Case Report

De novo myeloid sarcoma involving mandible in a child: Report of a rare occurrence

Moumita Sengupta, Indranil Das[1], Uttara Chatterjee, Boby Majumdar

Department of Pathology, Institute of Postgraduate Medical Education and Research, [1]Department of Pathology, Chittaranjan National Cancer Institute, Kolkata, West Bengal, India

Abstract

Myeloid sarcoma (MS) is a rare malignant disease defined as extramedullary infiltration of immature myeloid cells. We reporte a 2-year-old male of isolated MS who presented with swelling over the left side of the body of the mandible. Proper histological examination and adequate panels of immunohistochemical stain led to the accurate diagnosis. Early intervention with systemic chemotherapy regimens based on cytarabine is the treatment of choice. The role of chromosomal aberrations and genetic abnormality related to prognosis remain uncertain.

Key Words: Acute myeloid leukemia, chloroma, monoblasts, myeloblasts, myeloid sarcoma

Address for correspondence:
Dr. Indranil Das, 28/11 A. K. Mukherjee Road, Noapara, Baranagar, Kolkata - 700 090, West Bengal, India. E-mail: buntyrules83@gmail.com
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INTRODUCTION

Myeloid sarcoma (MS) is a rare neoplastic condition consisting of immature myeloid cells and occur at an extramedullary site that most frequently corresponds to bone, skin or lymph node although any part of the body can be affected.[1] MS most commonly consists of myeloblasts, with or without features of promyelocytic or neutrophilic maturation that partially efface the architecture. The term, "Chloroma," was given by King because such tumor often shows greenish cut surface.[2] MS involving head and neck region poses real diagnostic challenges because of the low frequency of this tumor and tumors of any lineage can occur in head and neck region.

CASE REPORT

The 2-year-old male patient presented with chief complaint of gradually increasing circumscribed swelling in the left side of the body of the mandible for last 1 year. The parents did not complain any symptom suggestive of pain in the swelling, but the child used to cry on touching it. There was no other associated complaint. On examination, a firm to hard, circumscribed, mildly tender swelling measuring 4 cm × 2.5 cm was found over the body of the left side of the mandible. Computed tomography scan of the head and neck region showed a soft tissue mass eroding bone over the body of the left side of mandible [Figure 1]. The report was suggestive of neoplastic soft tissue lesion involving underlying bone. The patient's blood count along with other hematological and biochemical parameters was normal. He underwent tru-cut biopsy from the lesion. Histological examination of the specimen showed mononuclear blast-like cells arranged in sheets with thin intervening fibrous septa [Figures 2 and 3]. The cells were of intermediate size and composed of round to oval nuclei with high nuclear-to-cytoplasmic ratio and prominent nucleoli and scanty basophilic cytoplasm [Figures 4 and 5].

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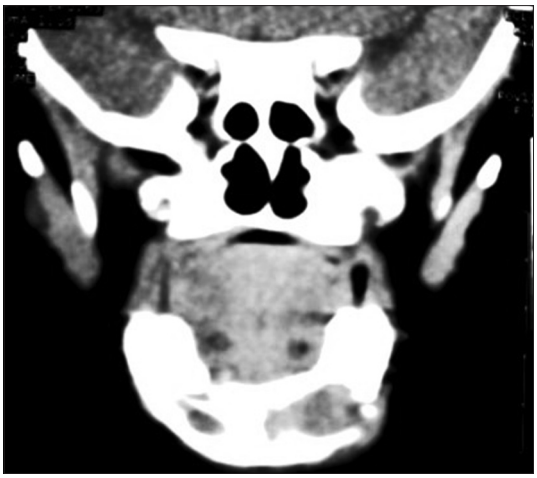

Figure 1: Computed tomography scan of the head-neck region showed a soft tissue mass eroding bone over the body of the left side of the mandible

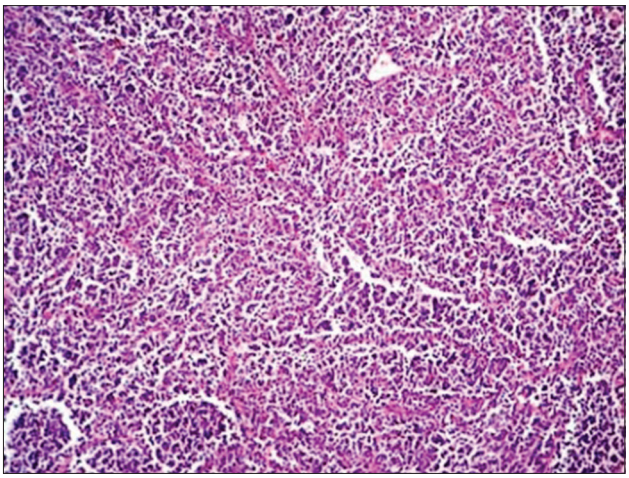

Figure 2: Histological examination of the specimen showed mononuclear blast-like cells arranged in sheets with thin intervening fibrous septa (H&E stain, ×40)

