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Mevalonate kinase deficiency: an early onset inflammatory bowel disease?

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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 Francophone 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_{25}=13.7; P_{75}=55.5); median MK activity: 2.2% (P_{25}=1.0; P_{75}=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 with 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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