CONFLICTS OF INTEREST

Dr Roberto Barriales-Villa, Diego García-Giustiniani, and Martin Ortiz-Genga belong to the steering committee of Healthincode. Dr Lorenzo Monserrat is managing director of Healthincode.

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Usefulness of Genetic Diagnosis in a Woman With Hypertrophic Cardiomyopathy and the Desire for Motherhood: Information Is Key. Response

Utilidad del diagnóstico genético en la miocardiopatía hipertrófica de una mujer que desea ser madre: la información es clave. Respuesta

To the Editor,

We appreciate the comments by Barriales-Villa et al on our "Scientific letter".[1] We agree that the interpretation of genetic studies is often complex and should be performed in national referral centers for familial heart disease, like ours. We would like to clarify that the study of causality of a genetic variant is based on the following points[2]: frequency of the variant in the population, conservation of amino acids in the species, predictive computer analyses, information on the variant within the family, and functional analysis.

A consultation of the public database with the most number of subjects (Exome Variant Server) shows that the G5R variant is only present in 7 out of 8311 individuals (0.08%). In addition, this variant affects a highly conserved amino acid in the species, specifically, the C0 domain, which is one of the sites of interaction with myosin regulatory light-chain kinase. This domain has been shown to be able to produce mild chemical alterations.[3] Moreover, the patient's father, who was a carrier of the G5R variant, has a hypertrophic cardiomyopathy phenotype, and the index case, with 2 variants, has a very severe phenotype. A more extensive cosegregation study within the family of the father was not possible given the poor relationship between the family members. Nevertheless, we believe that the data provided support the interpretation of the G5R variant as more than a simple polymorphism.

Finally, it is important to highlight that genetic counseling should be very restrictive.[4] In the case of doubt and in this particular clinical context, a variant should be considered pathogenic, as the patient will be undergoing an in vitro fertilization procedure with embryo selection. It would not be ethical to expose the patient to risk if there was a chance of developing fetal hypertrophic cardiomyopathy.

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