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IMAGES IN HEMATOLOGY

Mast cell sarcoma: 2 Mayo Clinic cases

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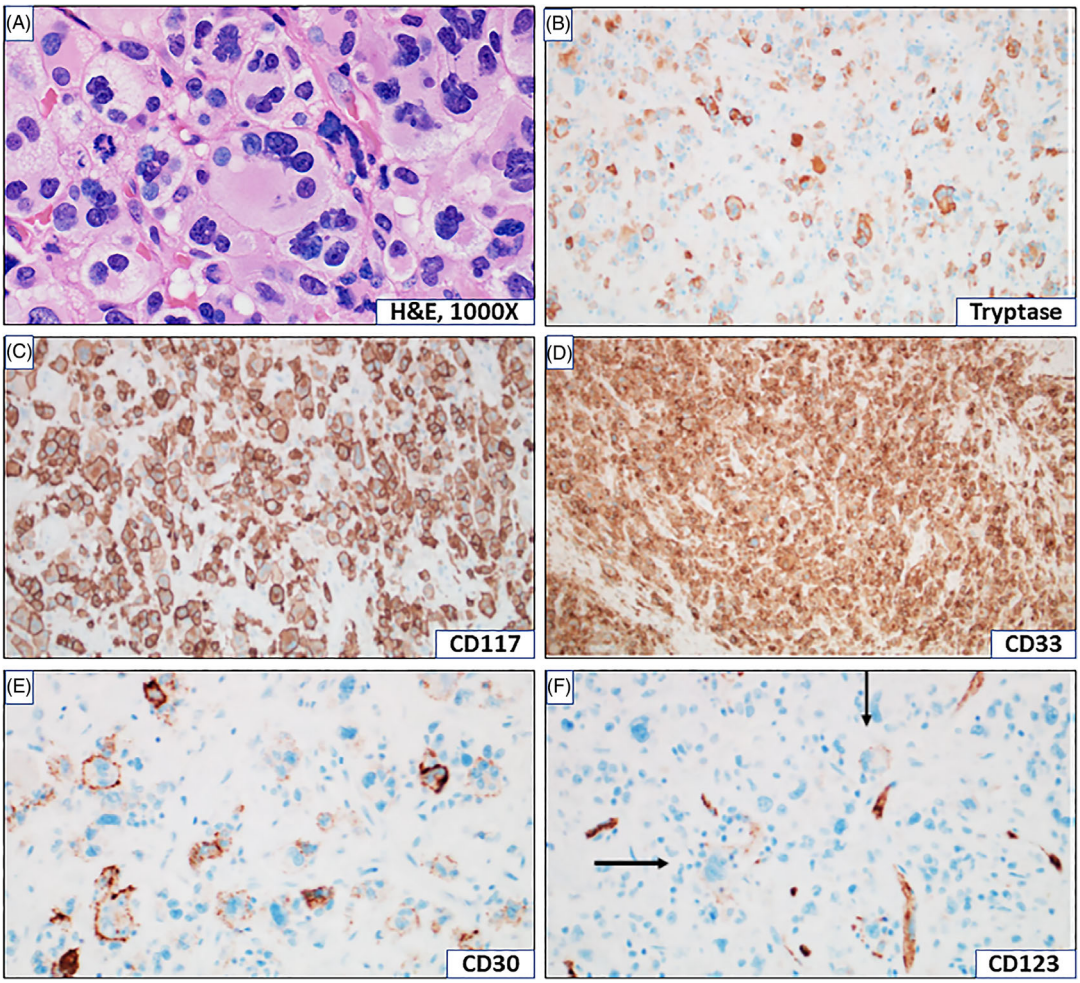

IMAGE 1 A 60-year-old man with femoral bone mast cell sarcoma. The neoplastic cell are large , some are multinucleated, with irregular nuclei, multiple nucleoli and abundant pink cytoplasm. The tumor cells expressed tryptase, CD117, CD33, CD30, and a small subset showing weak CD123 (arrows). They were negative for CD25 and CD2. *KIT* D816V mutation was not detected. *KRAS*G12C detected

