HYPERIMMUNOGLOBULIN D SYNDROME WITH SECONDARY AMYLOIDOSIS

Gustavo Roberto Lourenço^{1,*}, Rita de Cássia Menin¹, Iane Tamara Dondé¹, Patrícia Milani de Moraes¹, Carlos Augusto Rodrigues Padilha¹, Juliana de Jesus Boscolo¹, Renata Vaz de Oliveira¹, Danielly Dantas Pimentel¹, Maria Juliana da Silva Almeida¹

1.Faculdade de Medicina de São José do Rio Preto, São José do Rio Preto (SP), Brazil.

*Corresponding author: grlourenco@icloud.com

BACKGROUND

Hyperimmunoglobulin D syndrome is a rare, autosomal-recessive genetic disorder, due to compound heterozygous or homozygous mutation in the mevalonate kinase (MVK) gene. Clinically characterized by recurrent febrile episodes typically associated with lymphadenopathy, abdominal pain, elevated serum polyclonal immunoglobulin D (IgD) level and, rarely, with secondary amyloidosis.

CASE REPORT

A 21-year-old man evaluated in January 2015 with recurrent high fever (39 °C) since he was 3 months old, associated with cervical and inguinal adenomegaly, and arthritis of the right foot and ankle. On physical examination, he presents ataxic gait, without other alterations. Mutations in the MVK gene were confirmed (C.803-T>C and C.77A>C) and treatment was started with methotrexate 15 mg weekly and then associated etanercept due to treatment failure after 3 months. In March 2016, the patient evolved with recurrence of fever and adenomegaly, so we change the treatment to canakinumab 150 mg subcutaneous each 8 weeks, evolving with reduction of inflammatory markers and resolution of the fever and adenomegaly. In 2021, he developed a new episode of fever and adenomegaly. Laboratory tests: amyloid A protein 841 mg/dL. Abdominal ultrasonography: splenomegaly. Subcutaneous biopsy: search for amyloidosis by positive Congo red staining. We optimized the dose of canakinumab to 300 mg monthly and the patient remains under clinical follow-up.

CONCLUSION

Hyperimmunoglobulin D syndrome is a genetic disease with autosomal mutation in the mevalonate kinase gene located in the long arm of chromosome 12, an essential enzyme in the functioning of the cholesterol and isoprenoid synthesis pathways. There may be a significant reduction or complete absence of their MK activity, a condition known as mevalonic aciduria. Clinical manifestations consist of fever, usually with chills, adenomegaly (mainly cervical chain, bilateral and painful), skin rash, abdominal pain, vomiting, diarrhea, arthralgia/arthritis, headache, hepatomegaly, splenomegaly, oral ulcers, and serositis. The diagnosis is defined by searching for the MVK mutation. IgD levels are usually elevated (≥ 100 U/mL). During febrile crises, leukocytosis and increased inflammatory markers are common. Amyloidosis is a rare but serious long-term complication, manifesting with skin bruising, enlarged muscles, heart failure, hepatomegaly and nephrotic syndrome. Diagnosed by elevated serum levels of amyloid AA and biopsy of subcutaneous fat positive to Congo red dye. Treatment consists of using Anti-TNF or Anti-IL1, which is effective to control disease activity.

KEYWORDS

Amyloidosis, Secondary amyloidosis, Hyperimmunoglobulin D syndrome.