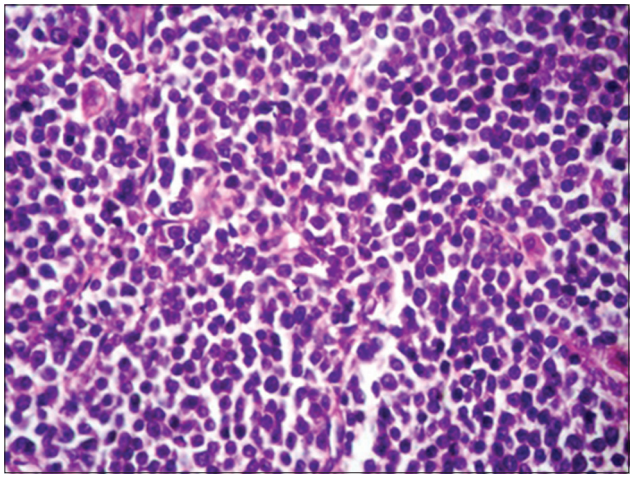

Figure 3: On histopathological examination, the cells were intermediate-sized and composed of round to oval nuclei with high nuclear-to-cytoplasmic ratio (H&E stain, ×100)

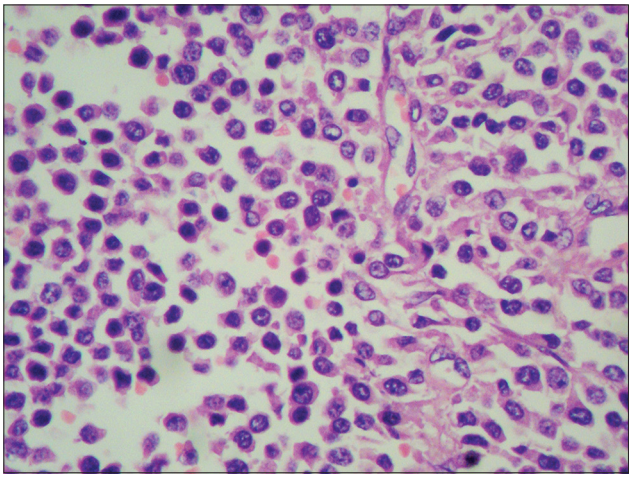

Figure 4: Histopathological examination shows the cells to have high N/C ratio, open chromatin and prominent single or multiple nucleoli (H&E stain, ×400)

Immunohistochemical stain of the paraffin-embedded tissue sections showed that the blast cells were positive for CD45, CD68 and lysozyme [Figures 6-8] and negative for CD3, CD20, CD99, terminal deoxynucleotidyl transferase (TdT), myeloperoxidase (MPO) and CD138. The histological and immunohistochemical findings confirmed the diagnosis of MS with monocytic differentiation. Then, bone marrow biopsy of the patient was done to detect whether bone marrow involvement was present or not but no abnormality was detected at that point of time. The patient was given cytarabine and anthracycline-based induction therapy followed by consolidation with cytarabine alone. On completion of chemotherapy, swelling completely reduced in size. The patient is now being followed up for any local recurrence or systemic relapse at an interval of every 6 months.

DISCUSSION

MS is a rare clinical condition and its diagnosis in a non-leukemic phase of a patient is often a challenge for clinician and pathologist. Pileri *et al*. in a large series of 92 patients reported that 35% of cases occurred concomitantly with acute myeloid leukemia (AML), 38% of cases had a previous AML history and 27% of cases presented as isolated MS.[1] The lesion could be solitary or show multifocal involvement. The clinical symptoms and signs varied depending on the involved anatomic area and tumor size. Pantanowitz and Thompson reported that MS could occur in any one of three clinical settings: (1) In patients who have a history of AML, during active disease or a recurrence, (2) in patients with chronic myeloproliferative disorders, who are at increased risk of blast transformation or (3) in patients with no history of hematologic disease

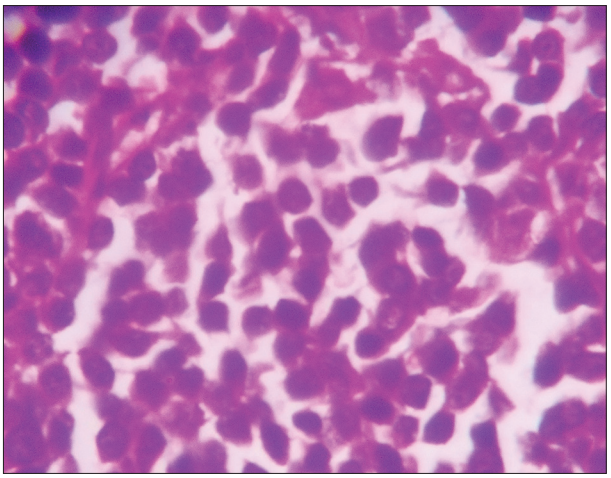

Figure 5: Oil immersion view shows more clear nuclear detail and slight to moderate rim of basophilic cytoplasm (H&E stain, ×1000)

