Granulocytic Sarcoma in Patients with Chronic Myeloid Leukaemia

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Abstract

Granulocytic sarcoma is an unusual variant of myeloid malignancy most commonly encountered in the course of chronic or acute myeloid leukaemia. Of 60 patients of chronic myeloid leukaemia studied over 21 months, we encountered 6(10%) cases of granulocytic sarcoma. Four of these had granulocytic sarcoma on their first presentation. All those who were receiving hydràxyurea did not fare well but one who was put on DAT (daunorubacin, cytosine arabinocide, 6 thioguanine)regiinen went into remission with complete disappearance of lesions (JPMA 45:180, 1995).

Introduction

Granulocytic sarcoma is an unusual variant of myeloid malignancy characterized by extramedullary tumor masses composed of immature myeloid cells. The tumor may occur as an isolated finding or may be associated with acute myeloid leukaemia, chronic myeloid leukaemia, agnogenic myeloid metaplasia hypereosinophilic syndrome and polycythaemia vera. Initially these tumors were called "Chloromas" because of the green appearance of the freshly cut surface of the tumor. This green colour is due to abundance of enzyme myeloperoxidase in the leukemic cells. Since not all myeloid cells are green, the term granulocytic sarcoma is now preferred. The most common sites of its origin are skin, lymph node and bones. Other sites include breast, gastrointestinal tract, ovaries, brain, testis, kidney, peritoneum and spinal canal. Granulocytic sarcoma may arise during the course of leukaemia or precede its development. It may be the first evidence of relapse in a patient with acute myeloid leukaemia on maintenance therapy. These tumors may also represent the initial manifestation of a blast crisis of chronic myeloid leukaemia. The diagnosis of granulocytic sarcoma can be suspected on morphological grounds and confirmed by the presence of specific myeloid enzymes, CD13 and CD33 expression and lack of T cell and B cell specific antigens. We describe characteristics and the course of six patients who developed granulocytic sarcoma in association with chronic myeloid leukaemia.

Patients and Methods

Sixty cases of chronic myeloid leukaemia were diagnosed and followed for 21 months (1st July, 1992 to 31st March, 1994). The diagnosis of chronic myeloid leukaemia was based upon blood complete picture, leucocyte alkaline phosphatase activity, cytogenetics, bone marrow aspiration and biopsy where indicated.

The blood counts were performed on Technicon™ haematology analyzer, which was calibrated and quality controlled using high, normal and low commercial controls obtained from TechniconTh4. The differential count was done by counting 300 cells on push smears stained with Leishman stain. Leucocyte alkaline phosphatase staining and scoring was carried out by the method described by
Bone marrow aspirations and trephine biopsies were performed and processed by standard techniques\(^7\). Bone marrow aspiration sample was used for cytogenetic studies. The procedure used for direct culture was that described by Younis\(^7\). The diagnosis of granulocytic sarcoma was made by fine needle aspiration of the growth or its biopsy and processed by standard techniques\(^7\).

Patients, after informed consent, were placed on induction therapy with hydroxyurea 35 mg/kg body wt/per day orally\(^9\). Maintenance dose of hydroxyurea was adjusted according to the haematological parameters determined at fortnightly intervals. The patient who presented with CML in myeloid blast transformation was placed on DAT 3+7 (Daunorubicin for 3 days and other two drugs for 7 days) chemotherapy\(^10\).

**Results**

Of sixty patients of CML, a diagnosis of granulocytic sarcoma was made in 6(10%). Four patients had extramedullary disease on presentation, while two developed it during the course of the disease. The clinical and laboratory profile of each patient at presentation is show in the table.

All except one case who presented in blast crisis, had clinical and laboratory findings typical of chronic phase CML. One patient, a young girl of 16, presented with multiple lumps in both breasts. The biopsy of the lump suggested presence of myeloid blast cells. Although her peripheral blood and bone marrow aspirate showed excessive blasts but her LAP score was at the lower limit of the normal and Philadelphia chromosome was demonstrated in the bone marrow aspirate. Thus a diagnosis of CML in blast crisis was made. She responded very well to DAT 3+7 regimen and is still in remission. The clinical response to hydroxyurea was less satisfactory. One patient showed progressive deterioration with laboratory features of accelerated disease after 3 months. He died of fulminant hepatic failure soon after. Another patient is also showing progression to accelerated phase of disease with constitutional symptoms and progressive viscemegaly despite therapy for 8 months. One patient died postoperatively after his extra medullary leukaemic tumor was removed from the spinal canal, remaining two patients did not report for follow up and were later reported to be dead.

**Discussion**

CML is known to be a biphasic or triphasic disease. The initial chronic phase usually lasts for three to four years. Then the disease enters accelerated phase and later transforms into blast crisis\(^11\). However, sometime the patient presents when the disease is already in accelerated phase or blast transformation. Several features have been identified that are associated with disease transformation. Granulocytic sarcoma is one of the unusual manifestations of disease evolution and progression. It may arise simultaneously with typical blood and bone marrow pattern of acute leukaemia, during the course of
blast crisis or antedate its development in the marrow by months\textsuperscript{12}. Although there are several reports of occurrence of granulocytic sarcoma in literature but the largest series reported by Terjanian et al\textsuperscript{3} have estimated its frequency at 7.9\% of CML patients. No other significantly large series has been reported in the literature. In our series the incidence is 10\%, which is higher than that reported by Terjanian et al\textsuperscript{3}. Our 4 patients presented with granulocytic sarcoma at the time of diagnosis of CML, which was an unusual finding and has not been reported previously in the literature\textsuperscript{2,3}. Most of the reported cases of granulocytic sarcoma have occurred during the course of CML. Conventional hydroxyurea dosage proved ineffective in controlling the lesions of granulocytic sarcoma. Patients of granulocytic sarcoma required somewhat higher doses of hydroxyurea than other patients of CML in chronic phase without extramedullary disease. More aggressive chemotherapy in these cases could be an alternate option. One case who presented with marrow blast crisis and granulocytic sarcoma responded well to DAT 3+7 induction therapy. She is in complete remission for over one year. To summarize, granulocytic sarcoma is an unusual manifestation of CML, which may be a presenting feature. Its detection characterizes poor risk patients and may call for more aggressive therapy.

References