Case Report

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A Case of Acute Promyelocytic Leukemia Presenting as Sternal Infiltrate

Kalyani Bapat*, Dia Mansukhani, Shanaz Khodaiji, Balkrishna Padate, Abha Dubey

P.D Hinduja Hospital

Abstract

Granulocytic sarcoma (GS) or myeloid sarcoma (MS) is a localized extramedullary tumor composed of immature myeloid cells which can develop de novo or concurrently with acute myeloid leukemia (AML), myeloproliferative disorders (MPN) or myelodysplastic syndrome (MDS). It can present before, along with or after the diagnosis of acute myeloid leukemia, MPN, MDS or may present as a manifestation of relapse in a previously treated AML patient. The occurrence of MS in an acute promyelocytic leukemia (APL) patient is a very uncommon clinical event especially as initial or primary presentation. APL is often associated with a life threatening coagulopathy making prompt diagnosis and initiation of therapy critical. Unusual clinical localization may lead to misdiagnosis, or delayed diagnosis and treatment. Hence being aware of such atypical presentations of APL is crucial. Here we report a patient with acute promyelocytic leukemia who presented with sternal infiltrate but without any systemic symptoms. The diagnostic challenges are of particular interest given the unusual clinical presentation along with atypical morphology of the abnormal promyelocytes.

Keywords: *Acute myeloid leukemia, Acute promyelocytic leukemia, Myeloid sarcoma*

Introduction

Myeloid sarcoma (MS) previously called as granulocytic sarcoma or chloroma is an extramedullary tumor of immature myeloid cells.[1]. MS develops in 2–8% of patients with AML and is also observed in patients with other MPN and MDS disorders [2] These tumors may precede or coincide with the occurrence of AML or present as a manifestation of disease relapse [1]. MS may involve any organ system, from the more common sites like skin, bone, soft tissue of the head and neck, frequently the orbits and lymph nodes, to rare cases involving the heart or small intestine. [2,3] MS is associated more frequently with a monocytic component (FAB M4 and M5), but it is seldom found in patients with acute promyelocytic leukemia (APL) [3,4].

APL is a distinct subtype of acute myeloid leukemia in which abnormal promyelocytes predominate and is defined by the balanced translocation between chromosomes 15 and 17 resulting in fusion of the promyelocytic leukemia gene (PML) with the retinoic acid receptor-alpha gene (RARα) [5] .It accounts for 5–8% of acute myeloid leukemias (AML) and is characterized by a favorable clinical outcome [6]. Although APL is considered the most curable form of AML, there remains a significant risk of death early in the disease course due to coagulopathy and bleeding thus early recognition of the disease with prompt initiation of therapy is critical [6]. APL blasts exhibit distinctive morphology in form of bilobed nuclei, multiple Auer rods/Faggot cells. In most cases, recognition of the characteristic clinical and morphologic findings allows for a presumptive diagnosis of APL at which point All trans retinoic acid therapy is initiated empirically. [6]. The diagnosis is confirmed by testing for the PML-RARα fusion using fluorescent in situ hybridization (FISH), or reverse transcription polymerase chain reaction (RT-PCR) [6].

MS is extremely uncommon in APL and in many of these cases, it usually occurs as a sign of relapse[1]. In such patients with relapsed APL, extramedullary leukemic infiltrates have been most often seen in the skin (leukemia cutis) and the central nervous system (CNS)[1]. Thus myeloid sarcoma as a presenting feature of APL is a rare entity with only a few case reports mentioning this.

