IJHOSCR

Case Report

International Journal of Hematology- Oncology and Stem Cell Research

Myeloid Sarcoma of the peritoneum at older ages: A case report and review of literature

Mozaffar Aznab[1], Naser Kamalian[2], Omid Beiki [3], Farhad Naleini[4]

[1]Medical Oncologist-Hematologist, Assistant professor, Kermanshah University of Medical Sciences, Kermanshah, Iran
[2] Professors, Tehran University of Medical Sciences, Tehran, Iran
[3] Research Center for Environmental Determinants of Health, Kermanshah University of Medical Sciences, Kermanshah, Iran
[4] Assistant professor, Kermanshah, University of Medical Sciences, Kermanshah, Iran

Corresponding author: Mozaffar Aznab, MD. Medical Oncologist-Hematologist, Assistant professor, Kermanshah University of Medical Sciences, Kermanshah, Iran
Tel: +989181313925
Fax: +988318370139
Email: draznab@yahoo.com

Received: 16, Feb, 2014
Accepted: 15, Apr, 2014

ABSTRACT

Myeloid sarcoma or granulocytic sarcoma (GS) is a rare disease with poor prognosis. It is characterized by the occurrence of tumor masses at an extra-medullary tissue. It is composed of myeloblastic cells and usually occurs in association with acute myeloid leukemia. Because of its nonspecific clinical and radiologic findings, its diagnosis might be challenging. It might be more commonly found in patients with specific cytogenetic abnormalities, particularly with the t (8; 21) translocation and less frequently the inv (16) type. We report a case of GS in a 62 years old man without particular previous pathologies, which brutally presented as an ascites and generalized edema. The laparoscopy showed involvement of greater omentum and peritoneum. The histologic examination of greater omentum showed granulocytic sarcoma. The bone marrow aspiration was normal. We started treatment of patient by standard acute myeloid leukemia's chemotherapy.

INTRODUCTION

The term granulocytic sarcoma or myeloid sarcoma was first described in the early 19th century by Rappaport[1], the original term was chloroma**.** This appearance is a result of the presence of myelo peroxidase enzymes in the immature myeloid cells. The favored name later changed to granulocytic sarcoma or myeloid sarcoma also known as extramedullary myeloid tumor, following descriptions of cases that were not green and had the gross features of a sarcoma. Granulocytic sarcoma is more common in patients with specific cytogenetic abnormalities e.g. t (8; 21) or inv (16) or FAB class M2[2]. Myeloid sarcoma occurs in 2 to 14% of cases of AML[3,4,5]. Granulocytic sarcomas may occur at diagnosis of AML or may precede the diagnosis; as the first manifestation of relapse in patients previously treated for primary or secondary acute leukemia. They have also been associated with myelodysplastic syndromes or myeloproliferative disorders and usually predict transformation to acute leukemia [3,4,5, 6]. In almost all reported cases of primary Granulocytic sarcoma (without a known pre-existing or concomitant acute leukemia), acute leukemia has developed shortly[2]. The tumors are usually localized; they often involve bone, periosteum, soft tissues, lymph nodes, or skin. The orbit and paranasal sinuses, gastrointestinal tract[7, 8], genitourinary tract, breast, cervix, salivary glands, mediastinum, pleura, peritoneum, and bile duct also have been reported[4]. The tissue biopsy for diagnosis is the preferred method [9]. The morphologic appearance on H&E (Wright /Giemsa stains) varies according to differentiation of the cells and recommends sending the specimen to immunohistochemistry, flow

cytometry, fluorescence in situ hybridization, and molecular analysis. The granulocytic sarcoma subclassified according to cell type into granulocytic, monoblastic or myelomonocytic and according to cell maturation into immature, mature and blastic types[5]. Pileri et al [5] histologically showed in a report of 74 patients, 50% of the tumors were of the blastic type, 43.5% either monoblastic or myelomonocytic and 6.5% corresponded to different histotypes. Immunophenotying and immunohistochemistry or immunocytochemical are crucial for the accurate diagnosis of MS [6]. According to the WHO 2008 classification, cytochemical stains for immunocytochemical include chloroacetate esterase (CAE), myeloperoxidase (MPO) and nonspecific esterase (NSE). Immunophenotyping can be done either in paraffin section or via fluorescence-activated cell sorting analysis on cell suspension derived from the tumor. Chen J, Yanuck R et al[10] in her study showed 30 cases CD117 reactivity in 87%, MPO, 97%; lysozyme, 93%; CD34, 47%; CD45, 84%; CD43, 97%; TdT, 37%; CD79a, 20%; CD20, 10%; CD3, 10%; and CD10, 1%. Pileri et al ., [5] showed 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%). After the diagnosis of MS, bone marrow aspiration and biopsy should be performed to rule out acute leukemia and other hematological malignancies [9]. Magnetic resonance or computed tomography is performed to localize and rule out other differential diagnoses of the tumor. These techniques also differentiate MS from abscess and hematomas especially in patients with AML[11] .The most common differential diagnoses include undifferentiated cancer, malignant melanoma, non-Hodgkin lymphoma, small round cell tumors (including neuroblastoma, rhabdomyosarcoma, Ewing's sarcoma), thymoma and myeloma [12,13] .These patients typically receive systemic chemotherapy. Although the optimal timing and treatment of isolated MS are not clear, delayed or inadequately systemically treated isolated MS will almost always progress to AML. In our practice, we use remission-induction chemotherapy similar to that used for AML.

