Isolated Mediastinal Myeloid Sarcoma: A Rare Presentation of Extramedullary Leukemic Tumor

Myeloid sarcoma is included as one of the subgroups of acute leukemia in the WHO classification and is most often found either concurrently or following a previously recognized AML. Less often it may occur as an isolated leukemic tumor or precede the appearance of blood or bone marrow disease [1]. The incidence of MS in AML is less than 1% and the involvement of the mediastinum is extremely rare [2-4]. Skin, gum, lymph nodes, soft tissue, periosteum, and bone are the most common involved locations [5]. The definitive diagnosis is usually based on immunohistochemistry. The use of only four markers (MPO, CD68, Lysozyme and CD34) has been proposed to distinguish the more common variants of myeloid sarcomas [6]. Molecular and cytogenetic studies are usually performed because the results have prognostic and therapeutic implications. The recommended treatment is AML-directed chemotherapeutic protocols. The role of Radiation therapy and hematopoietic stem cell transplantation has not been clearly established. Complete remission rates for isolated MS treated with AML-based induction regimens are comparable to those of AML without MS but with similar prognostic features, and a disease -free survival from 3.5 to 16 years has been reported [7]. We describe a patient with a bulky mediastinal myeloid sarcoma. We discuss the literature pertaining to clinicopathological features in MS, PET imaging and treatment options.

Materials and Methods

A 66-year-old male with a history of bladder cancer, colon...
cancer, and right knee histiocytoma (all in surgical complete remission; right knee also received adjunctive radiotherapy) presented with intermittent fever, chest heaviness, dry cough and dyspnea on moderate exertion. CXR showed a mediastinal mass (Figure 1 A and B). Subsequent CT of the thorax demonstrated a confluent anterior mediastinal soft tissue mass measuring 11.3 x 8.7 cm in largest dimension. The superior vena cava was encased and narrowed by the mass. In addition, enlarged right supraclavicular node, bilateral soft tissue nodes, subcarinal node and small left side pleural effusion were observed (Figure 2 A and B). That appearance initially led to a strong suspicion of Lymphoma.

**Figure 2.** A, B: Computed tomographic scan demonstrating a bulky.

![Figure 2. A, B: Computed tomographic scan demonstrating a bulky.](image)

Blood test results were: white blood cell count 5100/mcL, 78.1% neutrophils, 1.1% eosinophils, 0.4% basophils, 11.8% lymphocytes, 64.4% monocytes. No blasts were seen. Hemoglobin 10.6 g/dl, platelet count 404,000/ mcL. Clinical chemistry tests showed a uric acid level of 6.3mg/dL, LDH: 341 Units/L, BUN: 14mg/dL, Creatinine: 0.6 mg/dL, Calcium: 9.4 mg/dL. Hepatitis B, Hepatitis C and HIV serologies were negative. Percutaneous fine needle aspiration and biopsy of the mediastinal mass demonstrated a dense infiltrate of atypical mononuclear cells in a fibrous background, composed of predominantly intermediate sized cells with irregular nuclear contours, dispersed chromatin, inconspicuous to occasional small nucleoli and a scant cytoplasm (Figure 3 A). Immunohistochemical studies showed that the blastic cells were positive for CD33, CD34, and CD68 (Figure 3 B, C and D), and BCL2, with a Ki-67 proliferation index of 90%, while the neoplastic cells were negative for CD5, CD10, CD20, BCL6, MUM-1, C-MYC, CD117, TDT, Lysozyme and Epstein-Barr Virus (EBV)-encoded RNAs (EBERs). On bone marrow aspiration and biopsy, there was no evidence of leukemic infiltration. Molecular tests performed on the bone marrow specimens did not detect Fms-Like tyrosine 3 kinase 3 (FLT3) mutation. Kit mutation analysis on exon 17 was negative on the same specimens. Cytogenetic tests on bone marrow cells showed normal karyotype without clonal abnormalities in the mitotic population. FISH evaluation revealed del (13q) in 0.6% of the interphase cells examined, which is below the upper level of normal variation for this test. Based on these features a diagnosis of isolated mediastinal myeloid sarcoma was made.

