

Rare association of celiac disease with congenital heart disease

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Received - 14 February 2019

Initial Review - 19 February 2019

Accepted - 18 April 2019

ABSTRACT

Celiac disease (CD) is an autoimmune enteropathy caused by exposure to dietary gluten in genetically predisposed individuals. CD is a multisystem disease involving gastrointestinal, hepatobiliary, nervous, hematologic, and cardiovascular systems. Few associations of congenital heart disease have been reported with CD. We report a case of an 8-year-old female, who was presented to the hospital with severe anemia and undernutrition. She had severe pallor, clubbing, hepatomegaly, and a Grade III systolic ejection murmur. Echocardiography revealed a large ostium secundum type of atrial septal defect and patent ductus arteriosus. The increased levels of serum IgA anti-tissue transglutaminase (anti-TTG) antibody have arisen suspicion of CD, which was confirmed after the histopathological study of the duodenal biopsy. We are reporting this case to highlight the rare association of the CD with congenital heart disease.

Key words: Atrial septal defect, Celiac disease, Congenital heart disease, Echocardiography, Patent ductus arteriosus

Celiac disease (CD) is an immune-based reaction to dietary gluten (storage protein for wheat, barley, and rye) that primarily affects the small intestine in those with a genetic predisposition and resolves with the exclusion of gluten from the diet [1,2]. Clinical manifestations of this disease are abdominal pain, bloating, diarrhea, stools with bad smell, poor growth, or weight loss in children. Atypical manifestations are a metabolic bone disease, premature osteoporosis, anemia, unexplained weight loss, elevated liver enzymes, epilepsy, and ataxia [1]. Common associations of CD are dermatitis herpetiformis, diabetes mellitus type 1, inflammatory bowel disease, etc. [1,2]. The overall CD prevalence is 1.0% in Europe while in India and North India it is 0.6% and 1.2%, respectively [3]. Few case reports and case series are reported an association of CD with congenital heart diseases (CHD) [4-7]. Contributing to these rare studies, we hereby present a case of association of CD with congenital heart disease (atrial septal defect [ASD] and patent ductus arteriosus [PDA]).

CASE REPORT

An 8-year-old female was presented with a history of progressive abdominal distension for 2 months, pain in the abdomen for 15 days and difficulty in breathing for 10 days. There was no history of recurrent diarrhea or blood transfusion. On examination, her height was 95 cm and weight was 11.8 kg (severe stunting and thinness). She had tachypnea and tachycardia and had severe pallor and Grade II clubbing; the child had a protuberant abdomen with hepatomegaly (4 cm below costal margin). There was no

free fluid while her cardiovascular system examination revealed a Grade III systolic ejection murmur best heard over 2nd and 3rd intercostal space in the parasternal area along with thrill. The chest had bilateral crepitations.

Investigations revealed severe anemia (hemoglobin – 1.2 g%, packed cell volume – 6.9%, and microcytic hypochromic type), total leukocyte count – 10,600/ μ L, and platelet – 2 lakh/ μ L. Renal function test (urea – 39 mg/dL and creatinine 0.5 mg) and liver function test (total bilirubin – 0.6 mg/dL, alanine transaminase – 40 IU/L, and aspartate transaminase – 48 IU/L) were normal. Chest X-ray showed cardiomegaly. With a strong possibility of the CD, we did a clinical diagnosis of severe anemia with congestive cardiac failure accompanied by severe stunting and thinness. The patient was managed with oxygen, packed red cell transfusions and furosemide and her IgA anti-tissue transglutaminase (anti-TTG) antibody was raised (800 IU/mL). CD was confirmed after the histopathological study of the duodenal biopsy.

In view of the persistence of Grade III murmur after correction of anemia, echocardiography was done which revealed large ostium secundum type of ASD and 4 mm PDA. The child was referred to pediatric cardiology for management of heart disease and advised for a gluten-free diet. On follow-up, the child started gaining weight on a gluten-free diet and anti-failure drugs.