CASE REPORT

A 62-year-old man was admitted for a 30-day history of intermittent, abdominal pain accompanying by vomiting. The patient was referred with delay to our center. The patient also reported a 2-month history of constipation, abdominal distension and weight loss. On admission, the patient had dyspnea in long stretches, and the patient was normotensive with tachycardia. In physical examination of the patient, generalized abdominal tenderness was noted on palpation, without guarding or rigidity. The patients also had ascites, edema of bilateral lower extremity and scrotum. In physical examination, we did not detect lymphadenopathy. Laboratory examination including a complete blood count, erythrocyte sedimentation rate (ESR), liver and renal profile show anemia and elevated ESR and leukopenia. Stool and blood cultures were negative.

Imaging study

To localize and rule out other differential diagnoses of the tumor, enhanced computed tomography was performed showing ascites, mesenteric lymphadenopathies and stranding in mesenteric fatty tissue (Figure 1)

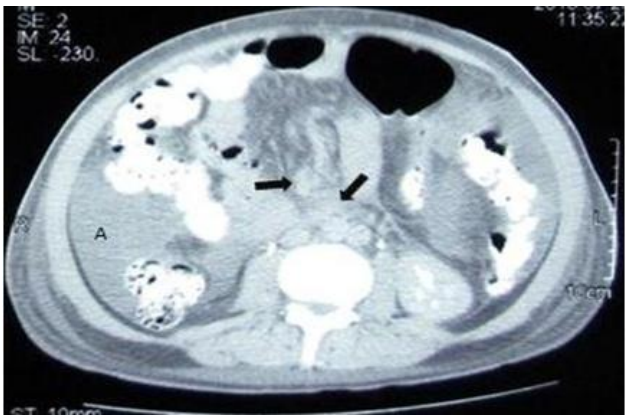

Figure1: Abdominal Enhanced CT scan showing ascites (A) and mesenteric lymphadenopathies (arrows)

Laparoscopy

Laparoscopy findings also included ascites and multiple nodules on the greater omentum, mesenteric lymphadenopathies and mild splenomegaly. We performed biopsies of the greater omentum and the peritoneum.

Pathology

Histopathology (Figure 2) with H&E staining of the biopsy showed cells with blastic appearance and scant cytoplasm. Immunohistochemistry (IHC) study revealed positivity for myeloperoxidase (MPO) (Figure 3). To rule out Non-Hodgkin lymphoma (including precursor T-cell or B-cell, Burkitt, some peripheral NK/T-cell and diffuse large B-cell lymphomas ,histiocytic lymphoma) IHC was performed for T-cell markers (CD3, CD5) ,B-cell markers (CD20, CD19, CD 30, CK) and IHC study revealed negativity. IHC proposed to distinguish Hodgkin lymphoma and IHC revealed negativity for CD15 and CD30. Patient was also investigated for leukemia. Bone marrow aspiration revealed cellularity 60% with preserved megakaryocytes, significant hyperplasia erythroid cells, decrease in myeloid series, no increase in blasts and no significant dysplasia change that might explain dysplasia(MDS).

Before starting chemotherapy, G-CSF began for the patient because the patient had leucopenia despite normal bone marrow aspiration, but a significant increase in cell count did not happen. We started chemotherapy with 7-3 regimen. On the seventh day, the patient became febrile neutropenia. During the hospital stay, the patient's condition steadily deteriorated, and he developed increasing abdominal girth and ascites, abdominal pain, and lower extremity edema. We started broad spectrum antibiotics and prescribed G-CSF for the patient. Clinically, the patient was evaluated on daily basis. No significant changes occurred in the reduction of ascites or scrotal edema, abdominal pain and we did not observe any response to treatment. During the follow-up, patient showed an increase in scrotal edema and got severe pain in the testicles. Testicular ultrasound showed necrosis in testicles. Adding anaerobic spectrum antibiotics did not prevent the worsening of overall condition. Pancytopenia was exacerbated and complication of testicles deteriorated, and infectious disease progressed. Finally, the patient died of septic shock.

