincristine and prednisolone were added. Post-therapy, the red cell agglutinates disappeared.

Anemia may be the first indication of transformation in CML. Our patient was of interest because RCA due to autoimmune hemolytic anemia (AIHA) was seen in CML, a very rare co-occurrence that caused rapid onset of severe anemia and could be picked up easily on low power microscopic smear examination.

RCA occurs in AIHA of the cold agglutinin type. Among malignancies, AIHA is common in lymphoproliferative disorders, particularly chronic lymphocytic leukemia (CLL) (10–20% cases) [1]. However, even here, the cold agglutinin variety is uncommon (2–3% cases only) [2]. Autoimmune hemolysis in CLL has been attributed to complex interactions between neoplastic cells, abnormally functioning T-cells and cells of the microenvironment [3].

AIHA is rare in CML. Maldonado et al. (1967), discussing their own and published papers, reported AIHA in 5 cases of CML [4]. Cold agglutinins were, however, not specifically mentioned. RCA was described in CML in 4/293 cases after allogeneic bone marrow transplantation [5] and Raynaud's phenomenon, presumably due to cold agglutinins, post-interferon in 2/48 patients [6]. The phase of the disease was not mentioned in these reports.

Among hematological malignancies, AIHA is overwhelmingly more common in lymphoid neoplasms. It is not possible to say on the basis of one case, such as we had, if AIHA was related to the blast crisis being lymphoid.

We conclude that though rare, cold agglutinin disease also should be considered, in CML patients who experience rapid and severe fall in hemoglobin; a simple low power

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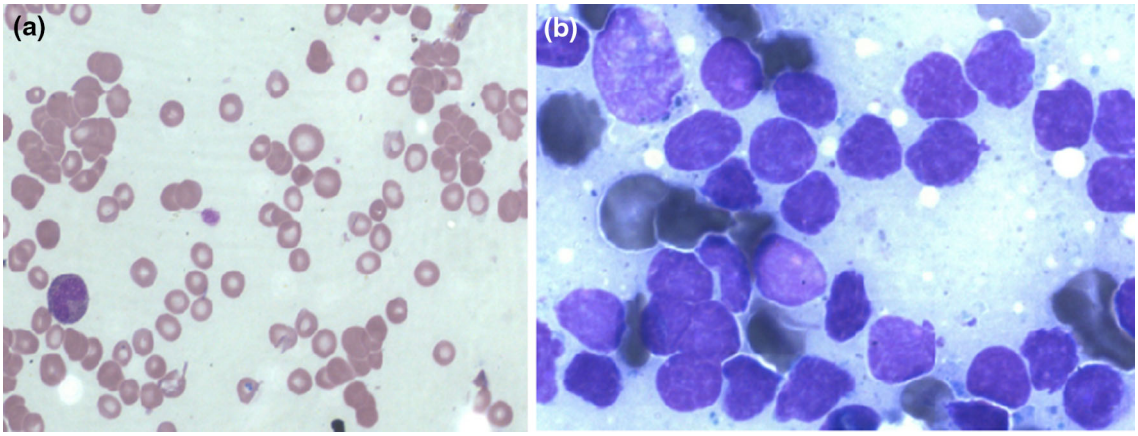

Fig. 1 **a** Red cell agglutinates (arrows) on peripheral smear in a case of chronic myeloid leukemia, blast crisis. **b** Bone marrow aspirate smear showing diffuse replacement with blasts, including several degenerated forms

examination provides the answer and helps appropriate management.

Compliance with ethical standards

Ethical Approval Peripheral blood smear, bone marrow examination and flow cytometric analysis was done as part of routine diagnostic work up. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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