
03 – Natural History

An Unusual Presentation of Gaucher Disease: Aortal Valve Fibrosis in a Patient Homozygous for a Rare G377S Mutation

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Introduction

Gaucher disease (GD) has variable clinical presentations, but cardiac involvement is generally an uncommon manifestation of the disease. Valvular calcifications, constrictive pericarditis and infiltration of ventricular myocardium have been reported so far. In the past 25 years, the underlying genetic disorder in GD has been well characterized, with almost 300 mutations identified in the glucocerebrosidase gene (GBA). Nevertheless, clear genotype-phenotype correlations have been confirmed only for the most frequent mutations.

Case report

We present a female patient, who was known to have aortic valve pathology from the age of 30, when she first presented with exertional dyspnea. Despite medical follow up, at the age of 60 she presented with heart failure (NYHA III). At that time echocardiography showed severe, fibrosed aortic valve stenosis with a mean AV gradient of 70 mmHg and concentric left ventricular hypertrophy. Valvuloplasty was planned when thrombocytopenia, previously considered to be autoimmune, became severe. Severe anaemia and mild leucopenia were also noted. Mild splenomegaly and severe bone marrow infiltration were found on MRI. Bone marrow aspiration revealed typical Gaucher cells and the enzyme activity assay confirmed the diagnosis of GD. DNA investigation showed that the patient is homozygous for the G377S mutation. Enzyme replacement therapy was promptly initiated.

Discussion

To our knowledge, of all mutations identified so far, only homozygosity for the D409H mutation has been associated with cardiovascular valvular disease in a patient with a rare type 3c GD. G377S, found in our patient, is a rare mutation, described before as a "dosage effect" allele, where homozygosity for the mutation appeared to result in type 1 while compound heterozygosity with a null allele led to the type 3 phenotype. This mutation has generally been reported as a "mild" mutation, because of the finding that homozygous patients were essentially asymptomatic or had mild disease. Our patient, also homozygous for the G377S mutation, had a severe form of type 1 GD, with rare cardiac valve involvement, which is a previously unreported clinical presentation for this mutation. This case further proves that patients with the same genotype can have different phenotypes, emphasizing the influence of other genetic and/or environmental factors.