Myeloid Sarcoma: An Unusual Case of Mediastinal Mass and Malignant Pleural Effusion with Review of Literature

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Abstract Myeloid sarcoma is an extramedullary tumor seen most commonly in patients with acute myeloid leukemia and less frequently in chronic myeloid leukemia, myelodysplastic syndrome and rarely, in an isolated form without any other underlying malignancy. Malignant pleural effusion in hematological malignancies is rare when compared with solid tumors. We present an unusual case of myeloid sarcoma in which a mediastinal mass with pleural effusion was the initial presentation. A 27 year old gentleman presented with complaints of fever, chest pain and swelling in the anterior chest wall for 6 months. Examination revealed a lump measuring 5 × 5 cm on the left side of the chest wall. Hematological evaluation showed hemoglobin-14.2 g/dL, platelet count-233 × 10⁹/L, TLC-117 × 10⁶/L with normal differential counts. Contrast enhanced computerised tomography (CECT) confirmed the presence of a soft tissue mass in the superior mediastinum abutting against the chest wall. Core biopsy was suggestive of myeloid sarcoma and immunohistochemistry was positive for myeloperoxidase and negative for CD3, CD 20 and CD 23. Pleural fluid analysis showed the presence of malignant cells. Bone marrow examination did not show an excess of blasts. A final diagnosis of extramedullary myeloid sarcoma with malignant pleural effusion was made. The patient was given induction chemotherapy (3 + 7 regimen) with daunorubicin and cytosine arabinoside. Repeat CECT done on day 28 showed

complete resolution of pleural effusion and significant reduction in the size of mediastinal mass. The patient has successfully completed three cycles of consolidation therapy following which there has been complete resolution of the mass. He remains asymptomatic on close follow up.

Keywords Myeloid sarcoma · Malignant cytology · Acute myeloid leukemia

Case Report

A 27-year old gentleman presented with complaints of fever, chest pain and swelling in the anterior chest wall for 6 months. Examination showed presence of a non-tender lump (5 × 5 cm) on the left chest wall which was fixed to overlying skin. Laboratory investigations showed hemoglobin-14.2 g/dL, platelet count-233 × 10⁹/L and TLC-11.7 × 10⁹/L with differential count of 65 % neutrophils, 13 % lymphocytes, 6 % monocytes, 16 % eosinophils with normal RBC indices and peripheral blood smear. Chest X ray showed mediastinal widening with left sided moderate pleural effusion (Fig. 1). CECT chest showed soft tissue mass in superior mediastinum abutting against the chest wall (Fig. 2). Positron emission tomography (PET) scan showed increased FDG avid uptake in the superior mediastinum (Fig. 3). A core biopsy from the mass was suggestive of myeloid sarcoma. Immunohistochemistry confirmed the presence of tumor cells that were positive for myeloperoxidase stain and negative for CD3, CD 20 and CD 23 (Fig. 4). Pleural fluid staining showed scattered population of hematopoietic cells intermixed with reactive cells while high power view showed increased cellularity with abundant blasts, myelocytes, metamyelocytes, eosinophils, neutrophils and scattered myeloblasts (Fig. 5).

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Fig. 1 Chest X ray PA view showing mediastinal widening with *left* sided moderate pleural effusion

Fig. 2 CECT chest showing soft tissue mass abutting against chest wall with *left* sided moderate pleural effusion

Blast cells had a high nucleus to cytoplasm ratio, immature chromatin, irregular nuclear margins and scanty to moderate cytoplasm (Inset of Fig. 5). Bone marrow examination did not show any evidence of leukemia. A final diagnosis of extramedullary myeloid sarcoma with malignant pleural effusion was made. He was started on induction chemotherapy with injection daunorubicin 90 mg/m² (D1–D3) and injection cytosine arabinoside 100 mg/m² twice daily (D1–D7). His pleural effusion resolved rapidly as evident on repeat chest X ray on day 8 of induction (Fig. 6). CECT chest done on day 28 of induction chemotherapy showed complete resolution of the pleural

Fig. 3 PET scan revealed increased FDG avid uptake in the superior mediastinum

effusion and significant reduction ~80–90 % in the size of the mediastinal mass. Comparative study of imaging before and after chemotherapy has been depicted in Figs. 7 and 8. Thereafter, he received three cycles of consolidation therapy with high dose cytosine arabinoside 3000 mg/m². No suitable sibling match was found for allogeneic hematopoietic stem cell transplantation. Complete clinical and radiological resolution of the mass was achieved at the time of completion of therapy and the patient remains on regular follow up.

