Myeloid Sarcoma: Presenting with Massive Cervical and Inguinal Lymphadenopathy

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Abstract A 21 year old Active Duty Marine presented with acute onset of diffuse lymphadenopathy and B-symptoms. Biopsy was conducted which demonstrated myeloid sarcoma. Myeloid sarcoma is diagnostic for AML but is only present in 2–8 % of patients with AML. Our article presents a classic presentation and histologic appearance and discusses the current status of the literature.

Keywords Myeloid sarcoma · Lymphadenopathy · Chloroma · Granulocytic sarcoma · Extra-medullary myeloid tumor · AML · Acute myeloid leukemia

Case Report

A 21 year old male Marine presented with a 1 week history of progressive cervical and inguinal lymphadenopathy associated with fatigue, malaise, night sweats as well as headaches, recurrent epistaxis, and exertional dyspnea. He

had lost 15 lb over the past month, which he attributed to his recent field exercise. The patient is a nonsmoker, nondrinker and was on no medications. His past medical history is remarkable for a benign reactive cervical lymph node excised 2 years earlier.

Physical examination of the neck showed numerous bilateral, enlarged, nontender, anterior, posterior, sub-mandibular, submental, and supraclavicular lymph nodes. The lymph nodes were all approximately 2 cm or less in size. In addition, the physical exam was notable for bilateral inguinal lymphadenopathy. The remainder of the physical exam was benign. A CT scan of the chest, abdomen, and pelvis confirmed the physical exam findings of diffuse axillary and inguinal lymphadenopathy and identified diffuse mesenteric lymphadenopathy (Figs. 1, 2). An excisional biopsy of a 1.5 cm submental lymph node was performed. The lymph node showed effacement of underlying tissue architecture by sheets of mononuclear cells with an interfollicular growth pattern (Fig. 3 lymph node, H&E low power Fig. 4 lymph node, H&E high power Fig. 5 lymph node, cells of interest are CD34 negative Fig. 6 lymph node, cells of interest are CD117 positive Fig. 7 lymph node, cells of interest are MPO positive). The mononuclear cells showed fine nuclear chromatin with clearing and prominent nucleoli. Admixed were eosinophil precursors and evenly distributed tingible body macrophages imparting a “starry-sky” pattern. Intact solitary germinal centers were present and located predominantly at the periphery of the lymph node. Flow cytometric immunophenotypic analysis showed ~55 % myeloid blasts with myelomonocytic features.

Subsequent chromosomal analysis of the bone marrow aspirate showed an abnormal male karyotype associated with an inv(16)(p13q22). (Fig. 8 H&E low power bone marrow core biopsy effaced by leukemia blasts admixed

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Fig. 1 Non-contrast CT of chest, abdomen and pelvis demonstrating diffuse axillary and mesenteric lymphadenopathy

with increased eosinophils Fig. 9 H&E high power bone marrow core biopsy Fig. 10 H&E low power bone marrow aspirate blasts admixed with increased eosinophils Fig. 11 H&E high power bone marrow aspirate blasts admixed with increased eosinophils)

What is your diagnosis?

Diagnosis Myeloid sarcoma

Myeloid sarcoma (MS) is an extramedullary proliferation of myeloid blasts that is diagnostic of acute myeloid leukemia (AML) regardless of bone marrow or blood status. Synonyms for MS include “chloroma”, “granulocytic sarcoma”, and “extra-medullary myeloid tumor” and it may be the first indication of AML. Myeloid sarcoma should not be considered a type of AML but rather an extramedullary manifestation of AML. In 2015, the National Cancer Institute estimates that there were 20,830 new cases of AML, accounting for 1.3 % of new cancer cases, and 10,460 deaths caused by AML, accounting for 1.8 % of cancer deaths in the U.S. [1]. If untreated, AML

Fig. 2 Non-contrast CT of chest, abdomen and pelvis demonstrating massive inguinal lymphadenopathy

follows an aggressive clinical course and may be rapidly fatal. Unfortunately, the current 5 year survival rate for AML from 2005–2011 is estimated at 25.9 % [1].

