



POSTER PRESENTATION

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PreS-FINAL-2200: Phenotype of V198M and Q703K NLRP3 variants

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Introduction

The term CAPS (Cryopyrin-Associated Periodic Syndromes) identifies a spectrum of autoinflammatory diseases caused by heterozygous mutations of the CIAS1/NLRP3. Affected individuals may present three different phenotypes: Familial Cold Autoinflammatory Syndrome (FCAS), Muckle-Wells Syndrome (MWS) and CINCA syndrome, the most severe form of the clinical spectrum. Clinical manifestations include urticaria-like rash, recurrent fever, arthralgia, conjunctivitis; chronic aseptic meningitis, cerebral atrophy and bone malformations in the severe cases.

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Objectives

To describe the long-term clinical course of a cohort of patients carrying two different low-penetrance NLRP3 mutations (V198M and Q703K).

Methods

Six patients were identified carrying the NLRP3 V198M mutation (mean age $10,35 \pm 4,73$ years, 4 males and 2 females), and 5 patients were identified carrying the NLRP3 Q703K (mean age $9,72 \pm 4,55$ years, 3 males and 2 females). All were Caucasians.

Results

In the V198M cohort the mean age at disease onset was $5,85 \pm 4,08$ years. All patients had symptoms consistent with recurrent inflammatory syndrome: 6/6 presented recurrent episodes of skin lesions and arthralgia, 4/6 of fever attacks, 3/6 of arthritis, 2/6 of headache and subcutaneous edema. One patient showed fatigue, conjunctivitis and recurrent abdominal pain. Half of the patients had a positive family history for recurrent inflammatory episodes. In 3 out of 6 patients the severity of phenotype and the persistence of elevated acute phase reactants, led to initiation of anti IL-1 therapy with immediate benefit. In the cohort of patients with Q703K variant the mean age at disease onset was $3,73 \pm 3,33$ years. All patients had skin rash, 4/5 patients presented recurrent fever, 3/5 arthralgia and myalgia, 2/5 subcutaneous edema, pharyngitis and lymphadenitis; 1 out of 5 patients had mild arthritis, headache and abdominal pain. Only in 1 case, symptoms were triggered or worsened by cold exposure. None of our patients had a family history relevant for autoinflammatory symptoms. Laboratory test showed no increase in acute phase reactants, with one exception. This patient presented also with recurrent fevers, treatment resistant epilepsy and carries a heterozygous MEFV mutation. She failed colchicine and anti IL-1 therapy was started with benefit.

Conclusion

The pathogenic significance of these NLRP3 mutations is still discussed. In our experience patients carrying Q703K mutation appear to have a milder and self-limited phenotype than those with V198M variant in which therapy with IL-1 inhibitor drugs is often necessary. The factors that affect the pathogenic consequences of these variants are still to be established.

Disclosure of interest

None declared.

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