We describe a case with rare presentation of APL in a young adult male who primarily presented for the first time with sternal infiltrate without any other systemic symptoms or coagulopathy. The abnormal promyelocytes in bone marrow also displayed atypical morphology further confounding diagnosis

Case Report

The patient was a 34-year-old male with no past medical history, who presented with complaints of recurrent dull aching non-radiating pain in the middle of the chest for the

last two months. There was no history of trauma. On examination, vitals were stable. No pallor, edema, lymphadenopathy, or hepatosplenomegaly was noted. ECG and 2D-ECHO revealed no abnormalities. Complete blood count (CBC) done showed hemoglobin of 13.9 gm%, with normocytic normochromic RBC morphology, Total Leucocyte count (TLC) of 9.01 x 10^9/L with 60% neutrophils, 31% lymphocytes, 6% monocytes, and 3% eosinophils, and platelet count of 1.99 x 10^9/L. ESR was elevated (44mm/1 hr.). MRI chest was suggestive of inflammatory changes in the sternal body and distal portion of the manubrium with periosteal reaction. In view of the above findings, he was given symptomatic treatment and advised a follow-up. After one month, he still complained of intermittent pain but no other systemic symptoms. CBC done as a part of routine investigations showed a drop in platelet count from his last count of 1.99 x 10^9/L to 0.76 x 10^9/L with normal hemoglobin and TLC of 11.1 x 10^9/L and differential leucocyte count of 89% neutrophils. The platelet count revealed a downward trend and within a week the platelet count crashed reaching nadir of 0.18 x 10^9/L. MRI was reviewed again, now a possibility of infiltrative disease was considered. Whole body PET CT Scan was performed which was suggestive of diffuse metabolic activity in the entire spine, pelvis, sternum, and 5th to 7th ribs. Bone marrow procedure was carried out. Aspirate showed mildly hypercellular marrow with trilineage hematopoiesis, adequate megakaryocytes, and increase in monocytoid cells about 15-18%, nature of which was inconclusive (Figure 1). These cells were medium-sized with moderate cytoplasm showing very fine granules and round to oval nucleus, some showing reniform shape. Few of these cells had salmon-pink cytoplasm. Neutrophils were also seen in the background. Biopsy was solidly cellular with focal areas of trilineage hematopoiesis (Figure 2). The predominant population comprised of medium-sized cells with vacuolated cytoplasm and few showing cleaved nuclei, resembling histiocytes (Figure 3). Immunohistochemistry (IHC) was performed on bone marrow biopsy with CD34, CD117, CD68. CD68 was diffusely positive while CD34 was negative, and CD117 was focally positive. Since the bone marrow aspirate and trephine were inconclusive, a decision was made to perform a dedicated open sternal biopsy after administration of platelet transfusions. Sternal biopsy showed sheets of cells with eosinophilic cytoplasm with reniform nucleus (Figure 4). Immunohistochemistry (IHC) done showed that the cells were MPO, CD68, and CD43 positive, thus confirming the diagnosis of myeloid sarcoma (Figure 5, 6). During this time, CBC continued to show a low platelet count along with WBC count of 11.17 x 10^9/L and drop in hemoglobin to 10.9 gm%. Left shift with few nucleated RBCs were noted in peripheral smear. In view of sternal biopsy report, bone marrow aspirate slides were sent for FISH panel for doing cytogenetics for AML which revealed the presence of t(15:17). Coagulation parameters done showed PT of 14.2 with INR of 1.32 and APTT of 24.6. Fibrinogen level was 110 mg/dL (200-400 mg/dL). He was thus diagnosed with acute promyelocytic leukemia (high risk). He was immediately started on All-trans retinoic acid (ATRA) and arsenic trioxide (ATO) with anthracycline. The patient completed induction and consolidation and had an uneventful course. Post induction and consolidation, PET-CT showed no evidence of disease. Post consolidation he achieved molecular remission as demonstrated by Real Time Quantitative PCR (RQ-PCR). Presently he is on follow-up 1 year after diagnosis and is on maintenance therapy.

Written informed consent was taken from the patient. Also, approval from the Institute's Ethics Committee was obtained.

