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Progressive course of isolated splenic myeloid sarcoma

Research Article

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Abstract: A previously healthy 40-year-old male presented with a 2-week history of fever and abdominal discomfort that was resistant to empirical broad-spectrum antibiotic treatment. The patient's blood cell count and complete biochemical panel was normal, except for an increased lactate dehydrogenase level. Ultrasonography and computed tomography of the abdomen showed a large, soft tissue mass had infiltrated superior part of the spleen. Splenectomy with total tumor mass removal were performed. The pathological examination of the tumor tissue confirmed diagnosis of isolated myeloid sarcoma with monoblastic differentiation. Despite intensive antileukemic therapy, patient died four months after diagnosis was established.

Keywords: *Spleen • Isolated myeloid sarcoma*

1. Introduction

Myeloid sarcoma (MS), also known as granulocytic/monoblastic sarcoma, extramedullary myeloid tumors, or chloroma, is a tumor mass comprising blasts or immature cells of the myeloid series that occurs at an anatomical site other than the bone marrow [1]. The condition was first described in 1811 by Burns [2] and later further described by King as tumors displaying a predominantly green color resulting from the presence of myeloperoxidase (MPO) [3]. In 1966, Rappaport proposed the term "granulocytic sarcoma" [4], and finally, in 2002, the term myeloid sarcoma was accepted by World Health Organization (WHO) [1].

Myeloid sarcoma can occur in patients with active acute myeloid leukemia (AML) and in patients with chronic myeloproliferative disease, where it may occur as the first manifestation of blast transformation, the first manifestation of AML relapse in previously treated patients, or isolated MS in patients without bone marrow infiltration [1]. In almost 90% of untreated patients who initially had no hematological disorder, if untreated, AML develops within 10.5–11 months. The incidence of MS is unknown and believed to be underestimated. Isolated myeloid sarcoma occurs in 2/1,000,000 adults, and in 0.7/1,000,000 children. Thus far, the involvement of the skin,periosteum, bowels, lymph nodes, genital system, central nervous system, heart, and lungs has been reported [5-12].

Several markers have been employed for identification of the myeloid origin of tumor infiltration in MS. Immunostaining with antibodies to myeloperoxidase (MPO), lysosomes, and chloroacetate esterase are important for identification of MS, bearing in mind that the myeloblasts in MS have an antigen profile similar to that present in the blasts and precursor cells of AML [10,11].

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2. Case report

A previously healthy 40-year-old male presented with a 2-week history of fever (up to 39°C) and abdominal discomfort that was resistant to empirical broad-spectrum antibiotic treatment. The patient's blood cell count comprised: hemoglobin 114 g/l; white blood cell count 14.9x10^9/l with 74% neutrophils, 2% eosinophils, 3% basophils, 15% lymphocytes, and 6% monocytes; and a platelet count 693x109/l. The complete biochemical panel was normal, except for the LDH level (680 U/l). Ultrasonography and computed tomography (CT) (Figure 1) of the abdomen showed a large, soft tissue mass (11x10 cm) that infiltrated superior part of the spleen.

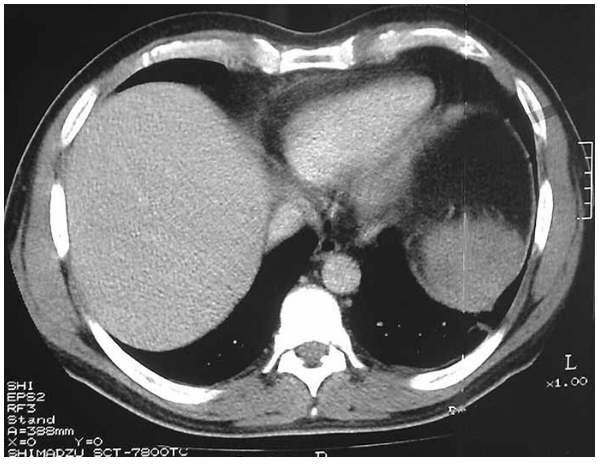

Figure 1. Initially computed tomography (CT) of the abdomen.

