PEDIATRIC RHEUMATOLOGY

POSTER PRESENTATION Open Access

Clinical and genetic features of Spanish patients with Mevalonate kinase deficiency

E Ruiz-Ortiz[1*], E Gonzalez-Roca[1], A Mensa-Vilaro[1], J Rius[1], S Plaza[1], C Anton[1], I Calvo[2], C Modesto[3], J Anton[4], C Arnal[3], C Alvarez[5], J Alvarez-Coca[6], E Becerra[7], N Bilbao[4], M Camacho[8], J Crespo[5], C de Diego[9], LF Diez-Garcia[10], L Espinosa[11], D Garcia-Escriva[12], F de Gracia[13], MI Gonzalez[2], E Iglesias[4], S Izquierdo[14], B Lastra[15], P Llobet[16], B Lopez[2], V Lopez-Gonzalez[17], R Martinez[18], MA Martin-Mateos[4], R Merino[11], L Ortega[19], ME Peiro[5], I Perez de Soto[8], C Perez-Mendez[20], V Rodriguez-Valverde[5], A Ribes[1], A Ruiz[21], B Sanchez[8], JL Santos[19], B Sevilla[22], J Sotoca[23], J Vilas[24], A Villoria[25], J Yagüe[1], JI Arostegui[1]

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 recessively-inherited autoinflammatory condition caused by *loss-of-functionMVK* mutations. This gene encodes for the enzyme mevalonate kinase (MVK), which catalyzes a crucial step of the biosynthetic pathway of cholesterol and isoprenoids. The partial deficiency of enzymatic activity causes the Hyper-IgD and periodic fever syndrome (HIDS), whereas it complete deficiency provokes the Mevalonic Aciduria (MA).

Objectives

The aim of this study was to describe the clinical and genetic features of Spanish patients with MKD diagnosed during the past 15 years.

Methods

The patients' data as well as the outcome of the administered treatments were collected from charts reviews. *MVK* analysis was performed by Sanger-based sequencing.

Results

Forty-one patients from different Spanish hospitals were included. Thirty-eight patients (92.7%) suffered from HIDS and three patients (7.3%) from MA. The MKD diagnosis was established in all of them by the detection of biallelic *MVK* mutations. Eighteen different *MVK* mutations were detected, with the p.[(V377I)] and p.[(I268T)] mutations as the most prevalent, accounting for 54.9% and 26.8% of mutated alleles, respectively. The majority of these mutations (96.4%) were missense mutations. The remainder mutations included premature stop (1.2%), frameshift (1.2%), and splice site mutations (1.2%). In the group of patients with HIDS (n: 38), twelve patients (31.6%) carried homozygous genotypes and twenty-six patients (68.4%) compound heterozygous genotypes. In the group of HIDS patients with homozygous genotypes (n= 12), ten patients (83.3%) carried the p.[(V377I)];[(V377I)] genotype. By contrast, in the group of patients with MA only one patient (33.3%) carried a homozygous genotype (the p.[(I268T)];[(I268T)]).

From a clinical point of view, the median age at the disease onset was 6 months (range 0-408), and the median duration of flares was 4.8 days (range 2-17.5). Mandatory vaccinations were identified as triggering factors for acute episodes in eleven patients (26.8%). The most prevalent manifestations during inflammatory episodes were fever (80.5%), lymphadenopathies (70.7%), abdominal pain (63.4%), diarrhea (58.5%), aphthous ulcers (53.7%) and arthralgia (51.2%). AA amyloidosis was only detected in one patient (2.4%), but had a severe course.

Conclusion

We herein provide a detailed description of the clinical and genetic features of a Spanish cohort of MKD patients carrying biallelic *MVK* mutations. Most of patients suffered from the mild MKD phenotype, the HIDS syndrome. Two prevalent *MVK* mutations, p.[(V377I)] and p.[(I268T)], were found in our cohort, and fever and lymphadenopathies were the most common features in enrolled patients.

[1]Hospital Clinic, Barcelona, Spain
Full list of author information is available at the end of the article

BioMed Central

© 2015 Ruiz-Ortiz et al. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/4.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. The Creative Commons Public Domain Dedication waiver (http://creativecommons.org/publicdomain/zero/1.0/) applies to the data made available in this article, unless otherwise stated.

Authors' details
[1]Hospital Clinic, Barcelona, Spain. [2]Hospital La Fe, Valencia, Spain. [3]Hospital Vall Hebron, Barcelona, Spain. [4]Hospital Sant Joan De Deu, Barcelona, Spain. [5]Hospital Marques De Valdecilla, Santander, Spain. [6]Hospital Del Niño Jesus, Madrid, Spain. [7]Hospital Universitario De Torrevieja, Alicante, Spain. [8]Hospital Virgen Del Rocío, Sevilla, Spain. [9]Hospital Virgen De La Salud, Toledo, Spain. [10]Complejo Hospitalario Torrecárdenas, Almeria, Spain. [11]Hospital La Paz, Madrid, Spain. [12]Hospital General De Valencia, Valencia, Spain. [13]Hospital Virgen De La Luz, Cuenca, Spain. [14]Hospital Miguel Servet, Zaragoza, Spain. [15]Hospital Central De Asturias, Oviedo, Spain. [16]Hospital De Granollers, Barcelona, Spain. [17]Hospital Universitario Virgen De La Arrixaca, Murcia, Spain. [18]Complexo Hospitalario Universitario De Ourense, Ourense, Spain. [19]Hospital Universitario Virgen De Las Nieves, Granada, Spain. [20]Hospital De Cabueñes, Gijon, Spain. [21]Hospital Son Espases, Mallorca, Spain. [22]Hospital San Cecilio, Granada, Spain. [23]Complejo Hospitalario Universitario De Albacete, Albacete, Spain. [24]Hospital De Pontevedra, Pontevedra, Spain. [25]Corporació Parc Taulí, Barcelona, Spain.

Published: 28 September 2015

doi:10.1186/1546-0096-13-S1-P36
Cite this article as: Ruiz-Ortiz *et al.*: Clinical and genetic features of Spanish patients with Mevalonate kinase deficiency. *Pediatric Rheumatology* 2015 **13**(Suppl 1):P36.

Submit your next manuscript to BioMed Central and take full advantage of:

- Convenient online submission
- Thorough peer review
- No space constraints or color figure charges
- Immediate publication on acceptance
- Inclusion in PubMed, CAS, Scopus and Google Scholar
- Research which is freely available for redistribution

Submit your manuscript at
www.biomedcentral.com/submit

BioMed Central