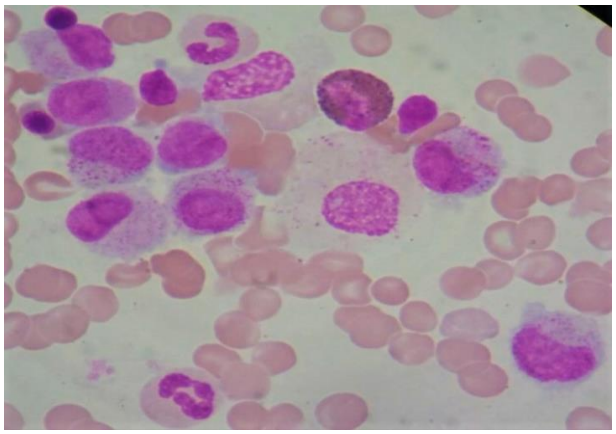

Figure 1: Bone marrow aspirate morphology showing monocytoid cells with round to oval nucleus and granular cytoplasm.(Leishman stain x1000, oil immersion)

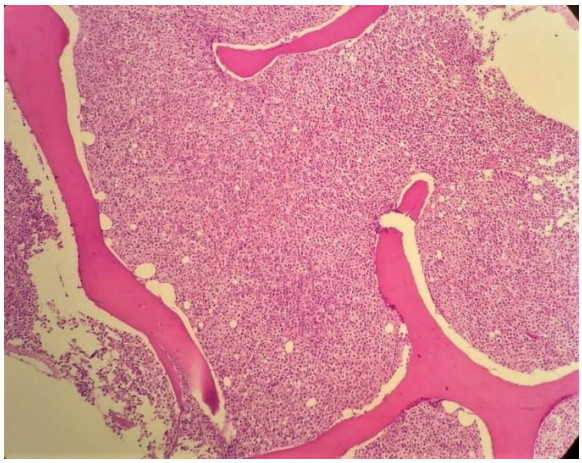

Figure 2: Bone marrow trephine biopsy showing solidly cellular marrow (H & E, x100)

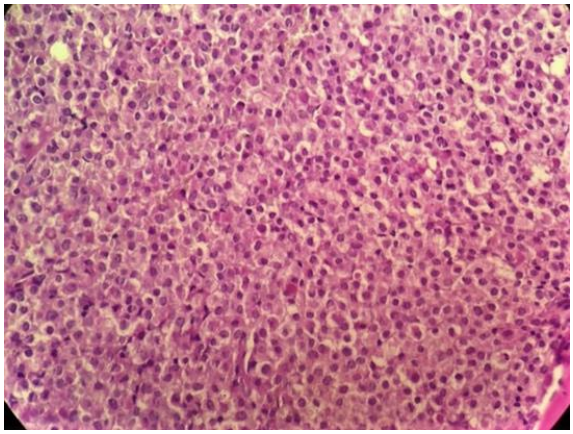

Figure 3: Bone marrow biopsy showing cells with eosinophilic and vacuolated cytoplasm, some with reniform nuclei (H&E x400)

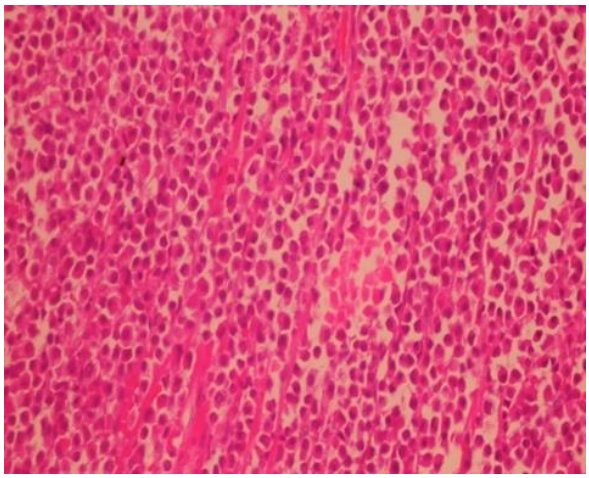

Figure 4: Sternal biopsy showing sheets of cells with eosinophilic cytoplasm and reniform nuclei. (H&E x100)