The patient was immediately taken to surgery. Splenectomy with total tumor mass removal and partial resection of the diaphragm (due to per continuitatem tumor involvement) were performed. The pathological examination of the tumor tissue showed large necrotic fields with tumor cells (Figure 2a) that were positive for CD14, CD68, lysozyme (Figure 2b,c,d), CD11c, CD163, CD33, CD13 but negative for EMA, myeloperoxidase, CD 34, CD43, CD117, HLA-DR, CD3,CD4, CD20, CD21, CD30, MUM1, CD38, CD138 and C56. The final histological diagnosis was myeloid sarcoma (MS) with monoblastic differentiation.

Despite removal of the tumor mass, the patient's symptoms did not resolve. Ten days after surgery, a multislice computed tomography (MSCT) scan showed a lobular, necrotic tumor mass had infiltrated the major curvature of the stomach, pancreas, diaphragm, and thoracic wall. A bone marrow biopsy and aspirate, with flow cytometric analysis, showed normal findings without criteria for any types of acute leukemia. Cytogenetic examination of the bone marrow cells revealed a normal karyotype.

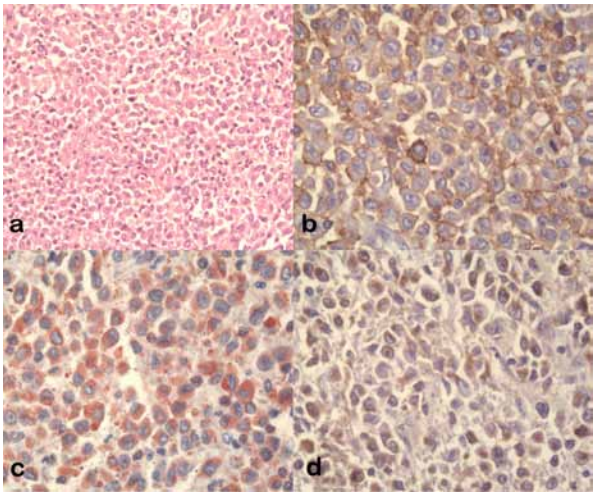

Figure 2a. The H/E staining of the tumor tissue.
c,d,e. Tumor cells were positive for CD14, CD68 and lysoyzyme.

One month after surgery, systemic induction chemotherapy was initiated, consisting of daunorubicin, given 45 mg/m^2 IV 1 hour daily on Days 1–3, cytarabine 200 mg m^2/day on days 1–10, and etoposide 100 mg/m^2 on Days 1-5.

The patient was remained febrile without a confirmed infection. Twenty-eight days after initiation of chemotherapy, a control MSCT of the abdomen was obtained. The initially detected tumor mass failed to reduce in size, and a new lesion was identified in the projection of the minor stomach curvature (Figure 3a,b).

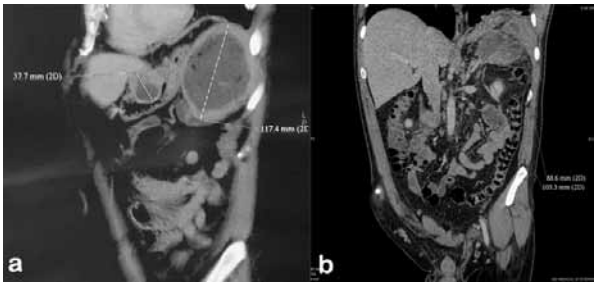

Figure 3. Multislice computed tomography (MSCT) scan of abdomen.

In an attempt to reduce the tumor mass, surgery was performed. Intraoperative findings confirmed the presence of a large necrotic tumor mass (Figure 4a,b) had infiltrated the diaphragm, colon, pancreas, stomach, and thoracic wall.

