Hypereosinophilia associated with dysplastic features and a constitutional translocation previously not described

We report an uncommon case of hypereosinophilia and splenomegaly in a young patient who showed marked morphologic and cytochemical dysplasia of eosinophils together with myeloproliferative and myelodysplastic traits. The patient bore a constitutional translocation not previously described.

Sir,

Many cytogenetic abnormalities have been described in patients with eosinophilia.1-3 It has been rarely associated with constitutions.2 In 1997, Brito-Babapulle published a review on hypereosinophil syndromes and clonal eosinophil disorders which clarified the differential diagnosis between them and establish criteria for the diagnosis of chronic eosinophilic leukemia (CEL). These are: mature eosinophils in peripheral blood, established clonality, absence of dysplastic morphological features, absence of Ph+/bcr-abl rearranged cells, absence of clonality.2 Nevertheless, the case of one of our patients suggests that these questions are not yet totally clarified. This patient probably suffers from a myeloproliferative disorder with trilineage myelodysplasia and atypical eosinophil proliferation together with a constitutional cytogenetic alteration not previously described.1,5,6

A 38-years old male with a normal phenotype was referred to our center because of large asymptomatic splenomegaly. His blood count was 9,400 WBC/µL (10% eosinophils, 1% basophils, 3% metamyelocytes, 9% bands, 58% neutrophils, 15% lymphocytes; 4% monocytes), Hb and platelets were within normal limits. A month later, the blood count was 4800 WBC/µL (23% eosinophils and the rest of the differential count similar to the previous one). Biochemical parameters, serology, and iron balance were normal. LAP score was 82 (normal). A bone marrow aspirate showed hypercellularity with 45% of eosinophils in different stages of maturation with numerous mitoses and marked morphologic abnormalities of eosinophils (ringed nuclei, nuclear hypersegmentation, cytoplasmic vacuolization, dyserythropoiesis and dysplasmoblasts). Cytochemical studies: eosinophils were PAS and chloroacetate esterase positive; 2% of ringed sideroblasts. A bone marrow biopsy was hypercellular with an increase of myeloid precursors and a great number of clusters of eosinophils. There were also two clusters of blasts and diffuse reticulin fibrosis.

The karyotype in bone marrow was 46 XY der(8) t(1;8)(p22;q24), and was identical in peripheral lymphocytes stimulated with PHA. Bcr-abl rearrangement

References

was negative. The patient was treated with hydroxyurea, which decreased the size of his spleen and the number of peripheral eosinophils. A few months later he underwent an unrelated bone marrow transplantation and was in remission a year later.

The diagnosis of CEL does not fit exactly the criteria proposed by Brito-Babapulle, since our patient has marked myelodysplasia. However the presence of fibrosis, hypercellularity in bone marrow, hepatosplenomegaly and the good response to hydroxyurea make diagnoses other than myeloproliferative disorder difficult.

The clonality of eosinophils, one of the key criteria could not be established directly since the detected cytogenetic alteration turned out to be constitutional. He fulfills other criteria proposed by Brito-Babapulle: major (medullary fibrosis, trilineage dysplasia, presence of ALIP) and minor (splenomegaly, normal levels of Ig, marked morphologic abnormalities of eosinophils). In resemblance of AML M4 Eo, in which the clonality of the eosinophils is well established, the cytochemical abnormalities of these cells are the same as in our case.

Finally, the presence of a constitutional cytogenetic alteration not previously described associated with any hematological disease raises two questions: does an uncommon traslocation have a possible pathogenic role in an also uncommon disease; and any undescribed cytogenetic alteration must be discarded as constitutional.

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References

Childhood Hemophagocytic Syndrome Associated with Kikuchi's Disease

We reported the cases of two children with Kikuchi's disease who developed hemophagocytic syndrome (HS) and responded well to intravenous immunoglobulin and corticosteroid therapy. Childhood HS may be associated with Kikuchi's disease and seems to have a less aggressive clinical course and better prognosis. Chemotherapy could be reserved for those who fail to respond to such a regimen.

Sir, Hemophagocytic syndrome (HS) is a histiocytic reactive process frequently associated with infection1-2 or malignancy.3 An etoposide-containing regimen has produced satisfactory results in non-familial childhood HS,4 but the patients' long-term survival is still uncertain.5 In contrast, subacute histiocytic necrotizing lymphadenitis or Kikuchi's disease is a well-defined and distinct clinicopathologic entity and usually follows a benign self-limited clinical course. There are only two reports of HS simultaneously associated with Kikuchi's disease in the literature4 5 but the prognosis and treatment strategy for HS in Kikuchi's disease is still unknown. We here report the cases of two children with simultaneous Kikuchi's disease and HS.

Case #1. A 14-year old boy had a two-week history of fever, fatigue, poor appetite and progressive cervical lymph node swelling. On examination, he had a temperature of 39°C and cervical lymphadenopathy (6 to 4 cm in diameter). The liver was palpable 6 cm below the right costal margin. The initial blood profiles were within normal limits. Elevation of acute C-reactive protein (CRP) level to 38.8 mg/L was noted. Despite the supportive and empirical antibiotic treatment, intermittent spiking fever and constitutional symptoms remained. Biopsy of lymph nodes revealed paracortical necrotizing lesions with typical features of Kikuchi's disease (Figure 1). In situ hybridization for Epstein-Barr virus (EBV) genome using the EBER-1 probe was negative. Progressive leukopenia, thrombocytopenia, coagulopathy and increasingly deranged liver function occurred in the subsequent days (Table 1). A bone marrow aspiration showed...