CASE REPORT
HYPEREOSINOPHILIA IN A PATIENT WITH ACUTE LYMPHOBlastic LEUKEMIA

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(Received 10 October 1986; accepted 5 March 1987)

A case of a coincident acute lymphoblastic leukemia and marked eosinophilia is presented. The clinical and 
pathological features of this case are discussed with special emphasis on the hypereosinophilic syndrome versus 
secondary hypereosinophilia that can be found to accompany ALL. Special immunological studies may be 
helpful in the diagnostic procedures.

Key words: Eosinophilia, Hypereosinophilic syndrome, Acute lymphoblastic leukemia.

INTRODUCTION
The hypereosinophilic syndrome (HES), represents idiopathic hypereosinophilia (blood eosinophil 
counts of over 1.5 × 10^9/l) of an unknown cause and has various clinical expressions.1,2 Three different 
forms have been described: (1) the benign HES with only lung involvement and angioedema, which often 
responds to treatment with steroids alone;3 (2) the intermediate HES with cardiac or CNS involvement, 
which in spite of treatment with steroids and cytotoxic drugs has a bad prognosis;4 and (3) the 'malignant' extreme of the HES featuring cytogenetic abnormalities of the eosinophils or other features of a leukemic disease.5

Secondary hypereosinophilia is often found to accompany a wide range of diseases including parasitic infestations, allergic diseases, skin diseases, pulmonary infiltration with eosinophilia and malignant diseases, including lung and gastrointestinal carcinomas, myeloproliferative disorders and myeloid leukemias.6 The present report deals with a patient in whom the presenting features could be attributed to either HES or acute leukemia and only immunologic studies helped to clarify the diagnosis of acute lymphoblastic leukemia.

CASE REPORT
A female, age 42 was admitted with a history of fatigue and diffuse muscle pain during one month. She had previously been well, had not travelled recently or been exposed to drugs or disease. One week prior to admission, fever, blurred vision and a skin rash had developed, and on admission, she complained of pain in her left arm. The temperature was 39.8°C, there were generalized petechiae and a flaccid paresis of the left arm. There was no lymphadenopathy and spleen and liver were not palpable.

The haemoglobin was 140 g/l, and the platelet count 48 × 10^9/l. The blood leucocyte count was 
9 x 10^9/l with 80% mature eosinophils, some with coarse eosinophil granules and hypersegmentation, and some larger than nor-

mal. No blasts were seen in the blood. The initial 
bone marrow was maximally hypercellular with 49% 
esoinophil granulocytes and 19% eosinophil myelo-
cytes and only 2% myeloblasts. The immunological 
phenotype of bone marrow cells was mainly 
myeloid, with a few cALLa+ (Common ALL 
Antigen) cells and no TdT+ (Terminal Deoxyribo-
nucleotidyl Transferase) cells (Table 1). Chromo-
some analysis of bone marrow cells with banding 
technique was normal. The serum B12 level was 
1522 pmol/l (normal range 200–600). Chest X-ray 
was normal, but ECG showed signs of ischaemia.
Table 1. Immunological phenotype of bone marrow mononuclear* cells

<table>
<thead>
<tr>
<th>Antibody</th>
<th>CD No.†</th>
<th>Day 1</th>
<th>Day 24</th>
</tr>
</thead>
<tbody>
<tr>
<td>B1 (Pan B)‡</td>
<td>—</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Leu5 (Pan T)§</td>
<td>CD 2</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Ia (HLA-DR)‡</td>
<td>—</td>
<td>70</td>
<td>68</td>
</tr>
<tr>
<td>J5 (cALLa)‡</td>
<td>CD 10</td>
<td>8</td>
<td>37</td>
</tr>
<tr>
<td>MO2 (Monocytic)</td>
<td>CD 14</td>
<td>15</td>
<td>33</td>
</tr>
<tr>
<td>My7 (Myeloid)‡</td>
<td>CD 13</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>My9 (Myeloid)‡</td>
<td>CD 33</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>TdT (Lymphoblastic)‖</td>
<td>—</td>
<td>0</td>
<td>40</td>
</tr>
</tbody>
</table>

