Case Report

CARDIAC INVOLVEMENT IN A PATIENT WITH MEVALONIC ACIDURIA

INTERESSAMENTO CARDIACO IN UN PAZIENTE CON MEVALONICO ACIDURIA

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Abstract. In this report we describe cardiac involvement in a patient whit Mevalonic aciduria (MVA).
Diagnosis was performed when she was six months by detection of large amount of mevalonic acid in urine. Left ventricular hypertrophy with reduction of ejection fraction was detected when she was one years old.

KEYWORDS
Mevalonate kinase deficiency, mevalonic aciduria, heart failure.

Abstract. In questo report descriviamo un caso di Mevalonico aciduria con interessamento cardiaco.
La diagnosi fu posta quando la paziente aveva sei mesi d'età tramite il dosaggio degli acidi organici urinari che misero in evidenza elevata escrezione di acido mevalonico. All'età di un anno fu riscontrata ipertrofia del ventricolo sinistro con riduzione della frazione di eiezione.

PAROLE CHIAVE
Deficit di mevalonato chinasi, mevalonico aciduria, scompenso cardiaco.

Introduction

Mevalonic aciduria (MVA) is a rare inflammatory disease due to Mevalonate Kinase Deficiency (MKD). At least 30 patients with MVA have been reported worldwide (1).
Action of Mevalonate Kinase (MK) is phosphorylation of Mevalonic Acid to form Mevalonic acid-5-Phosphate, which cholesterol, ubiquinone and other products generate from. Clinical features of enzyme deficiency ranging from periodic fever and hyper IgD, which clinical picture consists of recurrent fever, abdominal pain, vomiting, diarrhoea, cervical lymphadenopathy to most severe MVA.
Most of the MVA affected patients shows same picture as above, but they presented also severe failure to thrive, psychomotor retardation, ataxia, cerebellar atrophy, hepatosplenomegaly, cholestatic liver disease, dysmorphic features (triangular face, down-slanted eyes, dolichocephaly) and during recurrent febrile crises with vomiting, or diarrhoea, increase of hepatosplenomegaly, anaemia, lymphadenopathy, artralgia, skin rashes. Some patients had cataracts. At least has been described only one patient affected by bowel obstruction (2). The pathogenesis of inflammation is unknown, but urinary excrection of Leukotriene E4 was found to be highly increased (3, 4).

Case Report

The patients was the full-term product of a normal pregnancy. She was born from healthy unrelated parents came from the same small village in Western Sicily and she had three healthy siblings. Familiar history was negative for metabolic and cardiovascular diseases.
Diagnosis of Cow Milk Protein Intolerance was performed at the earlier age of life and she received hydrolized milk formula feeding because of recurrent crises of diarrhoea. Moreover clinical signs (anaemia, lymphoadenopathy and leucocytosis) were suspected for myelodysplastic syndromes and she had several admission before MVA diagnosis was made.
The diagnosis was performed by urinary organic acid analysis which revealed a considerably large peak of mevalonic acid when the patient was a six months child. The relevant clinical features were hepatosplenomegaly, jaundice, facial dysmorphism, postnatal failure to thrive, hypotonia, and recurrent characteristic crises

with fever, diarrhoea and lymphoadenopathy. She did not have systemic metabolic acidosis or elevated creatine kinase levels in blood. Mostly her levels of cholesterol was normal or just slightly low in serum and steroid profiles was normal. Later febrile crises were accompanied by polyarthritis involved knees and right wrist.

Six months after diagnosis she had one crisis characterized by diarrhoea, abdominal pain, polyarthritis and cervical lymphadenopathy and she was treated with Intravenous (I.V.) prednisone. During the crisis she experienced tachycardia and slight hypertension, ECG revealed changes of QRS suspected for left ventricular hypertrophy; echocardiography confirmed left ventricular hypertrophy with reduction of ejection fraction (about at 70%), but no antihypertensive drug therapy was performed because the patient was hemodynamically stable.

Echocardiography performed every six months did not showed worsening hearth failure for two years in which she experienced most febrile crises became more and more severe with occurrence of lymphadenopathy, transient morbilliphorm skin rashes and worsening of arthritis, that needed I.V. prednisone therapy.

The patient showed great mental retardation, poor muscle development and motor delay became more evident during her growing up: she was unable to sit without support, she never become able to walk and her speech was poor for age.

Since three years of age her cardiac involvement worsened, with increased hypertension and reduction of ejection fraction detected by echocardiography, digoxin and diuretic therapy was performed with no improvement of cardiac performance. Digoxin therapy was stopped after an episode of acute severe bradycardia that led her to death when she was four years old for heart and pulmonary failure.

Discussion

Wide diversity of clinical manifestation of MKD can lead to a delay or a lack in the diagnosis, as occurred at this patient which had several admissions in oncohematology division until she was six months old when MVA was diagnosed.

Recurrent characteristic crisis of fever, accompanied with diarrhoea and lymphoadenopathy can be confused with infectious diseases or gastrointestinal diseases, and its haematological and inflammatory signs (i.e. arthralgias and arthritis) can led to diagnosis of hematological diseases and juvenile rheumatoid. Most of patients reported so far, presents mental retardation and ataxia as a result of cerebellar atrophy became constant findings after infancy. In addition, stunted growth seems to develop in childhood. Cataract and optic atrophy may be accompanying symptoms of retinal dystrophy.

Even though MVA is variable in its clinical features, has been described only one patient with bowel obstruction as major symptom of MVK. This is the second case of cardiac involvement in a patient affected by MVA.

References

1. Haas D, Hoffmann GF. Mevalonate kinase deficienciencies: from mevalonic aciduria to hyperimmunoglobulinemia D Syndrome. Orphanet J Rare Dis. 2006;1:13.

2. Nimubona L, Laloum D, Rolland MO, Read MH, Guillos B, Duhamel JF. An intestinal obstruction in an eight month old child suffering from mevalonic aciduria. Acta Paediatr. 2002; 91 (6):714-6.

3. Frenkel J, Willemsen MAAP, Weemaes CMR, Doland L, Mayatepek E: Increased urinary leukotriene E4 during Febrile attacks in the Hyperimmunoglobulinaemia D and periodic fever Syndrome; Arch Dis Child 2001; 85:158-159.

4. Mayatepek E, Hoffmann GF, Bremer HJ: Enanched urinary excretion of LTE4 in patients with mevalonate kinase deficiency. J Pediatr. 1993;123:96-98.