AML is a heterogeneous group of hematologic malignancies that represent clonal proliferation of immature bone marrow-derived non-lymphoid cells that most classically involve the bone marrow and peripheral blood; however, in some instances may present in extramedullary tissue. The French-American-British Cooperative Group (FAB) described 8 AML subtypes based originally on morphologic and cytochemical features. Other studies, including immunophenotype and, in some cases, electron microscopy were later added defining features of some subtypes [2–4]. Although the terminology of the FAB classification continues to be used by pathologists/hematopathologists, the system is now considered obsolete

Fig. 3 Low power photograph of H&E stained lymph node demonstrating effacement of underlying tissue architecture by sheets of mononuclear cells with an interfollicular growth pattern

Fig. 4 High power photograph of H&E stained lymph node demonstrating effacement of underlying tissue architecture by sheets of mononuclear cells with an interfollicular growth pattern

owing to its inability to accurately identify prognostically significant disease types. The 2001 and subsequently the 2008 WHO classification incorporated and refined findings not included in the FAB classification, and took into account the significance of recurring cytogenetic abnormalities, various molecular subtypes, and treatment.

A complex approach is necessary for appropriate diagnosis and classification of AML or MS. The differential diagnosis of myeloid sarcoma versus lymphoma when there is extensive lymph node involvement is challenging on morphologic grounds alone. Such a differential typically involves diffuse large B-cell lymphoma, lymphoblastic lymphoma, blastic mantle cell lymphoma, and Burkitt's

Fig. 5 High power photograph of CD34 stained lymph node demonstrating cells of interest are CD34 negative

Fig. 6 High power photograph of CD117 stained lymph node demonstrating cells of interest are CD117 positive

lymphoma. Immunophenotyping, preferably using multi-color flow cytometric analysis and if needed additional immunohistochemical stains as well as submission of tissue for chromosomal analysis, are essential to the proper diagnosis and classification of myeloid sarcoma or AML.

The reported age range for myeloid sarcoma is 1–81 years old [5]. In patients with AML, MS is present in 2–8 % of these patients [5]. In adults, the true incidence of MS is unknown, although in roughly one third of cases it may occur concurrently with other myeloid diseases including myelodysplastic syndrome (MDS), myeloproliferative neoplasm (MPN) or MDS/MPN [6–11], but such an association is not required. In pediatric AML however, MS occurs in approximately 10 % of cases [11]. When involving extramedullary sites, MS most commonly

Fig. 7 High power photograph of MPO stained lymph node demonstrating cells of interest are MPO positive

Fig. 9 High power photograph of H&E stained bone marrow core demonstrating hypercellular bone marrow effaced by leukemia with increased eosinophils

Fig. 8 Low power photograph of H&E stained bone marrow core demonstrating hypercellular bone marrow effaced by leukemia with increased eosinophils

Fig. 10 Low power photograph of H&E stained bone marrow aspirate demonstrating leukemic cells with admixed increased eosinophils

involves the skin, followed by mucus membranes, orbits, central nervous system, lymph nodes, bones, gonads and other internal organs [12]. The clinical significance of myeloid sarcoma remains unclear. Other than rare cases of self-limited congenital forms, it is not clear whether MS confers any specific prognosis, particularly when cases are classified according to known risk groups [13, 14].

The current case was classified as an acute myeloid leukemia with a recurring inv(16) abnormality (FAB Subtype: M4 eos: myelomonocytic leukemia with abnormal eosinophils) which typically in absence of KIT mutation has a favorable prognosis [15]. The incidence of extramedullary disease (i.e. myeloid sarcoma) in AML

with inv(16) is reportedly as high as 50 %, higher than for most types of AML. In pediatric patients the inv(16) has been reported as occurring in 13 % of patients with MS [16]. Inv(16) has also been associated with, at least in some case reports, an intestinal presentation [8].

Initial treatment of AML with concurrent MS is systemic chemotherapy. Stem cell transplantation may be used during remission or recurrent disease. Low dose radiation therapy may be useful for the emergent treatment of life threatening or organ threatening (e.g. orbit or head and neck disease) MS.

Fig. 11 High power photograph of H&E stained bone marrow aspirate demonstrating leukemic cells with admixed increased eosinophils

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