Mast cell leukaemia (MCL) progressed from myelodysplastic syndrome (MDS) after acquiring *KIT* mutation

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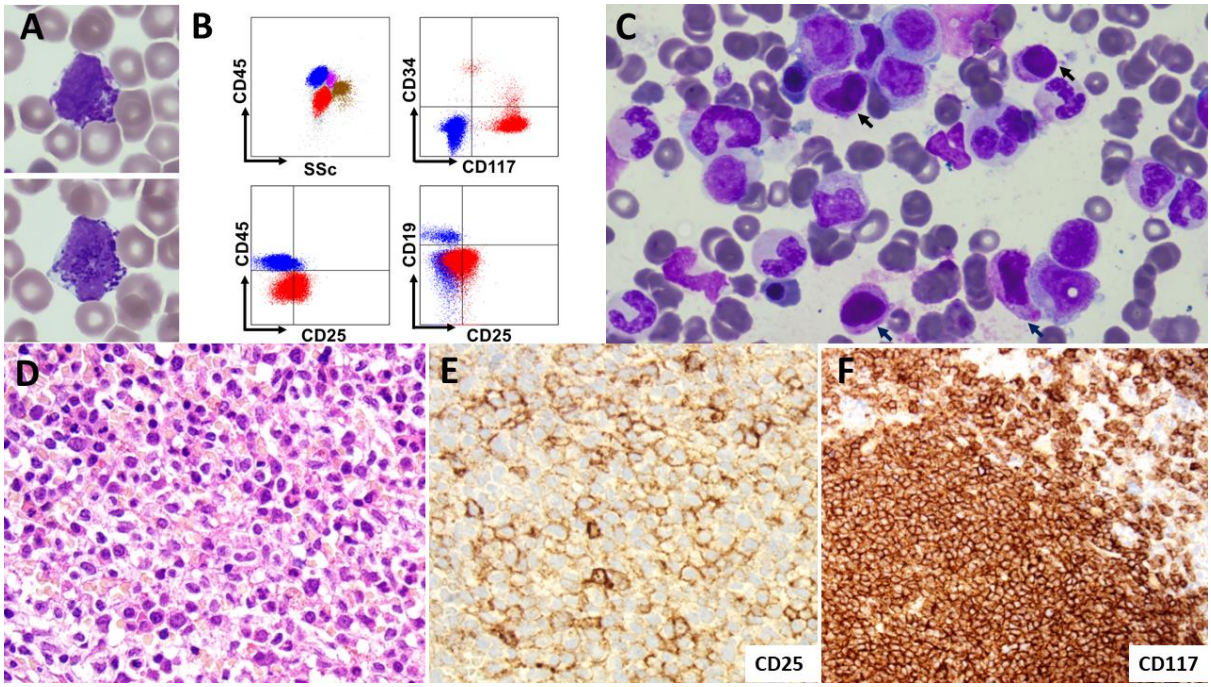

Figure 1, (A) Blood film (May-Grünwald-Giemsa stain ×100 objective); (B) Immunophenotyping; (C) Bone marrow aspirate (May-Grünwald-Giemsa stain ×100 objective); (D) Bone marrow trephine (haematoxylin and eosin stain ×40 objective); (E) Bone marrow trephine immunohistochemistry staining for CD25 (×40 objective); (F) Bone marrow trephine immunohistochemistry staining for CD117 (×40 objective)

A 69-year-old man was diagnosed with MDS with multilineage dysplasia, without any evidence of a mast cell disorder. Myeloid next-generation sequencing (NGS) (Archer Variantplex) identified pathogenic variants in *ASXL1* (variant allele frequency (VAF) 37%), *RUNX1* (VAF 44%), *TET2* (VAF 94%). Target fluorescence in situ hybridization (FISH) and molecular karyotyping (8x60K oligonucleotide arrays, Agilent) showed no abnormalities. He was treated with azacytidine when he progressed to MDS with

excess of blasts (12%). A bone marrow biopsy post cycle 4 of azacytidine showed systemic mastocytosis (SM) and persistent MDS without excess of blasts. The abnormal mast cell infiltrate (3%) showed multifocal aggregates of >15 masts cells. The mast cells express CD117, CD25 with focal expression of CD2. *cKIT* D816V mutation was detected (Plentiplex Real Time PCR assay). One year later, he lost response to azacitydine with worsening cytopenia and high serum tryptase level (>200 ug/L). He received midostaurin. Two months later, circulating immature cells (31%) was identified in blood film (figure 1.A, May-Grünwald-Giemsa stain ×100 objective). By flow cytometry (figure 1.B, red colour population), these immature cells were positive for CD117, CD25 and were in keeping with atypical mast cells. A bone marrow smear showed mast cell leukaemia involving >20% of the cellularity (figure 1.C, May-Grünwald-Giemsa stain ×100 objective, black arrow) in addition to persistent MDS (neutrophils are hypogranulation) with no excess of blasts. NGS again identified mutations in *ASXL1* (VAF 32%), *RUNX1* (VAF 48%), *TET2* (VAF 94%); a new mutation in *KIT* D816V (VAF 8%) was also present; indicating around 16% neoplastic mast cells were present in the specimen available for evaluation. Target FISH showed trisomy 8 and 21 in 20% of cells analysed. Trephine sample (figure 1.D) showed 40% mast cells. The mast cells express CD25, CD117(figure 1.E and 1.F) with focal expression of CD2. The patient received cladribine, but unfortunately passed away with persistent disease and organs failure.

MCL is an aggressive form of SM, characterized by at least 20% of mast cells in a bone marrow smear. The median survival time is less than six months. Most of MCL are aleukemic variant. *SRSF2*, *ASXL1* or *RUNX1* mutations adversely affect response to treatment, are poor prognostic variables [1, 2]. Here we presented a case of secondary MCL progressed from MDS after clonal evolution and acquiring *KIT* mutation.

Reference:

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