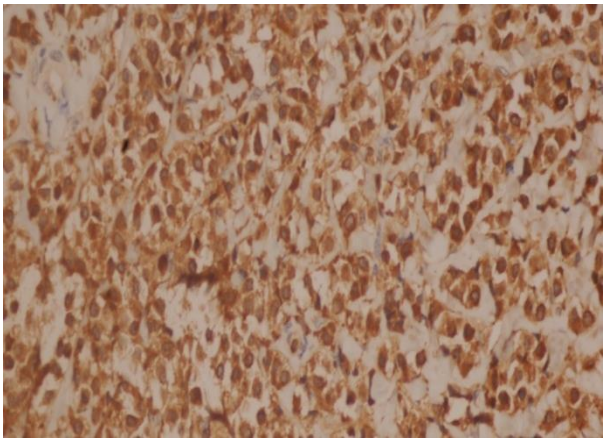

Figure 5: Sternal biopsy IHC with MPO stain showing diffuse positivity (X100)

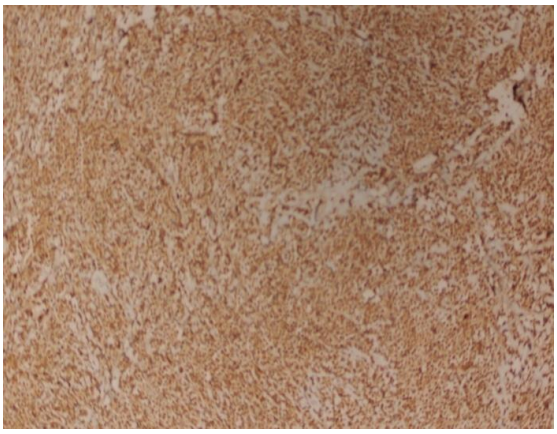

Figure 6: Sternal Biopsy IHC stain for CD68 showing diffuse positivity

Discussion

The presence of myeloid sarcoma (MS) is uncommon in APL at the time of initial diagnosis [4]. In rare cases, it can precede, or as in the presented case, coincide with APL. Most cases of MS in APL occur at the time of relapse . In these patients extramedullary disease most commonly occurs in the CNS and seems to be more common following therapy using ATRA rather than as the presenting sign [2,3,4,7]. More than 10% of hematological relapses are accompanied by CNS involvement [3]. Diagnosis is easier when MS is concomitant with leukemia, in which blasts or abnormal promyelocytes are present in the peripheral blood smear or bone marrow aspirate or when MS develops in patients in previously treated AML or MPN [3,4]. Diagnosis is more problematic when MS precedes acute leukemia especially in the isolated presentation without any signs of leukemia. [4]. Cases of MS are often misdiagnosed as other neoplasms, mainly as malignant lymphomas, Ewing sarcoma, or other hematopoietic neoplasm, often due to inadequate immunophenotyping of the malignancy [4,8,9]. Correct and timely diagnosis is thus a prerequisite for optimal treatment and outcome, in these cases especially establishing an accurate histological diagnosis is crucial for outlining the course of therapy [4,9].All diagnostic modalities like IHC, Flow Cytometry, FISH, karyotyping,and RQ-PCR are absolutely necessary to differentiate APL from other malignant disorders such as lymphomas, sarcomas, or other myeloid sarcomas. [10].

Regarding treatment the consensus is that all patients with MS should be treated with intensive chemotherapy. [4]. When left untreated, most cases progress to overt leukemia; a majority of the cases show AML transformation in about 10 months [4,8]. Hence AML-specific chemotherapy is recommended for treatment of MS. [2]. Standard treatment consists of ATRA combined with or followed by conventional anthracycline-based chemotherapy. This yields overall complete remission rates of 85–95% and 5-year overall survival rates of 65–70% . [2,11]. This approach

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provides favorable results in adults and children . [2,11].

