Case Report

Chronic Eosinophilic Leukemia presenting as Peripheral Neuropathy

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Abstract

Chronic Eosinophilic Leukemia (CEL) is a rare form of chronic myeloproliferative disorder of unknown etiology with no data on its true incidence. The disease has a wide variety of manifestations. Literature search has not shown peripheral neuropathy as the only presentation of CEL. Our case is probably the first such report case. Here we are reporting a 45 year old male patient who presented with progressive weakness of upper and lower limbs for 6 months and weight loss for 2 months. Neurological examination revealed findings consistent with bilateral sensorimotor polyneuropathy later confirmed by nerve conduction studies. Complete blood count revealed total wbc count – 51,870/mm³, eosinophil – 62.1% (32,315/mm³). Peripheral Blood film revealed eosinophilic leucocytosis. Superficial peroneal nerve biopsy showed mild perivascular infiltration with inflammatory cells. No granuloma or malignancy was seen. Bone Marrow examination showed hyperactive granulopoiesis with predominance of eosinophil series with progressive maturation along with presence of myelocytes, hypersegmented eosinophils and giant eosinophils. Blast cell was around 7%. Patient was treated with imatinib and prednisolone which showed excellent response.

Introduction

Chronic Eosinophilic Leukemia (CEL) is a rare form of chronic myeloproliferative disorder of unknown etiology with no data on its true incidence. An evidence of genetic clonality of eosinophils or an increase in blast cells in the blood or bone marrow is mandatory for diagnosis of CEL1. This disease may pose confusion during diagnosis owing to its wide variety of manifestations. Some of its manifestations may be overlooked or neglected causing delay or misdiagnosis which might result in significant amount of mortality and morbidity2. We report a case of 45 year old male with eosinophilic leukemia that presented as peripheral neuropathy.

Case Report:

A 45 years old male had a history of right sided nephrolithotomy with D-J stenting for bilateral nephrolithiasis with marked right sided hydronephrosis 7 months prior to admission. During pre-operative investigations, complete blood count revealed leucocytosis with eosinophilia. 6 months prior to admission, he presented with progressive weakness of upper and lower limbs. He developed weight loss and anorexia 2 months prior to admission. Patient was initially diagnosed as a case of Churge Strauss Syndrome (a type of vasculitis with eosinophilia) and was placed on a course of prednisolone. However there was no significant improvement in patient’s symptoms following course of steroid.

On admission, patient was found to be cachectic and anemic. Neurological examination revealed findings consistent with bilateral sensorimotor polyneuropathy of both upper and lower limbs. Muscle power was 1/5 for all 4 limbs. Complete blood count revealed Hb – 7.6 g/dl, total WBC count – 51,870/mm³, Polymorphs – 28.1%, Lymphocyte – 9.4%, Monocyte – 0.2%, Eosinophil – 62.1% (32,315/mm³), ESR – 37mm in 1st hour and platelet count within normal range. Peripheral Blood film revealed eosinophilic leucocytosis. Tests to determine the cause of eosinophilia were done. ANA, c-ANCA, p-ANCA, ICT for filarial and stool for ova all came back negative. Serum IgE level was 181.3 IU/ml (within normal range). Nerve conduction studies showed changes consistent with mixed sensory-motor polyneuropathy. Superficial peroneal nerve biopsy and histopathology showed mild perivascular infiltration with inflammatory cells. No granuloma or malignancy was seen. Bone Marrow examination showed hypercellularity, depressed erythropoiesis and hyperactive granulopoiesis with predominance of eosinophil series.

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Figure 1: 2 Blast cells from bone marrow smear (arrow)
These eosinophils showed progressive maturation along with presence of myeolcytes, hypersegmented eosinophils and giant eosinophils. Blast cell was around 7% (Figure 1). These findings were consistent with chronic eosinophilic leukemia. Fluorescent in-situ hybridization (FISH) assay for platelet derived growth factor alpha (PDGFRA) gene, which is commonly associated with chronic eosinophilic leukemia, came back negative. Liver functions tests and serum creatinine level were within normal range.

