Morphologic and immunophenotypic characteristics of the bone marrow in patients with hereditary α-tryptasemia

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Background

Hereditary α-tryptasemia (HaT) is a recently recognized condition characterized by the inheritance of multiple copies of *TPSAB1* gene which encodes for α-tryptase resulting in mast cell (MC) activation symptoms and increased basal serum tryptase (BST) levels. Although this condition may affect up to 5% of the general European population[1], there are only few reports addressing its morphologic features in the bone marrow or other tissues[2,3].

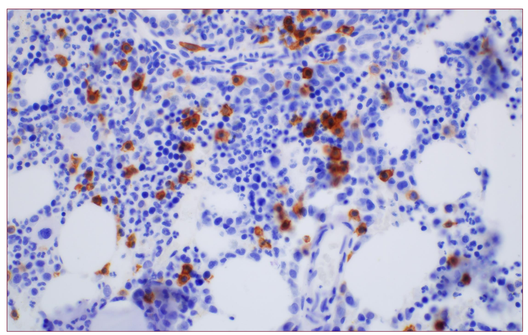
Material and Methods

12 patients with HaT, seen at the UofU Health.
- HaT is confirmed by molecular studies
- excluded patients with concomitant clonal MC disorders: CM or SM (5), CML (1)
- 6 patients were included in this study

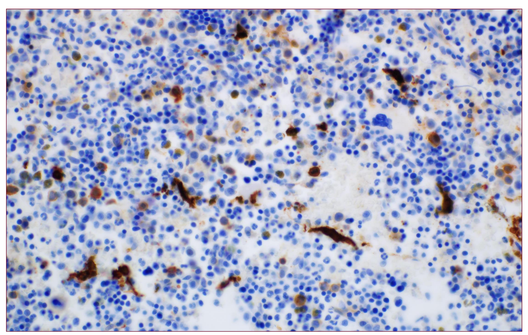
Assessed
- BM aspirate smears and cores
- Flow cytometry including CD117, CD2, CD25, CD30
- Immunohistochemistry: CD117, tryptase, CD25, CD30
- Molecular studies:
  - *KIT* ^{D816V} by PCR
  - *TPSAB1* copy number analysis by ddPCR, myeloid panel by NGS
- Karyotype analysis

Results and Conclusions

Pt	Age/ Gender	BST ng/mL	*KIT*^{D816V}	MCs in aspirate	MCs in core			
					MC # per HPF	Distribution	Spindled vs. round	Immuno phenotype
1	20F	25.5	Neg	not identified	12	Random interstitial	0/100	Normal
2	30M	21.7	Neg	round/oval, well-granulated	1	Random interstitial	10/90	Normal
3	40F	25.5	Neg	round/oval, well-granulated	10	Mostly random interstitial, rare clusters	2/98	Normal
4	50F	22.5	Neg	round/oval, well-granulated	6	Random interstitial	15/85	Normal
5	56F	37.5	Neg	round/oval, well-granulated	20	Random interstitial	5/95	Normal
6	72F	21.7	Neg	round/oval, well-granulated	10	Mostly random interstitial, rare clusters	10/90	Normal



Patient 3, BM core, Tryptase, 20x:
Increased number of MCs, focal clusters



Patient 4, BM core, CD117, 20x:
Increased number of MCs, a subset of spindled-shaped MCs

- In aspirate smears, the MCs were rare (<0.1%), appeared mature, and had normal cytoplasmic granulation;
- In the core, 4/6 individuals had an increased number of MCs (>4-6 MCs per HPF); 2/6 patients showed focal cluster formation (≤15 MCs, loose, not meeting criteria for dense MC aggregates);
- Spindle-shaped MCs were present in 5/6 cores, their fraction did not exceed 15%;
- Paratrabecular or perivascular concentration of the MCs was not appreciated;
- MCs in one case were moderately enlarged in size (x2 in relation to lymphocytes);
- None of the cases showed immunophenotypic aberrancies of the MCs, or the presence of *KIT* D816V mutation by digital PCR

Our cohort demonstrated an increased number of predominantly round/oval and well-granulated MCs, with a low number of spindled MCs, and occasional loose MC clusters (≤15 MCs). We, however, did not appreciate perivascular or paratrabecular MC localization or decreased cytoplasmic granulation.
Our investigation is limited by a small number of participants. Additional studies of the expanded cohort are warranted.

References

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