Rare presentations of APL: We reviewed the literature to identify case reports with myeloid sarcoma as the initial presentations of APL. APL presenting as an isolated myeloid sarcoma (extramedullary APL) has been increasingly recognized and we reviewed 17 case reports describing the same. The mean age was 26.7 years (median being 23 years), out of which 6 were children . Table 1 summarizes the clinical and laboratory features of all these cases [1-4,6,9-20] .The various sites reported were sternal mass in 1 [4] as also seen in the present case, spinal/paraspinal mass in 5 [1,3,17,19,13] , bony lesion of extremities in 2 [2,9] , breast mass in 1 [10] , vertebral or skeletal lesions in 2 [6,12] , mediastinum in 2 [16,18] , cerebellum in 1 [15] , lingual mass in 1 [14], mandibular mass in 1 [11] and 1 patient presented as painful 3rd molar [20]. Out of these 17 patients, 13 patients had presence of concurrent marrow disease along with extramedullary presentation. [1,2,3,6,10,11,12,13,14,15,16,19,20] Out of these 13, in 3 patients bone marrow morphology was negative for abnormal promyelocytes but the presence of disease was being demonstrated by either cytogenetics or molecular methods similar to present case [2,10,6]. While in remaining 10 patients disease was demonstrable on bone marrow morphology as well as on cytogenetics and molecular methods.

2/17 patients had isolated extramedullary mass with absence of disease in marrow even by molecular methods, nor did they develop a systemic disease later and were alive. [4,9]

Another 2/17 patients who initially presented as isolated extramedullary masses however later went on to develop systemic disease as demonstrated by bone marrow morphology and cytogenetics. [17,18] . Out of which one patient expired [18] .

All the 17 patients were treated with systemic chemotherapy by various protocols involving ATRA and either of the anthracyline drugs like cytarabine, idarubicin, daunorubicin. Out of 17 patients, 12 of them were alive ,most being in post maintenance phase.

In this review of 17 patients, 5 patients expired [10,15,16,18,20] . Table 2 summarizes the causes of death and possible contributing factors. Out of 4 patients in whom coagulation studies were done , 2 patients had prolonged PT , APTT and low fibrinogen values. These 2 patients suffered from intracranial bleeding and DIC [20,15] . High WBC count (more than 30.0x109/L) were seen in 2 patients [15,16]. One patient had evidence of CNS infiltration [10] . In one patient the disease was refractory to chemotherapy and was associated with widespread dissemination of leukemic cells as demonstrated on autopsy studies.[18] The patient had pleural and pericardial effusion and died of cardiac failure. Another patient, who completed induction and consolidation chemotherapy expired after having a hematological relapse.[16] .

Myeloid sarcoma by itself is not an adverse prognostic factor in acute promyelocytic leukemia, but it is reported that those associated with higher initial WBC count, CNS infiltration, are associated with poor prognosis [12].

Atypical morphology: In our case the atypical morphology of the abnormal promyelocytes further confounded the diagnosis . No faggot cells or Auer rods were demonstrated in the marrow aspirate smears, instead the cells looked monocytoid with low N/C ratio, moderate amount of cytoplasm showing few granules. Also substantial number of neutrophils were seen which is contrary to the finding usually seen in APL. On biopsy the cells had a foamy cytoplasm mimicking histiocytes. The morphological classification of APL as proposed by Sainty et al have proposed 15 categories of morphology of abnormal promyelocytes. [21] Our case resembled type 1 morphology wherein abnormal promyelocytes have regular round to oval nucleus, presence of few granules but without any Auer rods.

This case is being presented because it is an uncommon presentation of a common hematological malignancy and it adds to the database of such rare presentations of MS and APL It highlights the challenges involved in diagnosing such cases. Additionally, the pathologist should be aware of the fact that the promyelocytes can have variable morphology and neutrophils can be seen alongside these cells.

