The ever expanding clinical and genetic findings of DADA2

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Introduction:

ADA2 is an extracellular enzyme with a not entire known physiologic function but seems to promote monocytes and macrophage differentiation and also acts as a growth factor for endothelial and hematopoietic cells. The deficiency of ADA2 (DADA2, #615688) initially reported to be associated to monogenic forms of polyarteritis nodosa has also beem recently associated to ALPS-like phenotype and many other atypical or unusual clinical signs. Genetically, puntutal mutations and structural changes in ADA2 gene has been also associated to DADA2 disorder. The objective of this work is to describe a nove phenotype and genotype associated to DADA2.

Methods:

Prospective study of patients followed at a tertiary center. The study was carried out at the immunoderegulation clinic of the Clinical Immunology and Allergy Service of the Hospital das Clínicas, Faculdade de Medicina da USP.

Results:

Clinical, laboratorial and genetic data of two unrelated cases were retrospectively analyzed. **Patient 1:** A 14 years old boy, born and raised in the state of São Paulo that presented at the age of 3 years with a non-hodgkin lymphoma treated with clasical protocols of QT and RT. After that, recurrente episodes of systemic inflammatory sterile fever, associated to severe abdominal pain initiated. At the age of 12 a severe necrotic mouth ulcer ocurred leading to the loss of all teeth. **Patient 2:** A 2 years old girl, born and raised in the state of Minas Gerais with recurrent fever since the 6 months of live always associated to non-specific rash. At the age of 1,5 years, due to the persistence of the fever and the presence of large hepato and splenomegaly she was admittted to the hospital for investigation. Persistent and very high levels of acute reactant markers was found and all possible causes for the fever were rule-out. A sudden loss of conscience occured and a hemorragic stroke was diagnosed. **Genetic Sequencing:** Both patients presented with homozygous mutations in ADA2 gene (P1 already reported; P2 a novel mutation). **ADA2 measurement levels**: Low levels of ADA2 in P2 was found by western blot.

Conclusion:

The clinical presentation in patients with DADA2 has many faces. The highly variable clinical presentation renders early diagnosis difficult. Given the important morbidity and mortality, a high index of suspicion is needed for early diagnosis and intervention.

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Keywords:

DADA2, deficiency, phenotype, genotype