



ORAL PRESENTATION

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A novel mutation in the *PSTPIP1* gene is associated with an autoinflammatory disease distinct from classical PAPA syndrome

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Background

Hyperzincemia and hypercalprotectinemia, a rare condition within the spectrum of autoinflammatory diseases, is associated with recurrent infections, hepatosplenomegaly, arthritis, anemia, cutaneous inflammation, and failure to thrive. So far, no genetic cause has been identified in these patients. While the clinical appearance is heterogeneous, all affected individuals present with extremely elevated S100A8/S100A9 (calprotectin) serum concentrations (0.9-12.0 g/l (normal range < 0.001 g/l)).

Aim

The clinical phenotype of 8 patients was characterized. Screening of candidate genes *PSTPIP1* and *MEFV* was performed in 7 hyperzincemia and hypercalprotectinemia patients to identify disease-causing mutations.

Methods

Serum concentrations of S100A8/S100A9 were analyzed by an ELISA assay in 8 patients with hyperzincemia and hypercalprotectinemia and compared to PAPA patients with and without treatment. Candidate exons were amplified by PCR and sequenced on an ABI 3130 Genetic Analyzer.

Results

Seven of the eight patients were heterozygous carriers of a glutamic acid 250 (GAG)→lysine (AAG)/p.Glu250Lys/E250K substitution in exon 11 of the *PSTPIP1* gene. S100A8/S100A9 concentrations were extremely elevated

in these patients (0.9-12 g/l) compared to seven patients presenting with classical PAPA symptoms (0.02-0.35 g/l), whose levels again were significantly higher compared to normal controls.

Conclusion

The *PSTPIP1* E250K mutation causes an autoinflammatory disorder known as hyperzincemia and hypercalprotectinemia. The disease causes a heterogeneous spectrum of symptoms that only partially overlaps with the presentation of the classical PAPA syndrome. Elevated S100A8/A9 levels are a common hallmark and biomarker of disorders caused by mutations in the *PSTPIP1* gene.

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