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Case Report

Mast Cell Leukemia: Review of a Rare Disease and Case Report of Prolonged Survival after Allogeneic Stem Cell Transplant

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ABSTRACT

Mast cell leukemia is a rare and aggressive form of mastocytosis characterized by >20% mast cells found in the bone marrow aspirates of patients with signs of systemic mastocytosis-related organ damage. The prognosis for patients with mast cell leukemia is extremely poor, with resistance to both cytoreductive therapies and tyrosine kinase inhibitors being relatively common. While allogeneic hematopoietic stem cell transplantation has been associated with long-term survival in patients with advanced systemic mastocytosis, reports regarding its effectiveness in mast cell leukemia are limited to fewer than 20 cases described in the literature. Here, we report a patient with mast cell leukemia who remains in complete remission 24 months after allogeneic HSCT at the time of this writing, and briefly review the clinical, diagnostic, and therapeutic approaches to this rare disease.

1. Introduction

Mast cell leukemia is a rare and aggressive form of systemic mastocytosis. Mastocytosis is a heterogeneous collection of diseases (Table 1) characterized by the abnormal accumulation of mast cells; and until recently, has been listed under the umbrella of myeloproliferative neoplasms (MPN) [1]. Enhanced characterization of the clinical and molecular pathogenic differences between mastocytosis and the MPNs has prompted the extraction of mastocytosis out from under the umbrella of MPNs [2]. Diagnosing mast cell leukemia first requires the diagnosis of systemic mastocytosis, with the additional features of leukemic involvement of the bone marrow with >20% mast cells and signs of systemic mastocytosis related organ damage, such as prominent cytopenias. The prognosis for mast cell leukemia is exceedingly poor, with only a six-month median survival, and because of the rarity of this disease, little can be found in the current literature to help choose the best therapeutic approach. In particular, there is scant data regarding the efficacy of bone marrow transplantation in the treatment of mast cell leukemia [3,4]. We report a patient with mast cell leukemia who remains in complete remission at the time of this writing, 24 months after allogenic hematopoietic stem cell transplantation.

2. Case report

A 52 year old man with a long-standing history of psoriasis and psoriatic arthritis was evaluated for incidental thrombocytopenia and mild anemia. Bone marrow biopsy at that time revealed a hypercellular marrow with trilineage hematopoiesis, no significant dysplasia, and normal cytogenetic evaluation (including FISH testing for myelodysplastic syndrome). Given these findings, and after a second opinion, immune thrombocytopenia seemed most likely and the patient was treated with rituximab. However, his platelet count did not significantly improve, ranging from 20 to 50 K/μL for the following 3 years.

At the age of 55 years, the patient began experiencing night sweats, fatigue, dyspnea on exertion, and daily fevers. His thrombocytopenia and anemia had significantly worsened. A bone marrow evaluation was performed and the aspirate smear showed numerous mast cells (21%), many of which were spindle shaped. Eosinophilia (9%) and increased blasts (7%) were also present within a milieu of trilineage hematopoiesis that included occasional dysplastic megakaryocytes and erythroid cells with mild nuclear abnormalities. The core biopsy showed a markedly hypercellular marrow (100%) diffusely infiltrated by clusters of round to spindled mast cells as well as many eosinophils (Fig. 1). Immunohistochemical staining showed the mast cells co-expressed CD117, tryptase, CD25, and CD30 without CD2. Given that the background marrow displayed eosinophilia, mild dysplasia (occasional megaloblastic erythroid precursors and rare megakaryocytes with hypolobated nuclei), and increased blasts, correlative testing was performed to investigate the possibility of a concomitant clonal non-

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Table 1
WHO classification of mastocytosis, according to the 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia [2]

1. Cutaneous mastocytosis
2. Systemic mastocytosis
   a) Indolent systemic mastocytosis
   b) Smoldering systemic mastocytosis
   c) Systemic mastocytosis with an associated hematologic neoplasm
   d) Aggressive systemic mastocytosis
   e) Mast cell leukemia
3. Mast cell sarcoma

mast cell disorder such as myelodysplasia or eosinophilia-related abnormalities. These additional studies on the bone marrow aspirate showed *KIT* D816V mutation was positive, *BCR-ABL1* fusion by RT-PCR was negative, karyotyping was normal, and FISH studies for MDS-associated abnormalities as well as *FGFR1, PDGFRA, PDGFRB,* or *CBFB* (inv16) rearrangement were all negative. Given the extensive mast cell infiltrate (21% of cells on the aspirate smear), absence of circulating mast cells, and progressive cytopenias with systemic symptoms, the diagnosis of aleukemic mast cell leukemia without a concomitant clonal non-mast cell disorder was established.

