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آموزش مهارت های کاربردی در تدوین و چاپ مقاله
Acute Lymphoblastic Leukemia with Eosinophilia and *Strongyloides stercoralis* Hyperinfection

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**Abstract**

**Background:** Acute lymphoblastic leukemia (ALL) is the most common malignancy in children. Bone pain is an important symptom that can be severe. Eosinophilia without any other abnormal laboratory findings is rare in ALL. *Strongyloides stercoralis* in ALL causes disseminated fatal disease.

**Case Presentation:** This 9-year-old girl presented with bone pain in lumbar region. Bone pain was the only symptom. The patient didn’t have organomegaly. The BM samples were studied by flow cytometry, which showed pre-B cell ALL. Larva of *Strongyloides stercoralis* was found in fecal examination. Plain chest x ray showed bilateral para-cardiac infiltration. Strongyloidiasis was treated before starting chemotherapy. After two days treatment with Mebendazol the patient developed cough, dyspnea, respiratory distress and fever. The treatment changed to Ivermectin for 2 days. Chemotherapy started five days after diagnosis of leukemia.

**Conclusion:** The patient complained merely of bone pain in lumbar region without any other signs and symptoms. Peripheral blood smear showed eosinophilia without any other abnormality. Stool examination showed *Strongyloides stercoralis* larvae. We suggest that all patients diagnosed as ALL in tropical and subtropical regions should be evaluated for parasitic infection especially with *Strongyloides stercoralis*.

**Key Words:** Acute Lymphoblastic Leukemia; Eosinophilia; Strongyloidiasis

**Introduction**

Acute lymphoblastic leukemia (ALL) is the most common malignancy in children. Pallor, fatigue, bone pain, hepatomegaly, splenomegaly, lymphadenopathy, petechiae, purpura, bleeding, and fever are commonly present. Bone pain can be severe and is often associated with close to normal peripheral blood counts[1]. This finding may contribute to delayed diagnosis. Eosinophilia
of >600/μL is abnormal in the vast majority of cases. Eosinophilia without any other abnormal laboratory finding is rare in ALL [3,4]. Acute eosinophilic leukemia (a variant of the M4 phenotype), precursor B-cell ALL with T [5,14], and precursor T-cell lymphoblastic lymphoma with T [8,13] may be associated with eosinophilia. A broad variety of allergic, infectious, neoplastic, and idiopathic diseases are associated with increased blood and/or tissue eosinophils. The most common infectious causes for secondary eosinophilia are tissue invasive parasites such as Strongyloides stercoralis, hookworm, and Toxocara canis. Strongyloidiasis is endemic in tropical and subtropical regions and occurs sporadically in temperate areas [8]. Diagnosis requires identification of larvae in feces, body fluids, or biopsy of involved tissues. S. stercoralis infection 38 percent of patients with eosinophilia in some areas has been reported [9]. Manifestation of Strongyloides can range from asymptomatic eosinophilia in the immunocompetent host to disseminated disease with septic shock in the immunocompromised host [10]. It is thought that chemotherapy promotes the maturation of larvae from a quiescent rhabditiform stage. Successful management of hyperinfection syndrome requires early detection and initiation of therapy. Ivermectin can treat fulminant Strongyloidiasis [11].

Case Presentation

This 9-year-old girl presented with bone pain in lumbar region since 18 days before referring to our center. The patient had suffered a trauma in the lumbar region two months ago. Bone pain was the only symptom. Temperature was normal; no pallor. Normal heart sounds and respiratory rate. No lymphadeno-

Discussion

Our patient presented with bone pain in lumbar region without pallor, fatigue, fever, lymphadenopathy, hepatosplenomegaly, petechiae, purpura or bleeding that are common signs and symptoms in ALL [12]. Severe bone pain in children should be considered as an important sign of leukemia even though it may be associated with normal

Table 1: Laboratory findings at admission

|         | WBC × 10⁹/L | Hemoglobin (g/dl) | Platelet × 10⁹/L | Neutrophile | Lymphocyte | Eosinophil | ESR mm/hr | Stool exam      |
|---------|-------------|-------------------|------------------|-------------|------------|------------|-----------|---------------|
| At presentation | 5.600       | 12                | 307              | 19%         | 36%        | 45%        | 6         | S.S.larvae     |

WBC: Whit Blood Cell; ESR: Erythrocyte Sedimentation Rate; SS larvae: Strongyloides Stercoralis
peripheral blood counts\textsuperscript{[13]} and if noted, this may contribute to early diagnosis of the disease. In peripheral blood smear of our patient there was only eosinophilia without any blast cells or thrombocytopenia. Although stool examination showed \textit{Strongyloides stercoralis} larvae and this could cause high eosinophils, we should remember that eosinophilia is a herald for diagnosis of ALL especially when associated with severe bone pain. It is recommended to examine stool in tropical and subtropical regions in all patients diagnosed as ALL to evaluate parasitic infection especially \textit{Strongyloides stercoralis}. Burgers et al reported of bone marrow transplantation (BMT) in an acute lymphoblastic leukemia with peripheral blood eosinophilia, who developed moderate to severe pulmonary symptoms probably by pulmonary infiltration of \textit{Strongyloides stercoralis} after cytotoxic chemotherapy\textsuperscript{[14]}. Although \textit{Strongyloides stercoralis} hyperinfection syndrome (SHS) may develop in individuals with asymptomatic infection receiving immunosuppressive treatment, our patient probably had developed symptoms of SHS before starting chemotherapy, as she was an acquired immunodeficient patient (ALL). The patient became febrile and blood count showed severe neutropenia at that time. Blood culture was negative for bacteria. Some studies showed that SHS can predispose to Gram-negative sepsis and death\textsuperscript{[15,16]}. Therefore our treatment aimed to cover bacterial infection and Strongyloidiasis concomitantly. Bezares et al showed that disseminated Strongyloidiosis is fatal in acute leukemia\textsuperscript{[17]}. Our patient became afebrile and recovered from respiratory distress several days after treatment. The patient is in complete remission after 15 months. We had started chemotherapy after treatment of \textit{Strongyloides stercoralis} to prevent promotion of the maturation of larvae from a quiescent rhabditiform stage \textsuperscript{[18]}. It’s not clear that mebendazol induced severe leukopenia and dissemination of Strongyloides stercoralis or not? Ivermectin is preferred to other antihelmentic agents\textsuperscript{[19]}.

**Conclusion**

Before treating ALL we should rule out concomitant parasitic infections. It is preferred to treat Strongyloidiasis before starting chemo-

**Table 2**: Bone marrow Immunophenotype that is consistent with pre B-ALL

| CD2 | CD3 | CD5 | CD10 | CD13 | CD14 | CD20 | CD45 |
|-----|-----|-----|------|------|------|------|------|
| 4%  | 4.8%| 4.9%| 93%  | 8.2% | 0.2% | 76.9%| 85.9%|
therapy. We must consider *Strongyloides stercoralis* as a cause of fever and respiratory distress beside bacterial, fungal and viral infection in ALL in all phases of treatment. *Strongyloides stercoralis* may have been the unknown cause of death in many oncology centers in tropical regions. Finally, although high mortality rate is noted in disseminated Strongyloidiasis, it is still a curable disease when early diagnosis could be made and appropriate treatment applied.

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