Coeliac Disease in Down's Syndrome: A Case Report

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ABSTRACT

Down's syndrome is a trisomy with an incidence of 1/600. Coeliac disease is a malabsorption with an incidence of 1/2000. This is a case report of a Down's syndrome child with coeliac disease.

Leva et al.[1], reported a Down's Syndrome female who presented with coeliac disease malabsorption along with Coomb's positive haemolytic anaemia.[1] Bently[2] presented a male Down's syndrome who had coeliac disease and retinoblastma. Nowak et al.[3], reported 2 cases of Down's syndrome with coeliac disease. A case of Down's syndrome with coeliac malabsorption is presented in this case report which includes a discussion of the genetic association between congenital retardation and coeliac disease.

THE CASE

A baby boy was born after 35 weeks of gestation. The mother was 37 years at delivery. Birth weight was 2.4 kg, head circumferance 30.5 cm and length of 47 cm. The neonate showed signs of mongolism that included slanting of eyes, epicanthic folds, flat occiput, malformed ears, simian crease, telecanthis and hypotonia. At 8 months of age the diagnosis was confirmed by karyotyping and echocardiography excluded the presence of congenital heart disease. The baby exhibited developmental motor and mental delay, and experienced several attacks of chest infection. At the age of 2 years and 3 months, he presented with abdominal distension, passage of foul, bulky, pale stools with loss of weight. The patient weighed 8.8 kg and his height was 74 cm. On examination, the patient was pale but not jaundiced. The abdomen was distended but neither ascites nor organomegally was present. The patient had wasting of the proximal muscles. Complete blood count revealed a Hb of 8 gm/100 ml, MCV of 71 and a MCH of 23. Total proteins were 58 gm/1, and albumin was 30 gm/1. Calcium was 2.02 mmol/1, phosphate was 1.3 mmol/1, cholestrol was normal, SGPT was normal and serum carotene was low. Alkaline phosphates and Barium enema were normal. Barium follow through revealed a malabsorption pattern. Jejunal biopsy showed subtotal villous atrophy, elongation of the crypts and infiltration of lamina propria by lymphocytes. The diagnosis of coeliac disease was established and the patient was put on a gluten free diet. He improved clinically with disapperance of abdominal distension and improvement of stool consistency. After 10 weeks of the introduction of gluten free diet to the patient, a second jejunal biopsy was done which showed regeneration of the villi. A diet containing gluten was reintroduced to the patient, diarrhoea recurred and a third biopsy showed that the villi had again atrophied. The patient was followed for 2 years and he is now in good health.

DISCUSSION

A great advance occurred when Dicke (1850) showed that children with coeliac disease lost their symptoms when wheat and rye flour were removed from their diet. It soon became apparent that the harmful substance was in the gluten fraction of wheat and rye flour. The noxious component of gluten lies in the gliadin fraction and suggests that some form of immune mechanism is at work.[4]

There is no doubt that genetic factors play a role in the aetiology of coeliac disease. The incidence of the disease in relatives of coeliac sprue patients is significantly greater than in control population.[5] McDonald et al.[6], found as many as four biopsy proven cases of coeliac sprue in a single family and noted a total of 11 affected relatives among 96 people studied from 17 families. The symptoms are often either absent or so mild that some affected relatives were not aware of any abnormality. A 10% of first order relatives has subsequently been reported in several other studies. Although several relatives were affected in some hinderals, only a single case could be found in other carefully studied families. To confuse the matter further, both concordance and disconcordance for coeliac sprue have been documented in identical twin pairs.[6] That genetic factors play a role in coeliac sprue is supported by the observation that approximately 80% of coeliac disease patients carry the histocompatibility antigen HLA-B8 compared with 20% of control adult population. HLA-DW3 antigen, often associated with HLA-B8 through

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linkage disequilibrium, is also found in over 80% of the patients with coeliac sprue compared with less than 20% of normal persons. It has been suggested that the genetic basis of coeliac disease involves alleles at two loci, one being related to HLA-B8 or DW3 or an antigen associated with B8 or DW3 and the other related to the B-lymphocyte antigen.[7] In an effort to integrate the incidence that an immune response is involved with the available genetic data, it has been suggested that the genes involved code for a surface receptor that facilitate the interaction of gluten with lymphoid cells or interstitial absorptive cells or both. Although it has been established that genetic factors are significant in the pathogenesis of most of the cases of coeliac sprue, further studies are needed before the mode of inheritance is fully understood.[8]

Demonstration of IgG anti-gliadin antibody in the serum and intestinal secretions of patients with coeliac disease suggests a primary immunologic reaction as the mechanism of the disease. This may occur by immune complex formation directed against epithelial tissue. An alternate Hypothesis would be that an antibody-dependent lymphocyte mediated cytotoxic reaction may account for the observed villous injury. In such a reaction, antigliadin antibody would bind to a specific amino acid sequence of gliadin and the epithelial mucosa. The underlying mucosa would then be a larger area for cytotoxic injury by killer lymphocytes attacking the anti-gliadin antibody.[9] Supporting evidence for such immunologic injury include the observation that both the small bowel lamina propria of patients with active coeliac disease and organ culture specimens produce the similar cellular and humoral response expected in an immune mediated injury. The possibility that the observed immunologic reaction is simply a non-specific response to an already injured mucosa has not been excluded.[10]

Down's syndrome is a trisomy of the chromosome 21 with an incidence of 1/600. Several studies showed the association of Down's syndrome, hypothyroidism and diabetes mellitus. It is known that both insulin dependent diabetes mellitus and auto-immune diseases are associated with specific HLA haploid-lyses.[8] Fialkow showed that anti-thyroglobulin occur with a higher incidence among Down's syndrome patients and their relatives.[11]

The association of an histocompatible antigen with a certain disease suggests that the antigen may be instrumental in altering an individual's susceptibility to that disorder. It has been proposed that the histocompatibility locus is somehow linked to the immune response gene, implicating an alteration in immune surveillance as a factor in the genesis of a particular disease.[12]

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