Case 171

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History

50-year-old male who presented with a 2-cm firm, painless soft tissue mass above his left supraorbital ridge. He had no complaints of diarrhea, nausea, vomiting, syncope, or change in appetite. He did not demonstrate any constitutional symptoms. He had no lymphadenopathy or organomegaly. Of note, he also had an eczematous skin rash. Upon admission, he had the following laboratory indices: WBC: 8.7 x 10^9/L; Hemoglobin, 11.7 g/dL; Platelets: 370 x 10^9/L. A peripheral blood cell differential was normal. Lactate dehydrogenase levels were within normal limits. Serum tryptase level was slightly elevated at 12.8 ng/dL (normal: <10 ng/dL).

Radiologic studies revealed a lytic lesion involving the orbital wall, multiple lytic lesions in the left pelvis and scapula, and a pathologic fracture of the left femoral head.

Details

An excisional biopsy of the supraorbital mass was performed. H&E sections from the formalin fixed, paraffin embedded tissue revealed a polymorphic proliferation of atypical mononuclear cells intermixed with abundant eosinophils. The mononuclear cells had an immature/blastic appearance, characterized by scant vacuolated cytoplasm with coarse azurophilic or basophilic granules, increased nuclear to cytoplasmic ratio, fine chromatin and conspicuous nucleoli. These cells were best appreciated on touch imprints and were morphologically classified as basoblasts or mastoblasts.

Biopsy of the left femoral pathologic fracture showed similar findings but the nuclei of the mononuclear cells in the femoral lesion were more ovoid and occasionally bilobed. A random bone marrow core biopsy from the iliac crest showed large areas of fibrosis (>50%) with clusters of mononuclear cells, predominantly perivascular. A differential cell count on the bone marrow was as follows: 2% blasts, 12% myelocytes, 31% metamyelocytes/bands/ neutrophils, 8% eosinophils, 8% basophilic cells, 1% monocytes, 17% lymphocytes, and 21% erythroid normoblasts.

Immunohistochemistry and Flow Cytometry

Immunohistochemical studies performed on sections the orbital mass showed positive staining of the mononuclear cells for CD117, CD25 and CD68 with weak, patchy expression of myeloperoxidase. Approximately 15% of cells were weakly positive for tryptase and CD34. The blasts were non-immunoreactive with lysozyme, TdT, CD20 and CD3.

The mononuclear cells in the femoral pathologic fracture were strongly positive for CD117 and tryptase and predominantly negative for CD34.

The mononuclear cell clusters in the posterior iliac crest bone marrow biopsy were positive for CD117 and predominantly negative for tryptase by immunohistochemistry. Immunophenotypic analysis of the orbital mass by flow cytometry showed an immature population of cells predominantly localized to the basophil region when analyzed by CD45/side scatter. These cells showed aberrant co-expression of CD25; however, expression of CD59, CD63, and CD69 was lower than that typically seen in systemic mast cell disease.

Cytogenetic Findings

Conventional karyotyping on the bone marrow sample revealed a normal male karyotype.

Molecular Findings

Fluorescence in situ hybridization (FISH) for BCR-ABL1 gene rearrangements performed on freshly harvested bone marrow aspirate smears was positive in 30% of cells. BCR-ABL1 fusion signals were also observed in 89% of cells on touch imprints from the orbital mass. BCR-ABL1 fusion signal was demonstrated in CD117+ cells by FISH on the bone marrow core biopsy. Reverse transcription polymerase chain reaction (RT-PCR) for BCR-ABL1 fusion transcripts coding for p190 as well as for p210 and p230 products was negative by both a multiplex real-time PCR and by nested PCR. ICEPlex analysis demonstrated an e6a2 BCR-ABL1 fusion transcript in the orbital mass and PB.

Allele specific oligonucleotide PCR was negative for the KIT D816V mutation. Pyrosequencing was negative for a JAK2 V617F mutation.

Interesting Features/Discussion

This case is an unusual example of an extramedullary presentation of a *BCR-ABL1* positive myeloid neoplasm with increased blasts and mast cell differentiation. Given the clinical presentation, the presence of Philadelphia chromosome and the pattern of involvement in the bone marrow as well as the presence of immature, aberrant mast cells in an extramedullary site, appropriate classification of disease in this case was very challenging. The presence of increased blasts in the supraorbital mass raised the possibility of blast phase. Interestingly, the patient achieved complete remission upon therapy with tyrosine kinase inhibitor, dasatinib.

Proposed Diagnosis

Philadelphia chromosome-positive myeloid neoplasm with increased blasts and associated aggressive systemic mastocytosis vs. myelomastocytic differentiation (myeloid sarcoma) involving an orbital mass

Consensus Diagnosis

Aggressive systemic mastocytosis associated with BCR-ABL1-positive myeloproliferative disorder, involving an orbital mass with 15% blasts