Conclusion

This case highlights the difficulties in diagnosing rare and unusual presentations of acute promyelocytic leukemia. This patient not only had an atypical presentation but also had atypical morphology, which made this case challenging to diagnose. Moreover, it highlights the very rare association between granulocytic sarcoma and acute promyelocytic leukemia at presentation. A high level of clinical suspicion, extensive laboratory evaluation by doing a thorough examination of the aspirate smear, clot section, and core biopsy with the use of a comprehensive IHC panel and molecular diagnostics (RT-PCR) is necessary to arrive at a timely and correct diagnosis. Also, a multidisciplinary approach with correlation of radiological and histopathology findings is mandatory in the diagnosis of such rare presentations.

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Table 1: Summary of 17 patients of acute promyelocytic leukemia with MS at presentation with laboratory features and treatment

Reference	Site of involvement	Presence of Systemic disease	Bone marrow status	FISH /Molecular studies	Coagulation Studies	Treatment	Outcome
Worch J (2)	Lytic lesion in humerus, tibia and femur	Concurrent Presence as per molecular studies	No abnormal cells detected	RT PCR + for t(15:17) in both PB and BM	Not available	AML-BFM 2004 ATRA	Alive
Thomas X et al (4)	Sternal mass	No evidence	Normal with normal CBC	FISH + for t(15:17) on tissue biopsy RT PCR on PB and BM negative	Normal	French APL 2006 trial ATRA+ idarubicin+ Cytarabine	Alive 2 years follow up
Oravcova I (10)	Tumor masses in right and left breast	Concurrent presence as per molecular studies	Normal with normal CBC No marrow infiltration	RQ PCR of Marrow and PB of bcr 3 trasncript of PML-RARA FISH negative	Not available	Spanish LPA 2005 ATRA + idarubicin	Expired Post consolidation
Doucet M (1)	epidural paraspinal soft tissue mass T3-T5	Concurrent systemic disease present	Aspirate with 26% blasts/abnormal promyelocytes	FISH on marrow Positive for t(15:17)	Not available	Arsenic trioxide	Alive on Maintenance therapy
Kyaw T Z (3)	Extradural intraspinalmasses (T2-T4) Bony lesions over vertebral body and saccrum	Presence of concurrent systemic disease	CBC-pancytopenia Presence of Marrow infiltration of APL	RT PCR + for bcr1 type PML RARA fusion in marrow	Normal	ATRA + idarubicin	Alive on maintenance therapy
Winters C (6)	Osseous disease L3-L5	Presence of concurrent systemic disease	Normal CBC Marrow no morphological evidence	Karyotype and FISH positive for PML-RARA in marrow And PB	Normal	ATRA	Alive 14 months after initial diagnosis
Ajarim (16)	Thymus	Presence of systemic disease	Anemia + thrombocytopenia with leucocytosis with abonormal promyelocytes Marrow also involved morphologically and on cytochemistry	Karyotype negative	Normal	daunorubicin, ara-C, and 6-thioguanine.	Expired 8 months later from hematological relapse
Fukushima (15)	Left cerebellar hemisphere mass	Presence of concurrent systemic disease	CBC leucocytosis with 97% blasts with Auer rods , thrombocytopenia Marrow presence of abnormal promyelocytes	FISH positive for PML-RARA	Low firbrinogen	idarubicin, and arabino cytosine,	Expired

