Isolated Myeloid Sarcoma of the Maxillary Sinus: A Case Report and Review of Literature

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Abstract
Myeloid sarcoma is a rare malignant disease defined as extramedullary infiltration of immature myeloid cells and may precede or occur synchronously with acute myeloid leukemia. We reported a 35-year-old male of isolated myeloid sarcoma who presented with symptoms similar to chronic rhinosinusitis initially. Isolated myeloid sarcoma in the paranasal sinuses is exceedingly rare after reviewing the previous literatures. Through proper histological, adequate panels of immunohistochemical stain (positive markers including CD68/KP1, myeloperoxidase, CD 117, CD44, CD79a, terminal deoxynucleotidyl transferase and negative markers including CD3, CD20, CD45 and CD79a) and cytogenetic study lead to accurate diagnosis. Early intervention with systemic chemotherapy with cytarabine-based regimens is the treatment of choice. The role of chromosomal aberrations and genetic abnormality related to prognosis remain uncertain.

Keywords: Myeloid sarcoma; Sinus

Introduction
Myeloid sarcoma (MS) is a rare malignant disease defined as localized infiltration of immature myeloid cells occurring in extramedullary sites [1]. In 1811, the British physician Burns first described this condition and was later named as "Chloroma" by King due to the greenish color of tumors attributed to the enzyme myeloperoxidase [1,2]. The connection between leukemia and chloroma was discovered by Dock in 1904 [3]. Rappaport renamed the tumor as granulocytic sarcoma because their destructive nature developed from the immature cells of granulocytic series and the display of color other than green [4]. Myeloid sarcoma was defined as a subgroup of myeloid neoplasm and acute leukemia in the revised 2008 World Health Organization Classification and became the formal nomenclature [5]. Myeloid sarcoma occurs most commonly in the skin, bone and lymph nodes. It has been also reported in others organs such as central nervous system, orbits, heart, gastrointestinal tract, kidney, bladder and reproductive organs [5-7]. It is frequently occurred concomitantly in patients with acute myeloid leukemia (AML), myeloproliferative diseases or myelodysplastic syndrome (MDS) [6]. It could also be the initial manifestation of relapsing AML. In rare condition, myeloid sarcoma could be de novo occurrence and precede AML by months or years [8,9]. Here we report a rare case of isolated myeloid sarcoma presented initially as chronic rhinosinusitis. Endoscopic sinus surgery was performed in January 2009 and the specimen was sent for pathologic examination.

Histologic examination of the specimen demonstrated that the...
paranasal sinus mucosa was surrounded by a dense infiltration of mononuclear blast-like cells (Figure 2). The cells were intermediate-sized composed of prominent nucleoli and round to oval nuclei with high nuclear-to-cytoplasmic ratio. Immunohistochemical stain of the paraffin-embedded tissue sections showed that the blast cells were positive for terminal deoxynucleotidyl transferase (TdT), CD68/KP1, CD43, CD99 and CD117 (Figure 3). The myeloperoxidase (MPO), lysozyme, cyclin D1, TIA-1, CD1a and CD56 were all negative. The B- and T-lineage markers including CD2, CD3, CD4, CD5, CD8, CD20, CD79a and PAX-5 were all negative. The histologic findings confirmed the diagnosis of myeloid sarcoma.

The patient's blood cell count was normal at the time of diagnosis of nasal cavity myeloid sarcoma. Bone marrow study revealed normal cellularity on 3 February, 2009, and the chromosome analysis showed a 46 XY karyotype. The cytogenetic studies were negative for t(8;21) AML1-ETO translocations. The patient received induction chemotherapy with Daunomycin (60 mg/m²/day, days 1–3) and cytarabine (100 mg/m²/day, days 1–7) in February, 2009, and the chromosome analysis of nasal cavity myeloid sarcoma. Bone marrow study revealed normal cellularity on 3 February, 2009, and the chromosome analysis showed a 46 XY karyotype. The cytogenetic studies were negative for t(8;21) AML1-ETO translocations. The patient received induction chemotherapy with Daunomycin (60 mg/m²/day, days 1–3) and cytarabine (100 mg/m²/day, days 1–7) in February, 2009, and complete remission was achieved. In February 2010, his blood count showed pancytopenia (hemoglobin 11.5 g/dl, platelet count: 20,000/ul, WBC:1800/ul, Seg:22%, lym:71%, blast:0%) during routine follow-up. Subsequent bone marrow aspiration showed tumor infiltration (blast reported as 74%). The diagnosis of AML was then made. The flow cytometry revealed positive for CD13, CD33, CD34, CD56 and CD117 and negative for CD7, CD14, CD15, CD19 and CD64. The subsequent cytogenetic studies were negative for t(8;21) AML1-ETO translocations, CBFb-MYH11, MLL-PTD, NPM1 and FLT3 mutation. The chromosome study was 46, X, -Y, -21, +2mar[4]/45, X, -Y, -21, +mar[4]/46, XY[4]. The patient refused allogeneic hematopoietic stem cell transplantation. Reinduction chemotherapy with Etoposide (100 mg/m² for 2 days) and Cytarabine (100 mg/m² for 7 days) was initiated in April 2010. He had recurrent anal fistula with severe local infection and myelosuppression during routine follow-up. He received fistulectomy in February 2011 and local therapy for the wound afterwards. Recurrent pancytopenia occurred in May 2011, with bone marrow study showing relapsed AML and CT scan revealing a recurrent nasal cavity tumor. He received salvage chemotherapy with Mitoxantrone (12 mg/m² for 2 days), Etoposide (100 mg/m² for 2 days) and Cytarabine (1 g/m² q12h QOD for 3 days). The patient expired due to severe pneumonia with myelosuppression in May 2011.