Patient was placed on Tab. Imatinib (100mg) twice daily and Tab prednisolone at 1mg/kg daily and no blood transfusion was given. Within 7 days of treatment, patient's general wellbeing improved along with muscle power of all four limbs.

Table below shows improvement of CBC parameters during course of treatment

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Day of admission</th>
<th>Day 3</th>
<th>Day 10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin (g/dl)</td>
<td>7.8</td>
<td>8.2</td>
<td>9.0</td>
</tr>
<tr>
<td>WBC (/mm³)</td>
<td>51870</td>
<td>12130</td>
<td>10080</td>
</tr>
<tr>
<td>Eosinophil (%)</td>
<td>62.3</td>
<td>15.6</td>
<td>12</td>
</tr>
</tbody>
</table>

Discussion

The term chronic eosinophilic leukemia is often used in conjunction with hypereosinophilic syndrome (HES). Hypereosinophilic syndrome is defined by the following: (1) the presence of eosinophilia (>1500 eosinophils/mm³ for at least 6 months) that remains unexplained despite a comprehensive evaluation for known causes of eosinophilia (including parasitic helminth infections, HIV, drug hypersensitivity, nonhematologic malignancies, lymphomas, and primary allergic disorders) and (2) evidence of organ dysfunction directly attributable to the eosinophilia or otherwise unexplained in the clinical setting. Some authors classify chronic eosinophilic leukemia as a subtype of HES while others consider CEL as a mutually exclusive diagnosis from HES.

The modern diagnostic criteria as proposed by World Health Organization for CEL include:

- Persistent eosinophilia ≥1.5 x 109 /L in blood, increased bone marrow eosinophils
- > 5% but<19% myeloblasts in the bone marrow or 2% in the peripheral blood
- Clonality of myeloid cells
- No reactive eosinophilia due to allergy, parasitic, infectious, pulmonary, or collagen vascular disease
- No reactive eosinophilia due to other malignancies: T-cell lymphomas, Malignant lymphomas, Acute lymphoblastic leukemia/lymphomas, Hodgkin’s lymphoma, other myeloproliferative diseases, Myelodysplastic syndrome, acute myeloid leukemia including inv (16), t (16; 16), CML
- No T-cell population with abnormal cytokine production and aberrant phenotype

The neoplastic, monoclonal nature of eosinophils has been further substantiated by various cytogenetic studies showing a multitude of chromosomal abnormalities 5-9 and molecular genetic abnormalities particularly linked to eosinophil differentiation (such as formation of a FIP1L1- PDGFRA fusion gene). In our case, patient was negative for PDGFRA fusion gene.

The hyperproliferation of eosinophils and infiltration of end organs is responsible for the clinical symptoms. 11 The most common manifestations of CEL include weakness, fatigue, cough, dyspnea, myalgia, rash, and rhinitis. Progressive heart failure is a classical example of eosinophil-mediated organ injury and is the most common cause for mortality. Other important manifestations include lung fibrosis, eosinophilic gastritis, hypertension, encephalopathy, ataxia, and thromboembolism. Our case did not have any of these above features but instead presented as peripheral neuropathy. Although HES can present with peripheral neuropathy, no literature exists of CEL presenting as peripheral neuropathy and therefore we have no evidence of how they may be related. So we believe, this may be the first reported case of chronic eosinophilic leukemia presenting as peripheral neuropathy. Peripheral neuropathy in other forms of leukemia such acute lymphoblastic leukemia, acute myelomonoblastic leukemia, acute myelomonocytic leukemia, acute monoblastic leukemia and acute megakaryoblastic leukemia have been attributed to direct nerve infiltration of leukemic cells. However, in our case, nerve biopsy revealed no malignant infiltration of nerves. Therefore, we are speculating whether these neurological symptoms can be attributed to paraneoplastic syndrome as a result of CEL.

The mainstay of treatment of chronic eosinophilic leukemia is systemic steroids, hydroxyurea and the tyrosine kinase inhibitors imatinib, nilotinib, and sorafenib. Our patient showed dramatic improvement with imatinib and steroids.

References