The patient was subsequently treated with 2-chloro-dexoy-adenosine (2-CDA) for seven days at a dose of 0.1 mg/kg per every 24 hours, followed by the tyrosine kinase inhibitor dasatinib at a dose of 20 mg twice daily. After initial improvement, with resolution of fevers and systemic symptoms, the patient began to show signs of progression two months later heralded by progressive splenomegaly, recurrent fevers, and worsening cytopenias. Follow up bone marrow evaluations confirmed persistent residual disease with tryptase positive mast cells occupying approximately 20% of the marrow space. A decision was made to pursue allogeneic bone marrow transplantation and the patient was treated with an additional course of 2-CDA, again at dose of 0.1 mg/kg per every 24 hours, followed by myeloablative conditioning with busulfan and cyclophosphamide. Busulfan was given at 0.8 mg/kg every six hours on days 7, 6, 5, and 4 prior to bone marrow transplant. Cyclophosphamide was given at 60 mg/kg per day on Days 3 and 2 prior to related HLA-matched hematopoietic stem cell transplant.

Bone marrow biopsy performed 30 days post-transplant revealed a surprisingly hypercellular bone marrow (100%) with trilineage hematopoiesis, but no architectural distortion or discernable mast cell infiltrate by H&E staining. Tryptase staining did reveal increased numbers of largely non-clustered mast cells, initially thought to represent residual disease; however, CD30 staining was negative. CD25 staining was not performed, although negative CD25 staining would have provided further support for non-neoplastic mast cells. His post-transplant course was complicated by cutaneous graft-versus-host disease and cytomegalovirus reactivation. Bone marrow biopsy performed three months

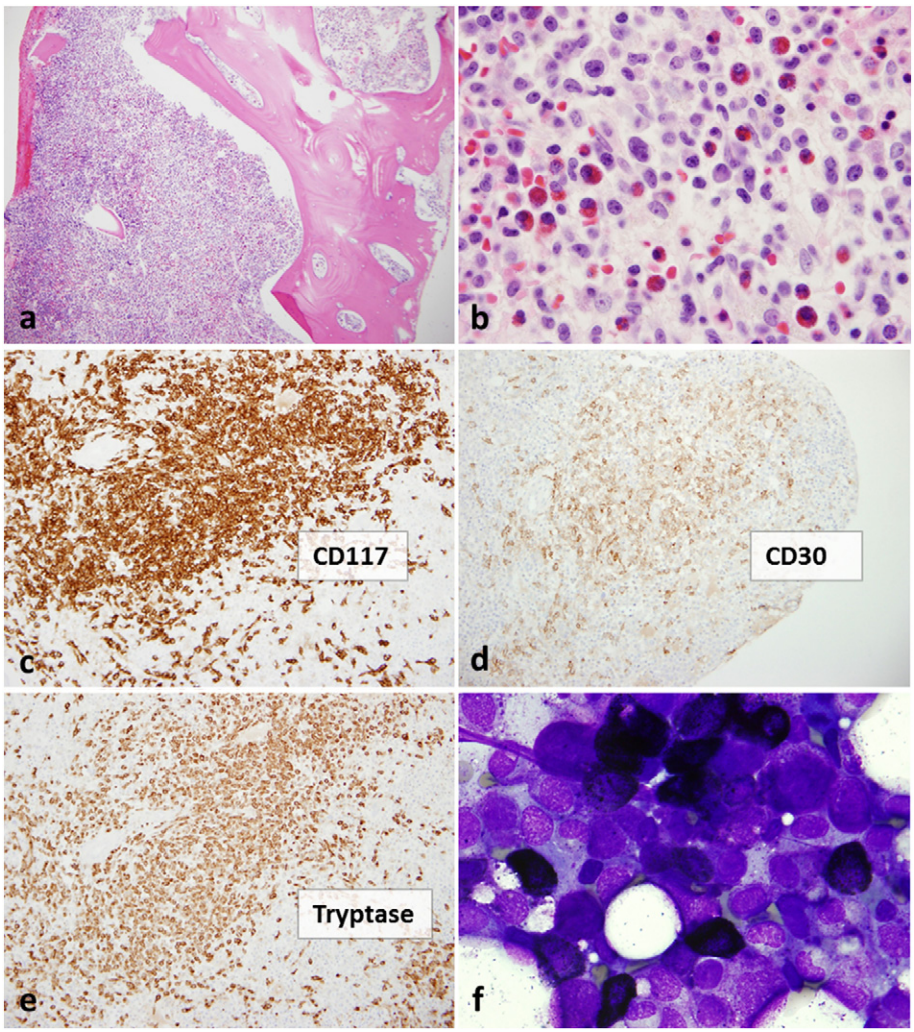

Fig. 1. Diagnostic bone marrow biopsy. **a)** Core biopsy showing a markedly hypercellular bone marrow and osteosclerosis with **b)** diffuse infiltration by round and spindled mast cells and increased numbers of eosinophils; H&E 20x and 100x magnification, respectively. The mast cells co-express **c)** CD117, **d)** CD30, and **e)** tryptase; all 20x magnification. **f)** The bone marrow aspirate showed 21% mast cells, many of which were spindle shaped; Wright-Geimsa 100× magnification.