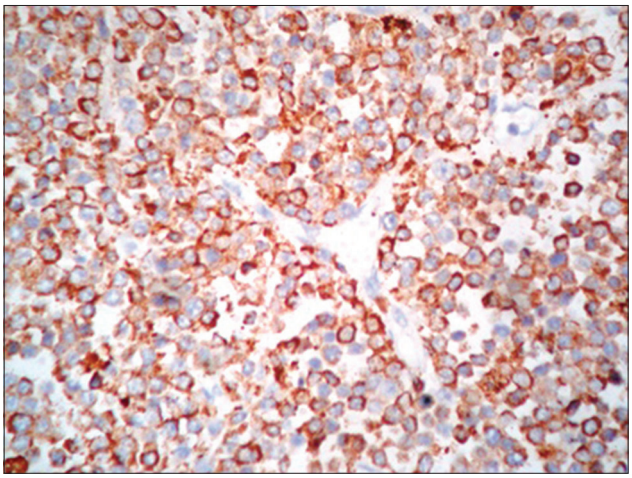

Figure 6: On immunohistochemical examination, blast cells were positive for CD45 (IHC stain, ×400)

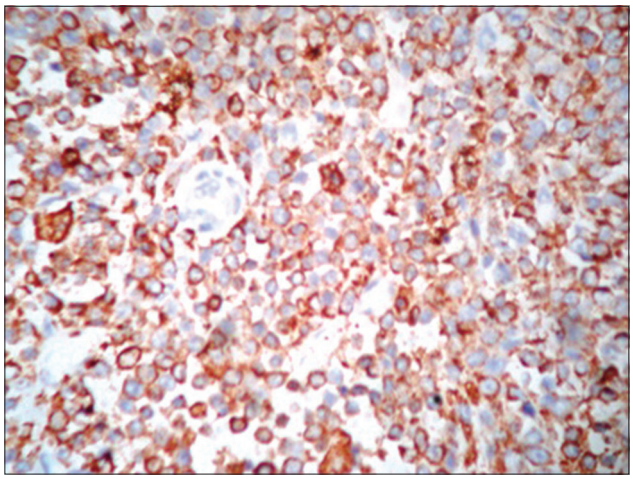

Figure 7: On immunohistochemical examination, blast cells were positive for CD68 (IHC stain, ×400)

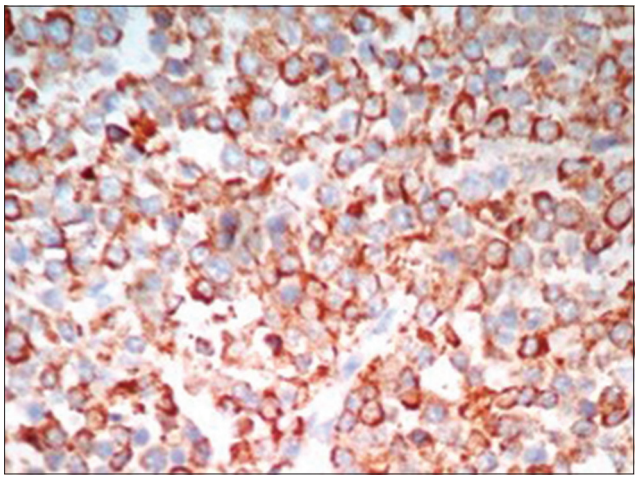

Figure 8: On immunohistochemical examination, blast cells were positive for lysozyme (IHC stain, ×400)