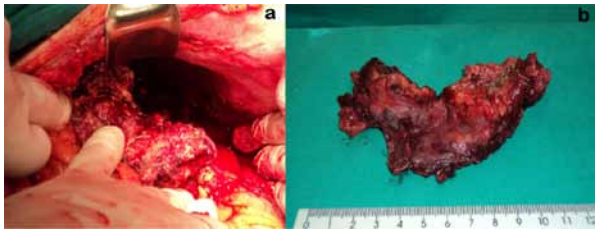

Figure 4. Large necrotic tumor mass.

Pathohistological findings was identical to those after splenectomy. After the second surgical intervention, only palliative therapy was continued and patient died four months after diagnosis was established.

3. Discussion

According to our knowledge, this is the first report of isolated splenic MS characterized with arare and therapeutically challenging presentation. Therefore, this report differs from previous reports in the literature which consider acute myeloid leukemia presenting together with myeloid sarcoma of the spleen.

Diagnosis of MS in patients poses a huge challenge, and earlier in the absence of hematological disorders, 46%–75% of patients were initially misdiagnosed. Myeloperoxidase, CD68, CD43, and lysozyme are frequently expressed in MS, but none of these are specific markers. To establish a definitive diagnosis, minimum panel of immunohistochemical markers should include the previously mentioned markers in addition to markers such as CD33, CD34, and CD117. In our patient, tumor tissue cells were positive for CD33, CD13, lysoyzyme, and CD68; these results confirmed monoblastic origin [9-12].

Considering that cytogenetic abnormalities are detected in approximately 55% of tested cases with MS, the identification of an AML-associated abnormality (i.e., trisomy 8, t(8;21)(q22;q22) or inv(16)(p13.1q22)/t(16;16)(p13.1;q22)) may assist correct diagnosis [1,11].

Our patient was resistant to applied therapy. There are a few possible reasons for that. first of all, at the moment of diagnosis disease was already disseminated. Despite extensive surgery there was a remaining mass that enabled further development of myeloid sarcoma until chemotherapy was started. Also, disease localization (diaphragm, thoracic wall) reduced chemotherapy effects. Another potential mechanism of resistance termed multidrug resistance (MDR) could be considered. MDR is related to the production of P-glycoprotein and cells expressing this protein exhibit reduced accumulation of different drugs, including many agents important in the treatment of myeloid sarcomas such as the anthracyclines, vincristin, amsacrine, mitoxantrone, and etoposide [13]. Also, there is limited information regarding the role of genetic mutation status in our patient. FMS-related tyrosine kinase 3 gene (*FLT3*) mutations have been reported in 35% of AML patients with normal karyotype and carry an unfavorable prognosis. In a small series, *FLT3* mutations were identified in 15% of MS cases but determination is technically very difficult because of specificity of tissue sample [14].

Several studies have summarized the outcomes of patients with MS and median overall survival for patients with MS the range is 7 to 20 months. The optimal timing and treatment of isolated MS are not clear, but delayed or inadequately treated isolated MS will almost always progress to AML within 10 months on average. Prognostic indicators suggestive of causes influencing the increased risk for development of AML have not been definitely established because only results of small series have been published. However, event free survival (EFS) considering extramedullary relapse or AML development was significantly longer in patients treated with systemic chemotherapy than in those treated with surgery or local irradiation (12 vs 3 vs 6 months). A recent study confirmed that patients treated with allogenic hematopoietic stem cell transplantation (HSCT) as post remission therapy had a longer EFS, except for a patient with high-risk cytogenetics who had poorer EFS and an increased incidence of relapse. However, the latter should be considered with caution as the cytogenetic data were missing in most cases of isolated MS [12,14-23].

According to the results of the published data, it is clear that in cases of suspected MS, employment of a wide spectrum of antibodies during immunohistochemical work-up of tumor tissue is mandatory. Timely diagnosis has a huge influence on treatment results, i.e., longer survival as a consequence of adequate therapy. Although prospective evaluations are needed, chemotherapy with allo-HSCT could be considered as the optimal therapy for isolated MS.

Moreover, the role of new molecular prognostic markers such as FLT3-ITD mutation in MS should be investigated.

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