**Figure 1.** A, B: Chest X ray shows widening of the mediastinum.

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Given this new diagnosis and its extensive presentation, no invasive surgical procedure was indicated. The patient was started on induction chemotherapy with anterior mediastinal mass encasing and compressing the great vessels.

Cytarabine 100 mg/ m² for 7 days and Daunorubicin 60 mg/ m² for 3 days. His course was complicated by atrial fibrillation, pericardial and pleural effusions. The mass did not respond to the treatment and the patient subsequently underwent radiation (2400 cGy in 12 fractions to the right mediastinum and chest wall) as well as reinduction chemotherapy. Follow up PET scan showed a decrease in the size and FDG avidity of the mass in addition to a new right supraclavicular lymph node which demonstrated myeloid sarcoma involvement. The patient then underwent allogeneic stem cell transplantation.
PET scan was done 77 days after transplantation and showed stable disease with decreased metabolic activity. However, one month after the PET scan, a surveillance bone marrow was suspicious, and 2 months after the PET scan, refractory myeloid sarcoma was documented in a palpable left supraclavicular node. The patient rapidly deteriorated and died 4.5 mos after allotransplantation.

Results and Discussion

Primary mediastinal myeloid sarcoma poses a diagnostic challenge for both physicians and pathologists. In a review of 72 patients with primary myeloid sarcoma, 47% of cases were misdiagnosed initially [8]. The most common alternative diagnoses being lymphoma, undifferentiated cancer, malignant melanoma, extramedullary hematopoiesis and inflammation [9]. Pathologically, the variable morphological appearance and absence of recognizable myeloid differentiation can be misleading [10,11]. So, immunohistochemistry and immunophenotyping are crucial for the accurate diagnosis of MS. Cytogenetic analysis in patients with MS is usually performed with reported cytogenetic abnormalities found in approximately 50% of cases [12]. Furthermore, the most common cytogenetic findings in MS complicating adult AML have been t(8,21) [13]. FLT3 and C-kit mutations can be found in MS and target them with tyrosine kinase inhibitors might be a new avenue in these settings [14,15]. Since few studies have focused on the treatment of MS, there is no consensus. The recommended treatment regimen in patients presenting with isolated MS or MS presenting concomitantly with AML is conventional AML chemotherapy [16]. In a study of 23 patients with nonleukemic myeloid Sarcoma received systemic anti-acute myeloid leukemia chemotherapy; the overall response rate was 91.3% and 56.5% of patients' experienced complete remission [17]. Other strategies have included involved field radiotherapy and consolidation hematopoietic stem cell transplantation. One study showed that combination treatment with radiotherapy and chemotherapy resulted in a better treatment failure-free survival than chemotherapy alone [18]. Chevallier et al reported 30 patients with isolated MS who received allogeneic stem cell transplantation with a median follow-up of 48 months. The 5-year overall survival was 33% and the 5-year cumulative incidence of relapse was 45% [19]. The results of autologous bone marrow transplant in two cases of MS showed variable outcomes, probably related to the difference in prognostic factors in each case [20]. Finally, two of five patients with CD 33 positive MS achieved complete remission after treatment with Gemtuzumab-ozogamicin, a drug-linked monoclonal antibody against CD33 [21]. FDG-PET is more accurate or at least equivalent to CT or MRI for the detection of MS [4]. In addition, there is a study that has shown FDG PET/CT is superior to detecting MS than CT or FDG-PET alone [22]. In our patient, the follow-up PET performed after reinduction chemotherapy and right mediastinal/chest wall radiotherapy demonstrated improvement within the RT field, but progression in a right supraclavicular node that was biopsy positive for myeloid sarcoma.

Conclusion

Interim PET-imaging performed after induction and/or at the end of the chemotherapy program may help to identify patients with persistent FDG uptake (as in our patient) who are at risk for relapse/progression, and may thus need intensification. The evidence to support PET scan imaging as a prognostic tool in such cases is not sufficient at present. The utility of this technique is promising but awaits larger studies [23, 22].

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References


