Eosinophilia Associated With Fludarabine Use in A Case With CLL

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ABSTRACT

Eosinophilia is a common finding in clinical practice and is seen in various conditions including allergic diseases, parasitic infections and some cancers. Some drugs may cause eosinophilia (cephalosporins, analgesics e.g.). Fludarabine is a purine analog and is used in the therapy of chronic lymphoproliferative disorders. Here we reported a case with chronic lymphocytic leukemia treated by fludarabine and hypereosinophilia occurrence after this therapy and reviewed the literature information.

Key Words: Eozinophilia, Fludarabine, CLL

ÖZET

KLL Hastasında Fludarabin Kullanımına Bağlı Eozinofili

Eozinofili, klinikte allerjik hastalıklar, parazitik enfeksiyonlar ve bazı kanserler gibi farklı durumlarda sık rastlanan bir bulgudur. Bazı ilaçlar da (sefalosporinler, analjezikler gibi) eozinofiliye neden olabilir. Fludarabin bir pürin analoğudur ve kronik lenfoproliferatif hastalıkların tedavisinde kullanılmaktadır. Bu yazıda kronik lenfositik lösemi hastasına verilen fludarabin sonrası gelişen hipereozinofili rapor edilmiş ve literatür derlemesi yapılmıştır.

Anahtar Kelimeler: Eozinofili, Fludarabin, KLL

INTRODUCTION

Fludarabine is a purine analogue used in the treatment of large granular leukemia (LGL), hairy cell leukemia (HCL) and Waldenström's macroglobulinemia (WM). Disease free survival (DFS) and progression free survival (PFS) is longer in cases treated with fludarabine, however overall survival (OS) does not affected by this therapy. The most important toxicity of fludarabine is immunesuppression and rarely it may cause eosinophilia in peripheral blood (1).

CASE REPORT

A 63 year old man admitted to our hospital on August 1995 and he was diagnosed as B cell chronic lymphocytic leukemia (CLL)-stage II (according to Rai classification). He had symptomatic disease and was treated with 6 courses of cyclophosphamide, vincristine and prednisone (CVP). Partial remission (PR) was obtained. His disease relapsed on March 2000. Fludarabine and cyclophosphamide (30 mg/m^2 and 300 mg/m^2 for three days, respectively) combination chemotherapy was given. At the end of 6 courses complete remission (CR) was obtained. However eosinophilia was determined at peripheral blood smear; WBC count was 6.9 x 10^9/L and eosinophil count was 1.3 x 10^9/L. Bone marrow aspiration showed an increase in eosinophil precursors. Figure 1 and 2 show eosinophils in peripheral blood and bone marrow. Etiologic factors for eosinophilia were looked for but there was no evidence of any other disorder related with eosinophilia. He was followed without medication and eosinophilia persisted for 13 months.

DISCUSSION

Alkylating agents are preferred drugs for the first line therapy of chronic lymphoproliferative disorders. In the last years, clinical trials have shown that fludarabine may be used as first choice in these disorders. Response rates of fludarabine are higher as compared with alkylating agents. However fludarabine causes immunosuppression and opportunistic infections are common in cases treated with fludarabine. For this reason, prophylactic antimicrobial therapy is proposed in these cases. Although toxic effect on T lymphocytes is most prominent, the development of pancytopenia is not rare (1-3).

Eosinophilia is a rare condition associated with fludarabine therapy, there are only limited number of cases in literature. Similarly hypereosinophilia has been observed in cases treated with 2-chlorodeoxyadenosine (2-CdA) which is another purine analogue. Underlying mechanism is not known but some hypothetical points are present. Some cytokines entering to the circulation from lysing malignant cells may a stimulating effect on bone marrow. Pancytopenia may be seen after the therapy and at this stage IL-5 secreted in large amount may stimulate eosinophilopoiesis. The other speculation is allergic reaction to drug, and in a few of these cases skin rash may be seen. These three mechanisms are only hypothetic and the cause of fludarabine associated eosinophilia is not known (4,5). Some authors proposed that hypereosinophilia developing after fludarabine therapy is a good prognostic indicator. This is explained by maximum tumor cell lysis and bone marrow stimulation by secreted cytokines. However in other cases it has not been shown a correlation between eosinophilia and response to therapy. So validity of this explanation is obscure. In summary, the association between fludarabine and eosinophilopoiesis is not clear and detailed molecular analysis are required for this situation (5,6).

The important point in cases reported in literature is the occurence of eosinophilia in a short time after therapy and diappearence in very short time again. The interesting point of our case was the appearence of eosinophilia after 6 courses of chemotherapy and continuation of 13 months after the cessation of therapy. This is the difference of our case from other cases.

In conclusion, hypereosinophilia may be seen after fludarabine therapy but the cause is not known. It can be said that there is no relation with response to therapy and/or prognosis. We need further observations and studies to determine the pathogenesis of this condition.

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