Mast cell sarcoma (MCS) is an extremely rare and aggressive variant of mastocytosis and typically presents as a unifocal mast cell tumor with high-grade cytology and destructive growth pattern.[1] MCS should be distinguished from systemic mastocytosis (SM).[2] A recent communication by Matsumoto, et al.[3] cited a total of 34 reported cases of MCS and described 10 new cases (median age 54 years), equally affecting men and women, with bone involvement in 90% of the cases; concurrent SM was documented in only one case, whereas mast cell mediator symptoms were reported in 3 patients and elevated serum tryptase in 6; two patients had prior history of germ cell tumors.[3] In the particular study,[3] cell morphology was described as being pleomorphic with large tumor cells expressing CD43, CD117, CD33, CD13, and mast cell tryptase, in all evaluated cases, while expression of CD25, CD2, CD30, and CD68 was variable; of note, none of the patients evaluated expressed *KIT*D816V, although two were reported to harbor other *KIT* mutations. The report from Matsumoto et al.[3] included two Mayo Clinic cases that are highlighted in the current report, which also provides additional diagnostic and treatment details and follow-up information.

A 60-year-old man (Image 1; patient 1) with a history of mediastinal testicular cancer presented in April 2021 with progressive right hip pain. A magnetic resonance imaging (MRI) scan revealed an expansile osseous lesion in the right intertrochanteric region extending to the hip (measuring 3.7 × 3 × 5.8 cm). A subsequent computed tomography (CT) scan of the abdomen and pelvis showed no additional findings. Biopsy of the right femur tumor was consistent with MCS and showed markedly pleomorphic, small to giant cells with bizarre nuclear features, hyperchromasia, multinucleation, and abundant pink cytoplasm (Image 1; patient 1); the tumor cells were positive for tryptase, CD117, CD33, and CD30 (majority of cells) (Image 1; patient 1). A small minority of the tumor cells were weakly positive for CD123 (Image 1). CD2 and CD25 staining were negative. Cytogenetic analysis revealed normal male karyotype. Sanger sequencing method was used, and KIT mutation in exons 8, 9, 10, 11, and 17 was not detected. The amplicon-based next-generation sequencing (NGS) assay was performed which showed *KRAS*G12C mutation (VAF = 60%). In May 2021, bone marrow biopsy did not show evidence of SM and PET scan was negative for any FDG-avid lesions or distant metastasis. In July 2021, the patient was started on adjuvant involved-field radiation therapy of 5000 cGy over 25 fractions. In August 2021, patient was started on midostaurin 100 mg twice-daily, which was continued until January 2022 when it was held because of increased liver function tests. In September 2021, a repeat PET scan was negative but hip x-ray

