Youngest reported child with tryptase >20μg/L, found to have hereditary alpha tryptasemia (HAT)

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INTRODUCTION

- Although cutaneous mastocytosis occurs relatively frequently in children, systemic mastocytosis (SM) is exceedingly rare
- Current guidelines recommend bone marrow biopsy in adults with tryptase >20μg/L to rule out SM
- Guidelines are less clear for pediatric patients
- Hereditary alpha tryptasemia (HAT) is a recently described phenotype caused by a duplication or triplication of the alpha-tryptase gene (*TPSAB1*), leading to overproduction of alpha-tryptase
- HAT is reported to affect 6% of the population, with autosomal dominant inheritance
- We report the youngest child reported with tryptase level >20μg/L, who is also the youngest child reported with HAT

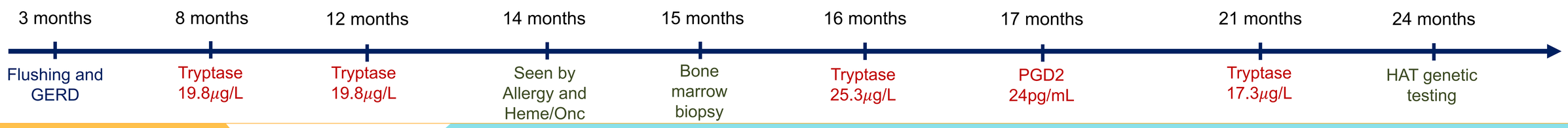
Test	Result	Reference
Tryptase	19.8μg/L (8 mos) 19.8μg/L (12 mos) 25.3μg/L (16 mos) 17.3μg/L (21 mos)	1-11.4μg/L
24-hour urinary prostaglandin D2 (PGD2)	24pg/mL	35-115pg/mL (adult ref.)
Abdominal US	Normal	
Bone marrow biopsy	Immunohistochemical stains for tryptase and CD117 negative; no evidence of mast cell infiltrate or *KIT* mutation	
HAT genetic testing	Duplication of the *TPSAB1* gene	

Table 1. Summary of results

DISCUSSION

- HAT presentation is highly variable – asymptomatic, retention of primary teeth, flushing, joint hypermobility, functional GI disorders, venom reactions
- Unclear whether enzymatically inactive alpha-tryptase plays a direct role in these findings
- Currently no data to suggest these patients have an activated mast cell phenotype
- HAT testing is quick, non-invasive (buccal swab) and inexpensive
- Bone marrow biopsy in children is invasive, requiring general anesthetic, and costly
- Given the rarity of SM in children, in the absence of a convincing history, we propose that HAT testing should be sent before a bone marrow biopsy

CASE DESCRIPTION TIMELINE



CASE DESCRIPTION

- 3-month-old girl with mosaic Turner syndrome presented to her family physician with daily episodes of flushing, with no identifiable trigger, and gastroesophageal reflux (GERD) requiring omeprazole
- Otherwise well, with no features IgE-mediated allergy or SM
- Mother worried about SM, so request serum tryptase
- Serum tryptase sent at 8 months, and elevated at 19.8μg/L (normal 1-11.4μg/L) on two measures, increasing to 25.3μg/L on subsequent measure
- Bone marrow biopsy normal, with negative immunohistochemical staining for tryptase and CD117, and no evidence of mast cell infiltrate or *KIT* mutation
- HAT genetic testing sent (buccal swab through Gene by Gene), which revealed a duplication of the *TPSAB1* gene, consistent with HAT

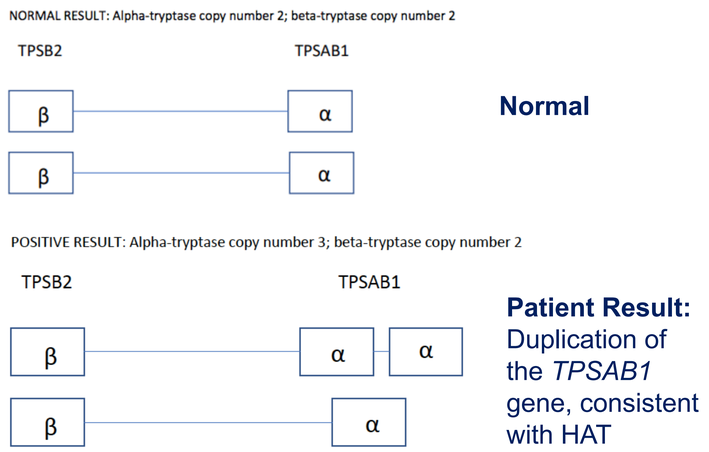


Figure 2. HAT genetic testing results

CONCLUSIONS

In the absence of a convincing history of SM, children with elevated tryptase should first have HAT genetic testing prior to bone marrow biopsy to avoid invasive testing given the rarity of SM in pediatric patients

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