

ORAL PRESENTATION

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# Mevalonate kinase deficiency: an early onset inflammatory bowel disease?

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From 8th International Congress of Familial Mediterranean Fever and Systemic Autoinflammatory Diseases Dresden, Germany. 30 September - 3 October 2015

## Introduction

Mevalonate kinase deficiency (MKD) is a rare autoinflammatory, autosomal-recessive defect on MVK gene. Clinical spectrum ranges from recurring febrile attacks to malformations and neurologic disorders. Gastrointestinal symptoms are cardinal. Severe gastrointestinal involvement has been described at the onset.

## Objective

To analyse severe gastrointestinal events (SGE) complicating MKD.

## Patients and methods

Retrospective observational French cohort of MKD patients. SGE were defined as complicated inflammatory involvement, requiring an abdominal surgery and/or enteral/parenteral nutrition. Data were collected from clinical charts provided by the members of the Franco-phone Society for Paediatric Rheumatism and Inflammatory Diseases (SOFREMIP).

## Results

From a 53-patient cohort, nine presented a SGE (17%). From these, disease onset median age was 1.0 months (0-12); one patient deceased (22 months) from a non-gastrointestinal event. Compound heterozygote mutations were found in 7/8, being Val377Ile the commonest (6/8). The main symptoms during febrile attacks were: diarrhoea (100%, 7/7), lymphadenopathy (89.9%, 8/9), skin lesions, joint pain (85.7%, 6/7 each), aphtous ulcers, abdominal pain (83.3%, 5/6 each), splenomegaly (66.7%, 6/9), hepatomegaly (62.5%, 5/8) and vomiting (57.1%, 4/7). Median mevalonic aciduria: 23.05 mmol/mol of creatinine

(P<sub>25</sub>=13.7; P<sub>75</sub>=55.5); median MK activity: 2.2% (P<sub>25</sub>=1.0; P<sub>75</sub>=24.0). The significant co-morbidities found in SGE patients in comparison with the global cohort were: failure-to-thrive in 85.7% (6/7), pulmonary diseases in 37.5% (3/8) and feeding disorders in 28.6% (2/7) (p<0.05).

Severe gastrointestinal involvement was the first event in 6% (3/50), representing 43% (3/7) of patients with severe gastrointestinal disease: abdominal adhesions (66.6%, 6/9) and colitis/enterocolitis (4/9, 44.4%) were mainly found. 87.5% (7/8) needed surgery and 44.4% (4/9) required enteral/parenteral nutrition. Despite digestive resection, disease progression remained; two patients needed re-intervention due to surgical complications. Aphtous/ulcerative damage was the main endoscopic feature (4/9, 44.4%). The most consistent microscopic finding was lymphocytic infiltrates. IL-1 antagonists were the most used/effective treatment (4/9), resulting in complete remission in all three patients with data available.

## Conclusion

MKD severe gastrointestinal involvement presentation has a non-negligible frequency. It usually appears as an aphtous/ulcerative disease involving any part of the digestive tract or as abdominal adhesions, frequently requiring surgery. The treatment with IL-1 antagonists resulted in complete remission in a majority of treated patients. Thus, MKD should be added to the list of monogenic early-onset inflammatory bowel disease.

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Published: 28 September 2015

doi:10.1186/1546-0096-13-S1-O56

**Cite this article as:** Martins et al.: Mevalonate kinase deficiency: an early onset inflammatory bowel disease? *Pediatric Rheumatology* 2015 13(Suppl 1):O56.

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