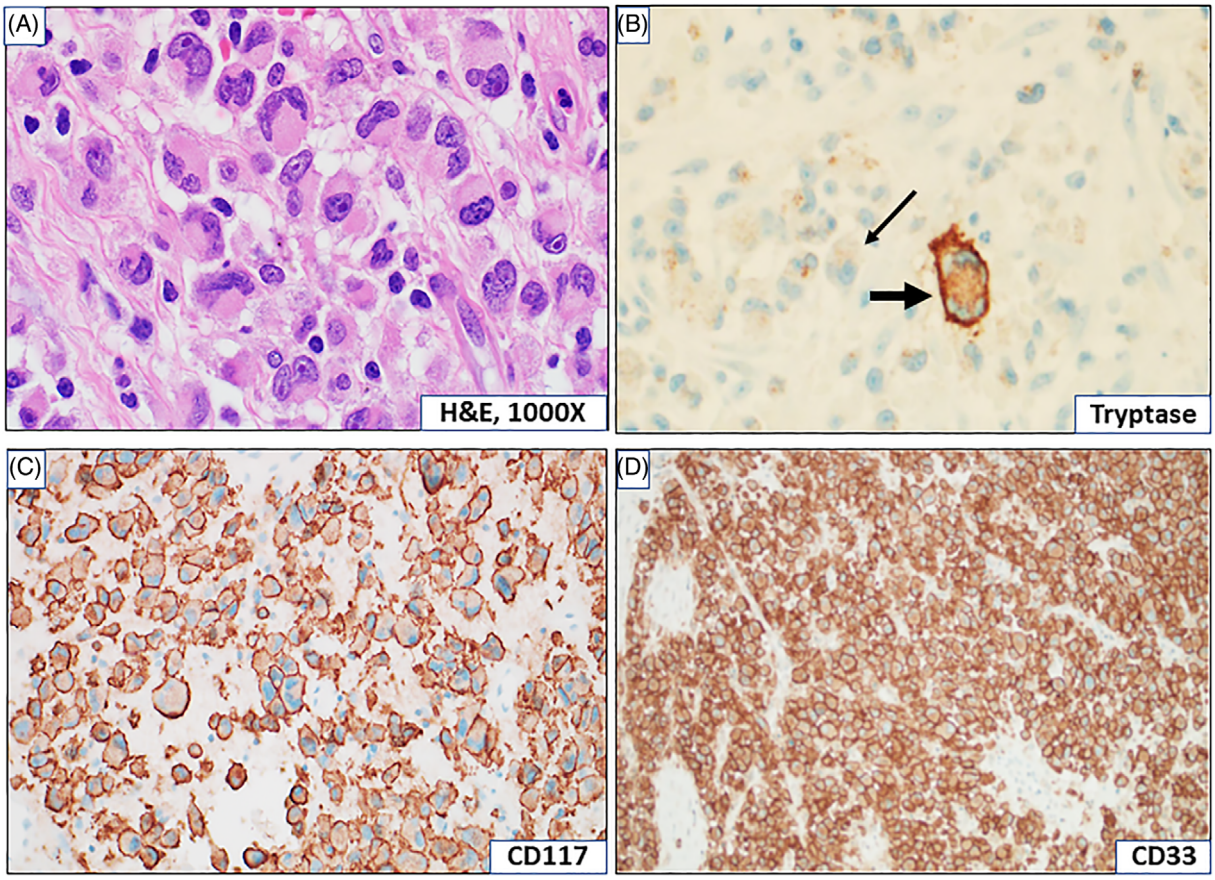

IMAGE 2 A 61-year-old man with mandibular bone mast cell sarcoma. The neoplastic cells are large showing irregular nuclear contours with and occasional single prominent nucleolus and abundant strongly eosinophilic cytoplasm. The tumor cells expressed CD117 and CD33. Tryptase staining was overall weak (thin arrow), but rare strongly positive cells were present (thick arrow). They were negative for CD30, CD123, CD2, and CD25. *KIT* D816V mutation was not detected. *TP53*, *ASXL1*, mutations and *KIT* VUS were detected

showed pathologic fracture and lytic lesion. The patient underwent total resection of the right proximal femur and pathology revealed viable MCS. In January 2022, CT skeletal survey and MRI showed no evidence of MCS recurrence.

A 61-year-old man (Image 2; patient 2) with a remote history of liposarcoma of his lower extremity presented in June 2009 with a one-year history of numbness and loosening of the teeth in the left mandible. Biopsy of the mandibular bone was performed and demonstrated predominantly large size cells with irregular nuclei, an occasional single prominent nucleus and abundant pink cytoplasm on hematoxylin and eosin stain (Image 1) were noted. Immunostains revealed that the majority of tumor cells are strongly positive for tryptase and CD33, weakly positive for tryptase (thin arrow; rare cell strongly tryptase positive Image 1; thick arrow) and negative for CD30, CD123, CD2 and CD25. Qualitative allele-specific polymerase chain reaction (PCR) assay showed negative *KIT* D816V. NGS showed *ASXL1* (VAF = 15%) and *TP53* (VAF = 53%) mutations, as well as a *KIT* variant of uncertain significance (VUS) c.1571_1573del; p.Pro524del (VAF = 32%). Bone marrow biopsy showed no evidence of SM. In October 2009, patient underwent radiation therapy with a total dose of 2500 cGy in 10 fractions to his left mandible. Unfortunately, post treatment, expansion of his mandibular tumor was noticed that led to mandibulectomy in December 2009. Subsequent follow-up information from outside records suggested possible disease progression and treatment implementation with dasatinib followed by nilotinib, until his demise in March 2012.

The observations from the current study and those of Matsumoto, et al.[3] confirm differences in neoplastic mast cell staining pattern and *KIT* mutation expression between MCS (often *KIT* unmutated and variable expression of CD25) and SM (often expressing both *KIT* mutation and CD25). Treatment outcome in MCS, often consisting of surgical resection and involved-field radiation, was poor and might warrant addition of chemotherapy, perhaps in the form of cladribine,[4] midostaurin,[5] or avapritinib.[6]

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

DATA AVAILABILITY STATEMENT

By request.

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