**Discussion**

Myeloid sarcoma is a rare clinical condition. Pileri et al. [8] in a large series of 92 patients reported that 35% of cases occurred concomitantly with AML, 38% of cases had a previous AML history and 27% of cases presented as isolated myeloid sarcoma [9]. The lesion could be solitary or multifocal involvement. The clinical symptoms and signs varied depending on the involved anatomic area and tumor size. Isolated myeloid sarcoma in paranasal sinus is exceedingly rare. We have reviewed the literatures in English, only 6 patients with MS involvement in nasal cavity were reported (Table 1) [10-15]. Among the patients, only two cases (case 1 and case 5) were isolated MS and the others presented with AML history or synchronous MDS. The present case is the third reported isolated MS involved paranasal sinus.

The pathogenesis of myeloid sarcoma regarding to 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 [16]. Faaij et al. [17] reported that the skin myeloid sarcoma among pediatric AML patients displayed the unique chemokine receptors including CCR5, CXCR4, CXCR7 and CX3CR1 and their interaction results in homing and retention of AML blast in the skin [17].

Diagnosis of MS in a nonleukemic patient is often a challenge for clinician and pathologist. The presenting symptoms are not specific, as in our case with the initial symptoms suggestive of chronic sinusitis. Menasce et al reported that all the 14 cases without previous history of myeloproliferative diseases were incorrectly diagnosed, with non-Hodgkin’s lymphoma the most common misdiagnosis [18]. The mainstay of diagnosis is histopathologic and cytologic confirmation. In histology examination, it must be differentiated from other small blue round cell tumor including lymphoma, neuroblastoma, rhabdomyosarcoma, Ewing’s sarcoma, primitive neuroectodermal tumor, and medulloblastoma, undifferentiated carcinoma or melanoma. Further classification of MS according to the cell type and the cell maturity were granulocytic, monoblastic or myelomonocytic types and immature, mature and blastic types respectively [13]. The immunohistochemical analysis is mandatory for accurate diagnosis if the hematoxylin and eosin stain demonstrated medium to large-sized pleomorphic cells with irregular nuclear outline, prominent
nucleoli and high nuclear-to-cytoplasmic ratio. The most common expressed positive markers for myeloid sarcoma were CD68/KP1, followed by myeloperoxidase (MPO), CD 117, CD 99, CD68/PG-M1, lysozyme, CD34, terminal deoxynucleotidyl transferase (TelT), CD56, CD61, CD30, glycophorin and CD 4. For myeloid differentiation of myeloid sarcoma, CD13, CD33, CD117 and MPO were the common markers, while CD14, CD163 and CD11c were the common markers for monoblast differentiation [19]. The B- and T-lineage markers including CD3, CD20, CD45ROI and CD79a should be examined for exclusion of lymphoma. In our case, the positive marker for TelT and CD 117 demonstrated the immaturity of hematopoietic progenitor cells. Positive markers for myeloid origin (CD68/kp1 and CD99) and negative markers for lymphoid organ (CD3, CD20 and CD79a) confirmed the diagnosis of myeloid sarcoma.

Further bone marrow biopsy is warranted to rule out concurrent bone marrow involvement once myeloid sarcoma confirmed. Cytogenetic and fluorescence in situ hybridization (FISH) analysis should also be performed as part of diagnosis because the reported incidence of chromosomal aberrations was found in approximately 54.3% of cases [8]. A variety of chromosomal abnormalities including 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 myeloid sarcoma [8]. The rate of t(8;21) AML1-ETO translocations in myeloid sarcoma was controversial, which is reported 43% (17/39)patients by Dusenberg et al. [20] and around 3.3% (1/30 patients) by Pileri et al. [8,20]. Another common chromosome rearrangement “inv(16)”, resulting in the fusion of CBFB and MYH11 genes, was found to present in myeloid sarcoma with intestinal involvement [21]. Nucleophosmin (NPM) 1 mutations and FMS-related tyrosine kinase 3 (FLT3) mutations, the common genetic abnormality in AML, were reported 15% of 181 MS patients by Falini et al. [24] and 33% of 9 MS with synchronous AML patients by Ansari-Lari et al. [22,23]. However, the clinical significances regarding to the prognosis or treatment effect for MS patient with above genetic abnormality remain to be discovered and compared with AML.

Myeloid sarcoma is a rare disease with poor prognosis. Meis et al. [24] 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) [24]. Therefore, treatment should be arranged shortly after initial diagnosis. Systemic chemotherapy with cytostatine-based regimens, as conventional AML type, is recommended currently [25,26]. The role of radiotherapy was mainly on patients with isolated myeloid sarcoma or treatment failure by chemotherapy, while surgery is reserved for tissue proof or patients with acute symptoms such as nerve compression [27]. Allogeneic hematopoietic stem cell transplantation (AHSCST) is another treatment of choice but needs further prospective studies for evaluation.

In conclusion, despite the rarity of the disease and diagnostic difficulty for clinician, myeloid sarcoma could be correctly diagnosed via adequate panels of immunohistochemical stains. The bone marrow biopsy, cytogenetic study and molecular analysis are also mandatory for the synchronous AML. Systemic chemotherapy should be administrated shortly once the diagnosis confirmed. Further prospective studies are necessary for stratification of the role of chromosome and genetic abnormality and the treatment outcomes.

References


