“Inner Allergy” – increased basal serum tryptase levels due to Hereditary Alpha-Tryptasemia and / or KIT D816V mutation may explain mast cell related symptoms

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Background & objectives

Increased basal serum tryptase (BST) levels as well as mast cell related symptoms occur in various mast cell-mediated pathologies, including Indolent Systemic Mastocytosis (ISM). Additionally, the genetic condition Hereditary Alpha-Tryptasemia (HaT) has recently been identified to be the most common cause for elevated BST levels. If symptomatic, individuals exhibit a strong decrease in quality of life while the underlying condition often remains undiscovered. HAT and ISM can be reliably detected using liquid biopsy.

The aim of this work is to characterize the clinical phenotypes of patients with BST levels at the upper limit of normal or above (≥8 ng/ml) who present with mast cell related symptoms to the allergy or oncology department. Gene variants causative for HaT and ISM are analyzed in peripheral blood samples and the genetic makeup is correlated with specific clinical phenotypes including allergies, BST levels and organ involvement. Furthermore, development of cKIT D816V mutation allele frequency in follow up samples of ISM patients will be observed.

Methods

A digital droplet PCR (ddPCR) triplex assay to detect amplification of alpha tryptase encoding TPSAB1 gene (determining HaT) and a ddPCR singleplex assay to detect cKIT D816V mutation (found in >90% of ISM patients) have been established and validated. HaT measurement is performed using genomic DNA (gDNA) from peripheral buffy coat cells. The cKIT D816V mutation is detected in cell free DNA (cfDNA) and gDNA from peripheral blood and from bone marrow. A questionnaire to record clinical characteristics has been designed.

Results

Symptom profiles of approximately 250 patients are currently investigated and differences between clinical phenotypes in HaT and ISM patients are identified. Overall, the percentage of HaT positive individuals is high (58%) in the patients presenting to the allergy department studied to date (n=62).

Conclusion

Characterizing clinical phenotypes associated with HaT and ISM will help to identify the underlying condition in patients presenting with hitherto unexplained symptoms in the future. The combined blood testing for HaT and ISM will help to establish the diagnosis. With established diagnosis, many patients experience mental relief by assigning their complaints to a cause. Additionally, suitable treatment strategies can be initiated.