Discussion

Pleural effusion secondary to leukemic cell infiltration is not a common phenomenon. In general, infective causes of pleural effusion are far commoner than malignant causes, of which hematological malignancies make up an even smaller portion. A retrospective analysis of pleural fluid cytological samples was performed at our institute by Awasthi et al. [1]. In this study, out of 898 samples of pleural fluid, only 164 cases were found positive for malignancy, the remainder being of infective etiologies. Further sub-categorization confirmed that only 30 cases were of hematological origin with the commonest etiology being non-hodgkin's lymphoma (20 cases) followed by acute lymphoblastic leukemia (four cases), multiple myeloma

Fig. 4 Immunohistochemistry of trucut specimen of mediastinal mass showing positivity for myeloperoxidase and negativity for CD 20 and CD 23

Fig. 5 High power magnification of pleural fluid sample on staining shows myeloid cells comprised of blasts, myelocytes, metamyelocytes, neutrophils and eosinophils. *Inset* shows blasts having high nucleo-cytoplasmic ratio, immature chromatin, irregular nuclear margin and scanty to moderate cytoplasm, some with cytoplasmic blebbing (MGG, $\times 1000$)

(four cases) and chronic myeloid leukemia (two cases). No case of acute myeloid leukemia was found. The two other major studies done by Cakir et al. [2]. Johnston et al.

Fig. 6 Chest X ray PA view done on day 8 of induction therapy shows complete resolution of pleural effusion with no mediastinal widening

Fig. 7 Comparison of two chest X rays done **a** before chemotherapy with pleural effusion and **b** on day 8 of chemotherapy with resolution of pleural effusion

Fig. 8 Comparison of two CECT chest done **a** before chemotherapy with presence of large soft tissue mass and **b** on day 28 of chemotherapy with significant reduction of mass size

Table 1 Malignant pleural effusion and hematological malignancies

Study	Pleural fluid samples studied (n)	Positive for cancer (n)	Hematological Cancer (%)	NHL	CML	AML	MM	ALL
Cakir et al. [2]	4684	364	13/364 (3.57)	9	1	1	2	0
Awasthi et al. [1]	898	164	30/164 (18.29)	20	2	0	3	4
Johnston et al. [3]	5888	584	93/584 (15.92)	NA	NA	NA	NA	NA

Table 2 Published data of myeloid sarcoma with pleural effusion, site of involvement, associated underlying malignancy and marrow infiltration

Study	Extramedullary site	Marrow involvement	Pleural effusion	Age/sex	Underlying malignancy
Guastafierro et al. [14]	Gingival swelling	No	Yes	56/F	Non leukemic
Singh et al. [7]	Mediastinal mass	Yes	Yes	35/M	AML
Kubonishi I et al. [8]	Mediastinal mass	Yes	Yes	23/M	AML M3
Rigamonti et al. [15]	Pericardium	No	Yes	52/F	AML
Takasugi et al. [9]	Mediastinal mass	Yes	Yes	50/F	AML
Dettrick et al. [17]	Head of pancreas	Yes	Yes	51/M	No leukemic
Hicklin GA et al. [12]	Lung, pleura	No	Yes	36/F	No leukemic
Khan et al. [11]	Pleura, peritoneum	Yes	Yes	–	MDS → sec.AML
Disel et al. [20]	Pleura	Yes	Yes	–	AML M3 relapse
Park J et al. [13]	Pleura	No	Yes	41/M	AML relapse (post BMT)
Rege K et al. [16]	Thymus gland	Yes	Yes	–	AML
Lo CD et al. [10]	Mediastinal mass	Yes	Yes	–	AML
McCarty et al. [6]	Mediastinal mass, Spinal mass (T9-T12)	No	Yes	33/M	Non leukemic

suggested similar findings [3]. These studies showed that malignant pleural effusion is an uncommon phenomenon in patients with hematological malignancies (Table 1). The incidence of malignant pleural effusion occurring in a patient with myeloid sarcoma in the absence of any detectable medullary disease is therefore, exceedingly rare and unusual.