*Heparinized bone marrow aspirate was Ficoll-Hypaque [Lymphoprep (R)] separated and incubated with the antibodies listed (all monoclonal except TdT) in the 1st step and fluorescein isothiocyanate-conjugated rabbit anti-mouse antibody in the 2nd step. Read in a Leitz immunofluorescence microscope, analyzing 2 × 50 cells per marker.
†Cluster Designation Number (3rd International workshop, Oxford, UK 1986).
‡Coulter Clone (R).
§Becton Dickinson (R).
‖BRL Bethesda Research Laboratories (R).

The CSF was normal and a brain CT-scan also normal.

A tentative diagnosis of eosinophil leukemia was made based on the high WBC and the extreme hypercellularity of the bone marrow with depressed erythropoiesis and thrombopoiesis, although the absence of blasts made the diagnosis of acute eosinophilic leukemia less likely and, based on the normal chromosome analysis, a chronic eosinophil granulocytic leukemia was also less likely.

Following antibiotic treatment the patient became afebrile and at day 7, antileukemic treatment with Daunorubicin (DNR) 45 mg/m² daily for 3 days, continuous infusion of Cytosine Arabinoside (Ara-C) 100 mg/m² daily for 7 days, and prednisone 100 mg per day was started. This regimen reduced the WBC to 7.2 × 10⁹ at day 24, but still with 68% eosinophils. However, the bone marrow at this date was still hyperplastic and the morphological feature at this time was a predominance of mainly lymphoblastic cells. This was confirmed at immunological examination (Table 1), showing approximately 40% cALLa+, TdT+ cells. The TdT+ cells were clearly mononuclear blasts that could easily be distinguished from the polymorphonuclear eosinophils with strong, unspecific fluorescence of cytoplasmic granules (Fig. 1). These mononuclear cells did not express any myeloid antigens (My7, My9, MO2), on the surface membrane. However, doublestaining was not performed to document this.

Consequently, the working diagnosis was revised to possible ALL with secondary hypereosinophilia, and to the second treatment series of Ara-C and DNR, started at day 30. Vincristine was added, Prednisone 60 mg per day still given. At day 39, the WBC was reduced to 4.1 × 10⁹ with 31% eosinophils.

At this time congestive heart failure developed and the patient was digitalized and diuretic treatment started. An ultrasound heart scan on day 25 showed no mural thrombi and no evident endocardial disease. However, at day 40 the patient suddenly died.

At autopsy, the endocardium was covered by massive mural thrombi, recent subendocardial infarction and necrosis without eosinophil infiltrates was found. Scattered fibrosis was found in the myocardium. The bone marrow was now normocellular without blastic or eosinophil predominance, consistent with remission.

DISCUSSION

Hypereosinophilia with organ involvement can arise as a primary process, as seen in HES, or secondarily to other disease, as we believe happened in this patient. It may be difficult to identify this underlying process because of the massive eosinophilia, and special studies, employing, e.g. immunological or cytogenetic techniques may in such cases be useful.7

Although the final diagnosis in this case cannot be entirely settled, we consider ALL with hypereosinophilia a most likely diagnosis, based on the presence of cells with lymphoblastic morphology and a pre-B cell phenotype in the midst of a huge population of mature eosinophils with no signs of maturation arrest in that cell line. (In fact, the eosinophil granulocytes were so dominant that they were richly represented in the cell pellets even after Ficoll separation.) If a biphenotypic leukemia was present, such a maturation arrest would have been expected, whereas in a biclonal leukemia, e.g. an eosinophil granulocytic leukemia with an incipient lymphoblastic blast crisis, the Philadelphia chromosome should be present. In a normal adult, a proportion of 40% TdT+ pre-B cells is not likely to be encountered, not even in a regenerating bone marrow.8 Retrospectively, the finding of 8% cALLa+ cells in the first bone marrow specimen might have represented the evolving lymphoblastic clone, although any TdT+ cells were not detected at that time.

The huge proportion of Ia+ cells at the first