Granulocytic Sarcoma of Colon in a Patient with Acute Promyelocytic Leukemia

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Abstract Granulocytic sarcoma in a patient with acute promyelocytic leukemia (APML) has been described often in the relapse setting, however primary presentation of APML as granulocytic sarcoma is rare. We present a case of a 29 year old male who was evaluated for thrombocytopenia with haematochezia and a diagnosis of acute promyelocytic leukemia was established after the colonic biopsy was reported as a granulocytic sarcoma.

Introduction

A granulocytic sarcoma (chloroma, granulocytic sarcoma, extramedullary myeloid tumor), is a rare neoplastic condition consisting of immature myeloid cells and occurring at an extramedullary site that most frequently corresponds to the bone, skin, or lymph node, although any part of the

body may be affected [1]. In other words, it is an extra-medullary manifestation of acute myeloid leukemia; a solid collection of leukemic cells occurring outside of the bone marrow. MS most commonly consists of myeloblasts, with or without features of promyelocytic or neutrophilic maturation that partially or totally efface the tissue architecture. In a significant proportion of cases, it displays myelomonocytic or pure monoblastic morphologic features [2]. Here we present a case of granulocytic sarcoma in a patient of acute promyelocytic leukemia.

Case Report

Mr. M. P. S a 29 year old male was evaluated for fever with pancytopenia at another centre and treated as sepsis of unknown focus and? Macrophage Activation Syndrome on the basis of high ferritin, triglycerides and low fibrinogen levels. He was referred to our center with history of fever and haematochezia of one day's duration. At admission his Hemoglobin was 8.7 gm/dl, WBC count of 3,300/cu.mm and platelet count of 30,000/cu.mm. His PT, APTT and Fibrinogen were within normal limits. A gastroenterology consultation was obtained for the haematochezia and a colonoscopy was done which showed multiple ulcers in colon and ileum (Figs. 1, 2) which was biopsied. The biopsy was reported as a granulocytic sarcoma (Fig. 3) which on immunohistochemistry revealed neoplastic cells expressing MPO, CD43, CD3 (reactive T-cells), Ki-67 (70 %) and were negative for LCA, CK, CD20. Meanwhile a repeat bone marrow aspiration biopsy (Fig. 4) with immunophenotyping was done, which was reported as acute myeloid leukemia. On the basis of strong MPO positivity, immunophenotyping (CD13, CD33, MPO+ve and HLA DR-ve), and FISH for *t* (15, 17) positive (Fig. 5),

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Fig. 1 Caecal ulcer

Fig. 2 Ileal ulcer

Fig. 3 Biopsy of Colon—granulocytic sarcoma

Fig. 4 Bone marrow aspirate $\times 100$

Fig. 5 FISH for $t(15;17)$ showing one red (Chr 15–PML), one green (Chr 17–RARA) and one yellow-white (PML–RARA Fusion gene) signals by LSI PML/RARA translocation probe. (Color figure online)

a diagnosis of AML M3—Hypogranular variant, was made. Chemotherapy was started with Daunorubicin and all trans-retinoic acid (ATRA). One additional dose of Daunorubicin (80 mg) was given during the course of treatment due to very high counts. Platelet count, serum fibrinogen and PT PTT were regularly monitored and adequate supports were provided. Bone marrow assessment on day 28 showed features of differentiation and reported as a normal marrow in remission. He had bilateral blurring of vision due to retinal bleed which was treated conservatively. Patient tolerated the therapy well without any serious acute bleeding or ATRA syndrome. At the time of discharge his counts had stabilized and he was in a stable condition.

Discussion

The condition now known as chloroma was first described by the British physician A. Burns in 1812, although the term chloroma did not appear until 1853 [3]. This name is derived from the Greek word chloros (green), as these tumors often have a green tint due to the presence of myeloperoxidase. The link between chloroma and acute leukemia was first recognized in 1902 by Dock and Warthin [4]. However, because up to 30 % of these tumors can be white, gray, or brown rather than green, the more correct term granulocytic sarcoma was proposed by Rappaport in 1967 [5], and has since become virtually synonymous with the term chloroma.

Chloromas may occur in virtually any organ or tissue. The most common areas of involvement are the skin (also known as leukemia cutis) and the gums. Skin involvement typically appears as violaceous, raised, nontender plaques or nodules, which on biopsy are found to be infiltrated with myeloblasts. Other tissues which can be involved include lymph nodes, the small intestine, the mediastinum, epidural sites, the uterus, and the ovaries. In the largest series so far, described by Pileri et al. [1], the male-to-female ratio was 1.42:1. The median age was 55.8 years (range 16–87). The commonest sites of MS presentation were the skin (28.2 %), lymph node (16.3 %), testis (6.5 %), intestine (6.5 %), bone (3.25 %) and central nervous system (CNS) (3.25 %). Histologically, 50 % of the tumors were of the blastic type, 43.5 % either monoblastic or myelomonocytic and 6.5 % corresponded to different histotypes. CD68/KP1 was the most commonly expressed marker (100 %), followed by myeloperoxidase (83.6 %), CD117 (80.4 %), CD99 (54.3 %), CD68/PG-M1 (51 %), CD34 (43.4 %), terminal-deoxy-nucleotidyl-transferase (31.5 %), CD56 (13 %), CD61/linker for activation of T cells (2.2 %), CD30 (2.2 %) and CD4 (1.1 %). Foci of plasmacytoid monocyte differentiation were observed in intestinal cases carrying inv16. Chromosomal aberrations were detected in about 54 % of cases: monosomy 7 (10.8 %), trisomy 8 (10.4 %) and mixed lineage leukemia-splitting (8.5 %) were the commonest abnormalities, whereas t (8:21) was rare (2.2 %). Symptoms of myeloid sarcoma at these sites are related to their anatomic location; myeloid sarcomas may also be asymptomatic and be discovered incidentally in the course of evaluation of a person with acute myeloid leukemia.

The clinical behavior and response to therapy do not seem to be influenced by any of the factors like age; sex;

anatomic site; de novo presentation or clinical history related to AML, MDS, or MPN; histotype; phenotype; or cytogenetic findings [1]. Importantly, these patients have to be treated like any other acute myeloid leukemia and patients who undergo allogeneic or autologous bone marrow transplantation seem to have a higher probability of prolonged survival or cure.

Extra medullary tumors in APML are not very common and there are only a few reports of APML presenting as granulocytic sarcoma has been described in the literature more often in relapse setting [6]. One case of APML presenting as colonic ulcer has been described [7] and one case report of a tumor in a supraclavicular lymph node has been described when the marrow was in remission [8]. Central nervous system involvement is the commonest site that has been reported [9, 10]. Leukemia cutis is also a rare occurrence in APML. In view of such a rarity of these extra medullary tumors we report this case.

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