We performed a systematic review of all studies investigating myeloid sarcoma with leukemic pleural effusion published between 1977 and 2013. The National Library of Medicine database was searched using the MeSH terms “Myeloid sarcoma” and “pleural effusion”. We limited the literature search to articles on human subjects and those written in English. Pleural effusions secondary to infectious processes, heart failure, renal failure or hypoalbuminemia were not included. We reviewed and limited our discussion to only pleural effusion with positive cytology for malignant cells. In total we found 13 related articles as per our criteria (Table 2).

Lymph nodes, bone, skin, orbit and soft tissue are the most common sites of involvement by myeloid sarcoma however involvement of rare sites have also been reported [4, 5]. In our literature review we found that the most

common extra medullary site of myeloid sarcoma was the mediastinum [6–10] followed by pleura [11–13]. McCarty et al. reported a case of a 33-year old man who developed myeloid sarcoma at two sites (mediastinum and paraspinal mass) within a span of 12 months along with right sided malignant pleural effusion [6]. Mediastinum (six cases) was the most common site of involvement among the nine cases of intrathoracic myeloid sarcoma studied by Takasugi et al. [9]. Malignant pleural effusion was noted only in a single case of a mediastinal myeloid sarcoma. Lo et al. [10] reported a patient with granulocytic sarcoma of the mediastinum who presented with esophageal obstruction and compressive symptoms. The involvement of rare sites like gingival [14], peritoneum [11], pericardium [15], spine [6], thymus [16] and the head of pancreas [17] have also been reported in literature.

Usually, myeloid sarcoma occurs in conjugation with previous or concurrent AML or in patients with other myeloid malignancies such as CML or MDS [18]. Rarely, myeloid sarcoma can be seen in patients without any evidence of hematologic disorders [19].

Nine out of thirteen case reports reviewed by us had acute myeloid leukemia. Five cases had non-promyelocytic

AML [7, 9, 10, 13, 15, 16], two had acute promyelocytic leukemia [8, 20] and one had AML secondary to pre-existing MDS [11]. In the cases reviewed by us, we found that apart from our case there were four cases with biopsy proven myeloid sarcoma and malignant pleural effusion without concurrent acute myeloid leukemia. Three out of the four above mentioned cases had lung nodules with pleural involvement, gingival swelling and lesions in the head of pancreas [17]. Only one case had a mediastinal mass as seen in our patient [6].

Myeloid sarcoma may be considered as a herald or precursor of AML in some cases. Aggressive management of this tumor on the lines of AML with systemic chemotherapy is necessary as most patients may develop full blown AML if only local therapy or radiation alone is given. Imrie et al. reported that 71 % of patients diagnosed with myeloid sarcoma who did not receive anti leukemic chemotherapy subsequently developed AML within a median time of 7 months (21).

Conclusion

Isolated myeloid sarcoma in the absence of other features of acute myeloid leukemia is an unusual presentation. Management of myeloid sarcoma should be on the lines of systemic disease due to the high incidence of progression to AML in patients treated with local therapy alone. Malignant pleural effusions are rare in patients with AML. This case illustrates a rare presentation of a myeloid sarcoma presenting with a mediastinal mass and malignant pleural effusion.

Ethical statement and conflict of interest On behalf of all the co-authors (listed above) I would like to state that this work has not been submitted elsewhere in any other journal. Also there is no associated conflict of interest to be disclosed. No involvement or participation of human/animals requiring ethical clearance.

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