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Kubonishi (18)	Anterior mediatinal mass	8 months later developed APL	Normal CBC 8 months later PB showe d promyelocytes with marrow showing 33% abnormal promyelocytes.	Not done	Normal	Combination chemotherapy	Expired 14 months after diagnosis of mediastinal mass
Mohammed (14)	Ulcerated tongue lesion	Systemic disease +	PBS Leucocytosis with abnormal promyelocytes Bone marrow abnormal promyelocytes +	FISH positive for t (15:17)	Not available	ATRA + daunourubicin + cytarabine	Remission in first cycle of chemotherapy
Savranlar (17)	Extradural intraspinal lesion T2-T5	10 months later developed APL	Normal PBS and bone marrow At 10 months PBS- 76% abnormal promyelocytes Marrow -90% abnormal promyelocytes	t (15: 17) + by FISH	Normal	Cytosine + daunorubicin (3+7)	In remission alive referred to to other center
Yamashita (11)	Mandibular mass	Presence of systemic disease	Bone marrow morphology positive	FISH showed PML-RARA fusion	Normal	AML-P05 protocol e Japanese Pediatric Leukemia/Lymphoma Study Group. ATRA + anthracycline	1 year alive post maintenance
Tosi (19)	L3-L4 mass	Present	Leucocytosis with thrombocytopenia 47 % promyelocytes Marrow abnormal promyelocytes seen	Karyotyping positive t (15:17)	Abnormal coagulation profile	ATRA and 3+7 chemotherapy	CR after 4 th cycle of chemotherapy Alive with follow up of 1 year
Swanhey et al (9)	Intramedullary mass right proximal humerus	Absent	Normal CBC and marrow	FISH and RT-PCR negative for t(15: 17) Both PB and Bone marrow	Not available	Loco et al ATRA+ arsenic trioxide	Post consolidation alive on maintenance
Surarez et al (20)	Painful 3rd molar	Presence of systemic disease	Pancytopenia 6% blasts Bone marrow 80% abnormal promyelocytes	FISH + t(15: 17)	Abnormal coagulation	ATRA + daunorubicin	Expired due to IC bleed
Stankova (13)	Extradural mass L2-L5	Present	Bone marrow biopsy infiltration by blasts	t (15: 17) by RT PCR on tissue biopsy Marrow cell cultures negative	Normal	Group B APL protocol ATRA	21 months post completion of treatment alive
Nair (12)	Lytic lesions of skull and pelvis	Present	Marrow showed blasts	FISH t(15:17)	Normal	PETHEMA ATRA+ anthracycline	Alive post consolidation

Table 2: Summary of patients who expired with possible contributing factors

Reference	Site of MS	Cause of death	Coagulopathy	Other factors
Surarez (20)	Painful 3 rd molar	IC Bleed DIC	Present Prolonged PT, APTT and low fibrinogen	Delayed diagnosis and initiation of treatment due to atypical presentation
Kubonishi (18)	Anterior mediastinal mass	Cardiac failure Diffuse systemic infiltration of leukemic cells	No DIC	Refractory to chemotherapy
Fukushima (15)	Left cerebellar hemisphere	DIC	Abnormal coagulation	High WBC count
Ajarim (16)	Thymus	Hematological relpase	Normal coagulation	High WBC count Maintenance treatment not given.
Oravcova (10)	Breast mass	CNS failure	Not available	CNS infiltration as shown by positive CSF cytology and flow cytometry Complications due to cytopenia following consolidation RQ-PCR:PML-RARA bcr3 transcript