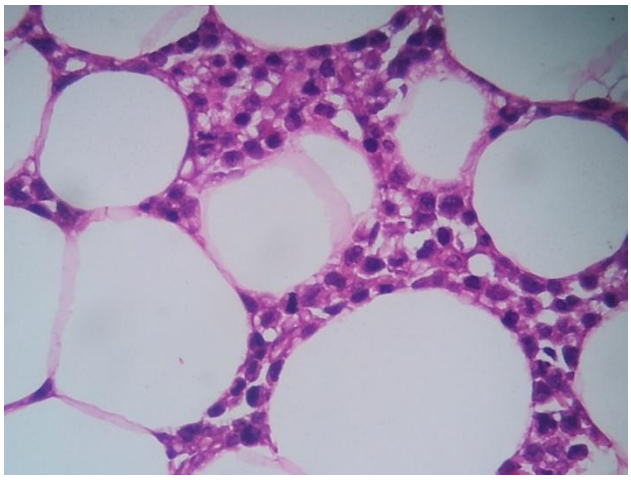

Figure 2: Photomicrography of peritoneal biopsy revealing an infiltrate of cells with prominent nucleus and scant cytoplasm (hematoxylin and eosin stain × 400)

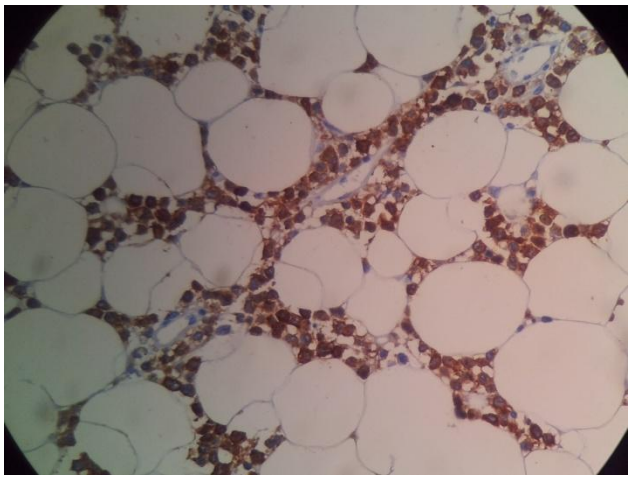

Figure 3: Immunohistochemical stain for MPO showing staining of the tumor cells (myeloperoxidase × 400).

DISCUSSION

GS is a challenging diagnosis and might presents clinically, radio logically, and histo-pathologically similar to several other tumors such as soft tissue sarcoma, non-hodgkin lymphoma, malignant melanoma. It is more common in young age. Most patients with GS tend to have leukemia at

presentation, or they will eventually develop leukemia. Treatment is similar to that for AML, even in cases of isolated tumors with no blood or bone marrow involvement. Lan et.al have pointed out that early diagnosis with biopsy and early chemotherapy seems to improve survival outcome. In the treatment of GS, systemic chemotherapy, surgical resection, radiotherapy or a combination of these approaches are used on a case-by-case basis. There was no targeted therapy for patients with MS but new agents such as FLT 3 inhibitors, Gemtuzumab ozogamicin(GO) ,farnesyl-transferase inhibitors studied in patients with AML could be considered as an option for MS patients [14].Vedy and et al[15] reported successful therapy with imatinib mesylate in a patient presenting with AML and paravertebral leukemic masses. There was no more accurate no data concerning the possible efficacy of Gemtuzumab ozogamicin for MS until report Piccaluga and et al[16] in which treated 24 patients relapsed and refractory AML and myeloid sarcomas CD33-positive with Gemtuzumab ozogamicin in which among the five patients with MS of the skin or bones, two achieved a complete remission, one was resistant and two showed a complete response of the extramedullary tumor. Piccaluga and colleagues conclude that GO is effective as a single agent in AML and myeloid sarcomas. Ando and et al[17] describe a 54-year-old male patient who developed AML with multiple sites of extramedullary relapse in soft tissue and bone 120 days after after allo-HSCT, the patient was treated with GO as a single agent. We recommend that IHC for CD33 done on biopsy of tissue of patients with myeloid sarcomas and if CD 33 positive is better complementary therapies done with Gemtuzumab ozogamicin. We have reported a case of myeloid sarcoma that has happened at older age. Patient received systemic chemotherapy drugs in adjusted-dose that did not help the patient, and he died due to no response to treatment. The delay referral from primary care center might be the most important reason for no response to treatment.

CONCLUSION

For elderly patients, we recommend immediate treatment and target drug therapy if IHC is positive for CD 33 (Mylotarg) along with low-dose chemotherapy. Fully supportive care should also be considered.

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