although it commonly predates the development of leukemia, often within 1 year.[3] When there is no concomitant leukemia, the diagnosis of MS becomes difficult and challenging also, particularly in the case of children where lymphoma and small blue round cell malignancy is a common occurrence. Our case also imposed a diagnostic challenge due to age, site and presentation. The pathogenesis of MS regarding extramedullary infiltration is still under investigation. In contrast to the normal homing signals of normal leukocyte in vascular and lymphatic system, Stefanidakis *et al*. proposed a study that supramolecular complex composed of B2 integrins and MMP-9 in AML derived cell is required for pericellular proteolysis and migration.[4] The differential diagnosis of MS in the head and neck region includes several types of malignant lymphoma (B-cell and T-cell) and small blue cell tumors of childhood. Perhaps the most common error is to misdiagnose cases of MS as diffuse large B-cell lymphoma. This is particularly likely for cases of immature MS, where no evidence of differentiation is observed. In general, the cells of diffuse large B-cell lymphoma have thick nuclear membranes and basophilic nucleoli, unlike myeloblasts or monoblasts, which have thin nuclear membranes and pinpoint nucleoli. In addition, cases of diffuse large B-cell lymphoma express pan–B-cell antigens and are negative for myeloid antigens. MS also can exhibit a prominent, starry-sky appearance with numerous apoptotic cells and mitoses and resemble Burkitt lymphoma. However, immunohistochemical studies readily distinguish MS from Burkitt lymphoma because the latter is positive for pan–B-cell antigens, CD10 and BCL-6 and is negative for myeloid antigens.[5] The expression of CD99 is shared by subsets of MS and pediatric small blue cell tumors. However, small blue cell tumors of childhood lack myeloid antigens, such as lysozyme and MPO. In addition, tumors such as alveolar rhabdomyosarcoma, neuroblastoma and other childhood tumors have distinctive immunophenotypic or molecular profiles (e.g., muscle markers and chromosomal translocations characteristic of alveolar rhabdomyosarcoma) to

Table 1: Differential antigen expression of monocytic and histiocytic malignancies

Neoplasm	CD13/CD33	CD1a	CD14	CD64	CD68	CD21	CD35	S100	CD34	CD117	HLA-DR
Acute monocytic and monoblastic leukemia	+	−	+	+	+	−	−	−	±	+	±
Acute myelomonocytic leukemia	+	−	+	+	+	−	−	−	+	±	+
Histiocytic sarcoma	−	−	−	−	+	−	−	±	−	−	+
Langerhans cell histiocytosis	−	+	−	−	+	−	−	+	−	−	+
Interdigitating dendritic cell sarcoma	−	−	−	−	±	−	−	+	−	−	−
Follicular dendritic cell sarcoma	−	−	−	−	±	+	+	±	−	−	+

HLA-DR: Human leukocyte antigen-diabetic retinopathy

establish the correct diagnosis. The most commonly expressed positive markers for MS were CD68/KP1, followed by MPO, CD117, CD99, CD68, lysozyme, CD34, TdT, CD56, CD61, CD30, glycophorin and CD4. For myeloid differentiation of MS, CD13, CD33, CD117 and MPO were the common markers, while CD14, CD163 and CD11c were the common markers for monoblastic differentiation [Table 1]. MS is a rare disease with poor prognosis.[6] Meis *et al.* revealed that 87% (13 of 15) of patients diagnosed with granulocytic sarcoma subsequently develop AML in a mean time period of 10.5 months (range from 1 to 49 months).[7] Further bone marrow biopsy is warranted to rule out concurrent bone marrow involvement once MS is confirmed. Cytogenetic and fluorescence *in situ* hybridization analysis should also be performed as a part of diagnostic workup because the reported incidence of chromosomal aberrations is found in approximately 54.3% of cases. A variety of chromosomal abnormalities including mixed-lineage leukemia (MLL) rearrangement, t(8:21), monosomy 7, trisomy 8, MLL splitting, inv (16), trisomy 4, monosomy 16, 16q–, 5q–, 20q– and trisomy 11 were found to be associated with MS. However, the clinical significances regarding the prognosis or treatment effect for MS patient with above genetic abnormality remain to be discovered and compared with AML.[1] In conclusion, despite the rarity of the disease and diagnostic difficulty for the clinician, MS could be correctly diagnosed through adequate panels of immunohistochemical stains. The current recommended treatment regimen in patients presenting with isolated MS or MS presenting concomitantly with AML is conventional AML-type chemotherapeutic protocols. This recommendation is based on the observation of a higher rate of progression to AML in isolated MS patients receiving localized treatment (88–100%) compared with patients given systemic chemotherapy (42%).[8] The role of radiotherapy in addition to systemic chemotherapy is not established although it is often given. Tsimberidou *et al.* suggested that radiotherapy may prolong failure-free survival but not overall survival in patients presenting with isolated MS.[9] However, Lan *et al.* found no effect on survival in MS patients (isolated or following the diagnosis of AML) treated with radiotherapy in addition to chemotherapy compared to chemotherapy alone.[8] The role of hematopoietic stem cell transplantation (HSCT) in patients with MS was not studied prospectively, but the outcome of patients undergoing HSCT was shown in several retrospective reports.[1] The results in case reports have variable outcomes, probably reflecting the difference in prognostic factors in each case. In our case, only chemotherapy was given and follow-up studies are being carried out to detect early systemic or local recurrence.

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Conflicts of interest

There are no conflicts of interest.

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