Reference

1. Doucet M and SchmieJ: "A rare case of acute promyelocytic leukemia with focal bone marrow involvement presenting as a paraspinal myeloid sarcoma." J Hematopathol (2016) 9:161–166.
2. Worch J, Ritter J, Frühwald MC. "Presentation of acute promyelocytic leukemia as granulocytic sarcoma." Pediatr Blood Cancer 2008;50:657-60.
3. Kyaw TZ, Maniam JA, Bee PC, et al. "Myeloid sarcoma: an unusual presentation of acute promyelocytic leukemia causing spinal cord compression." Turk. J. Haematol. 29(3), 2012, 278–282.
4. Thomas X, Chelghoum Y. "Promyelocytic sarcoma of the sternum: a case report and review of the literature." Korean J Hematol. 2011;46:52–6.
5. Swerdlow SH, Campo E, Harris NL, Jaffe ES, Pilleri SA, et al. "WHO Classification of Tumours of Hematopoietic and Lymphoid Tissues." Lyon: IARC; 2017 Revised edition.
6. Winters C, Chen A I, Moore S, Traer E, Dunla J. "Acute promyelocytic leukemia presenting with features of metastatic osseous disease." Leukemia Research Reports 2018, 36–37.
7. Evans, G. D., and D. J. Grimwade. "Extramedullary disease in acute promyelocytic leukemia." Leuk. Lymphoma 33, 1999, 219–229.
8. Neiman S.R., Barcosm., Berard C., Bonnerh., Mannr., Rydell R. E. & Bennett J. M. (1981) "Granulocytic sarcoma: A clinicopathologic study of 61 biopsied cases." Cancer 48, 1426-1437.
9. Sawhney S, Holtzman NG, Davis DL, Kaizer H, Giffi V, Emadi A, & Koka1 R. "Promyelocytic sarcoma of the right humerus: an unusual clinical presentation with unique diagnostic and treatment considerations." Clinical Case Reports 2017;5(11):1874–1877.
10. Oravcova I, Mikuskova E, Leitnerova M, et al. "A unique clinical presentation of de novo acute promyelocytic leukemia as a myeloid sarcoma of the breast." International Journal of Hematology, 108, 550-553, 2018.
11. Yamashita, Y., N. Isomura, Y. Hamasaki, M. Goto, et al. "Case of pediatric acute promyelocytic leukemia presenting as extramedullary tumor of the mandible." Head Neck 35.
12. M. Nair, P. Kusumakumary, P.S. Nair. "Rare presentation of pediatric acute promyelocytic leukemia as multiple lytic bone lesions: case report and review of literature." J. Cancer Res. Therapeut. 10(2), 2014, 381–383.
13. J. Stankova, D. Mitchell, C. Bernard, J.P. Farmer, R. Faingold, N. Jabado. "Atypical presentation of acute promyelocytic leukaemia." Br. J. Haematol. 132(3), 2006, 379–380.
14. Mohamedbhai, S., M. Pule, B. Conn, C. Hopper, A. Ramsay, and A. Khwaja. "Acute promyelocytic leukaemia presenting with a myeloid sarcoma of the tongue." Br. J. Haematol. 141, 2008, 565.
15. Fukushima S, Terasaki M, Tajima Y, Shigemori M. "Granulocytic sarcoma: an unusual complication of acute

promyelocytic leukemia causing cerebellar hemorrhage. Case report." J Neurosurg 2006;105:912-5.

16. Ajarim DS, Santhosh-Kumar CR, Higgy KE, el Saghir NS, Almomen AK, Shipkey FD. "Granulocytic sarcoma of the thymus in acute promyelocytic leukaemia." Clin Lab Haematol 1990;12:97-9.
17. Savranlar A, Ustündag Y, Ozer T, et al. "A thoracic-epidural granulocytic sarcoma case that was diagnosed preceding the onset of and that recurred co-incidental to acute promyelocytic leukemia, which developed after surgical treatment." Acta Med Okayama 2004;58:251-4.
18. Kubonishi I, Ohtsuki Y, Machida K, et al. "Granulocytic sarcoma presenting as a mediastinal tumor. Report of a case and cytological and cytochemical studies of tumor cells in vivo and in vitro." Am J Clin Pathol 1984;82:730-4.
19. Tosi A, De Paoli A, Fava S, et al. "Undifferentiated granulocytic sarcoma: a case with epidural onset preceding acute promyelocytic leukemia." Haematologica 1995;80:44-6.
20. Suárez-Cuenca JA, Arellano-Sánchez JL, Scherling-Ocampo AA, Sánchez-Hernández, Pérez-Guevara D, and Chalapud-Revel JR. "Rapidly progressing, fatal and acute promyelocytic leukaemia that initially manifested as a painful third molar: a case report." Journal of Medical Case Reports 2009, 3:102.
21. Sainty D, Liso V, Cantu`-Rajnoldi A, Head D, Mozziconacci MJ, Arnoule C, et al. "A new morphologic classification system for acute promyelocytic leukemia distinguishes cases with underlying PLZF/RARA gene rearrangements." Blood 96, 2000, 1287-1296.

Corresponding Author:

Dr. Kalyani Bapat
Email: kalyanibapat2812@gmail.com

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