DISCUSSION

We hereby discuss a patient of severe anemia with undernutrition who was diagnosed as a case of CD and acyanotic CHD (ASD

and PDA). CD is an immune-mediated systemic disorder elicited by gluten and related prolamines in genetically susceptible individuals characterized by a combination of gluten-dependent clinical manifestations, anti-TTG antibodies enteropathy [2]. Silent CD is a combination of positive celiac antibodies and biopsy findings without sufficient symptoms to warrant clinical suspicion of celiac. The latent CD is described as positive CD antibodies without villous atrophy. The patient has had a gluten-dependent enteropathy but the patients may/may not have symptoms. The potential CD is positive antibodies without villous atrophy where the patient may/may not have symptoms and may or may not develop CD [2].

CD is screened by detection of celiac antibodies: IgA anti-TTG antibody, IgA endomysial antibody, IgA, and IgG-deamidated gliadin peptides. The anti-TTG antibody is the preferred test. The diagnosis is confirmed by intestinal biopsy. HLA-DQ2/DQ8 genotyping testing should be used to effectively rule out the disease in selected clinical situations. This includes equivocal small-bowel histological finding (Marsh I-II) in seronegative patients, patients with discrepant celiac-specific serology and histology, patients with suspicion of refractory CD and patients with Down's syndrome [1]. HLA testing can also be used to confirm the diagnosis of CD in cases where anti-TTG antibody titer is more than 10 times the upper limit of normal antibody titer thereby omitting the need of invasive procedure of endoscopy and biopsy [1]. The present case was diagnosed by high levels of IgA anti-TTG antibody and duodenal biopsy.

In the present case, the child had abdominal distension, growth failure, and severe anemia. Common associations of the CD are type 1 diabetes, Down's syndrome, autoimmune thyroid disease, Turner syndrome, Williams syndrome, IgA deficiency, and autoimmune liver disease [2]. Uncommon associations are dermatitis herpetiformis, pulmonary hemosiderosis, inflammatory bowel disease, epilepsy, ataxia, peripheral neuropathy, infertility, and amenorrhea [1]. Case reports and studies have shown various cardiac manifestations with CD such as cardiomyopathy, myocarditis [4], significantly lower contractility indices, higher left ventricular dimensions [5], systolic dysfunction of the left ventricle [6], and increased risk of atrial fibrillation [7].

In the present case, the association of CD with CHD (ASD and PDA) was found as shown in a few previous case reports and studies. In the study conducted by Wingren *et al.* in Sweden, CHD was one of the most common congenital anomalies accompanied by CD [8]. McNeish and Anderson (1974) reported a coarctation of the aorta in two cases of CD [9]. In India, Kumhar *et al.* reported a 14-year-old girl with celiac and ASD [10]. Shahramian *et al.* conducted a case-control study on 1002 children in two groups of CHD patients (n=402) and healthy controls (n=600). Serum anti-TTG levels were investigated in both groups. Serum anti-TTG levels were significantly higher (11%) in patients with CHD than the control group (3.5%).

Theories proposed for the increased incidence of CD in patients with CHD are: First, endothelial damage in CHD patients exposes the immune system to gluten initiating CD process in susceptible patients. Second, patients with CHD commonly fail to thrive, which may result in the early introduction of cereal in the diet that can be considered as a logical reason for developing CD [11].

CONCLUSION

This case is being reported as an association of congenital heart disease with CD is rare. An alternate etiology, like CD, should be considered if failure to thrive is out of proportion in a congenital heart disease patient. No guidelines are available for screening of CD in cases of congenital heart disease. There is a need to formulate guidelines for the same.

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Funding: None; Conflict of Interest: None Stated.

How to cite this article: Bhargava R, Singh A, Aggarwal A, Narang M. Rare association of celiac disease with congenital heart disease. *Indian J Child Health*. 2019; 6(5):255-256.

Doi: 10.32677/IJCH.2019.v06.i05.016