

IgG4-related Disease in Monozygotic Twins

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Background:

IgG4-related disease (IgG4-RD) is a recently recognized chronic fibro-inflammatory disorder occurring more frequently in males over 50 years. Pathophysiology is largely unknown but genetic studies in Japanese patients with pancreatic, salivary and lachrymal involvements have shown some associations with haplotypes, genes, or gene polymorphisms. However, familial aggregation has not been reported.

Methods:

Case report of IgG4-RD in monozygotic twins.

Results:

First patient is a 62 years old Caucasian man who presented with enlargement of the pancreas, serum IgG4 level increase (2.5 g/L) and lymphoplasmocytic infiltrates with fibrosis in pancreatic needle biopsy. The patient also presented sclerosing cholangitis and bilateral renal hypodense lesions on CT scan.

Second patient is the twin brother of the first patient. We consider them to be monozygotic twins because birth records described a single placenta, and the twins resemble each other physically. The second patient had abdominal pain, jaundice and weight loss at 63 years. CT and MRI showed a mass in the hepatic hilum, surgically removed. Pathological analysis showed polyclonal lymphoplasmocytic infiltrates, periductal fibrosis, and obliterative phlebitis. Immunohistochemistry showed 100 IgG4⁺ plasmocytes/high power field with an IgG4/IgG ratio of 80%. Serum IgG4 level was increased (3.85 g/L), HLA testing revealed HLA class I A*02:32 B*27:51 and HLA class II DRB1*01:03 and DQB1*02:05.

The patients have not lived close to each other since the age of 20, and have had completely different professional activities. The father of the twin patients is 85 years old with normal serum IgG4 level and no history suggestive of IgG4-RD. The mother of the twin patients is deceased; she had no history suggestive of IgG4-RD in her medical record. The first patient has 2 sons (41-year old twins) and a daughter (24 years of age) in good health and with normal serum IgG4 levels.

Conclusions:

These observations in monozygotic twins demonstrate a genetic basis of IgG4-RD in our patients and suggest at least 2 genetic hypotheses: a *de novo* mutation in one of the parents with autosomal dominant transmission; alternatively, an autosomal recessive transmission with both parents heterozygote for the candidate gene.