Celiac Disease in a Boy with Duchenne Muscular Dystrophy: A Double Jeopardy!

Sir,

A 7-year-old boy presented with a history of walking difficulty and recurrent falls from 5 years of age. He had trouble in getting up from sitting and supine position. He was noted to have progressive enlargement of bilateral calves. There was no history of similar illness in other family members. In addition, he also had a history of progressive abdominal distension, pallor, and poor weight gain from 2 years of age. He received twice packed red blood cell transfusions in the past for anemia. A possibility of celiac disease (CD) was considered at 2 years of age and confirmed with upper gastrointestinal endoscopy, which showed typical features of grooving and scalloping in the duodenum [Figure 1a], and elevated tissue transglutaminase IgA (>128 U/mL; normal <7). Histopathological examination of duodenal biopsy tissue showed subtotal villous atrophy (Marsh 3B stage), crypt hyperplasia, and increased intraepithelial lymphocytes. He was started on a gluten-free diet (GFD), nutritional supplements at 2 years of age; however, compliance remained poor.

On examination, his weight, height, and head circumference were less than −3Z score for age and sex, suggestive of wasting and stunting. Neurological examination showed proximal muscle weakness and wasting of bilateral posterior axillary folds with pseudo-hypertrophy of the deltoid, infraspinatus [Figure 1b], and calf muscles. His Gower's time and 10-m walk time were 5 and 12 s, respectively. Brook's upper limbs' score was 1 and lower limbs' Vigno's score was 2, suggestive of an early ambulatory phase of Duchenne muscular dystrophy (DMD).

Investigations showed elevated serum creatine kinase levels (7204 U/L, normal: 26–308 U/L) and lactate dehydrogenase levels (1001 U/L, normal: 140–271 U/L). A complete hemogram revealed hemoglobin of 10.6 g/dL. Thyroid profile was normal, and antithyroid peroxidase antibodies were negative. Tissue transglutaminase IgA levels were elevated (>128 U/mL). DMD gene analysis by multiplex ligation-dependent probe amplification revealed deletion of exons 46–52, an out-of-frame deletion confirming the diagnosis of DMD. He was initiated on oral prednisolone (0.75 mg/kg/day), along with standard care including physiotherapy, muscle stretching exercises, and orthotic devices. He was also advised for GFD adherence, however, compliance to GFD remained poor. improvement in neurological symptoms. For DMD, he is on regular follow up, on oral steroids, and is in the early ambulatory stage.

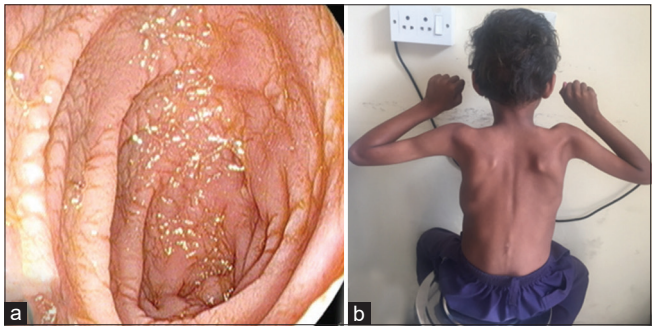

Figure 1: Upper gastrointestinal endoscopy showing typical features of grooving and scalloping in duodenum (a). Photographs of the child showing wasting of posterior axillary folds with hypertrophy of deltoid and infraspinatus muscles (valley sign) (b)

CD is an "immune-mediated systemic disorder caused by gluten and related prolamines in genetically susceptible individuals." CD is characterized by a variable combination of gluten-dependent manifestations, CD-specific antibodies, human leukocyte antigen (HLA)-DQ2 or HLA-DQ8 haplotypes, and enteropathy.[1] Neurological manifestations are one of the most common extraintestinal features of CD and are reported in 5%–10% of patients. These include epilepsy, headache, migraine, breath holding spells, attention-deficit hyperactivity disorders, cerebellar ataxia, cognitive impairment, dementia, multifocal encephalopathy, cerebral calcification, psychosis, vasculitis, and rarely neuromyelitis optica.[2] Neuromuscular disorders observed in association with CD are peripheral neuropathy, proximal myopathy, mononeuritis multiplex, inclusion body myositis, dermatomyositis, and polymyositis.[3] Neurological symptoms are more often late complication in patients with CD, but rarely can be the presenting feature. The mechanism of neurological complications in CD is mostly unknown and is believed to be due to micronutrient deficiency, immunedysregulation, or a combination of the two.

Muscular dystrophy is uncommon in association with CD. Ravindra *et al.*[4] reported a 27-year-old female who presented with gastrointestinal symptoms and 8 months later developed neurological symptoms suggestive of myotonic dystrophy. However, her neurological symptoms did not improve on GFD. Suthar *et al.* reported a case of proximal myopathy as presenting feature of CD in a 4-year-old girl. The pathogenesis was attributed to vitamin D deficiency, secondary hyperparathyroidism, and immune-mediated myopathy.[5]

The association of DMD and CD is unique in the index case and never reported in the literature. Gastrointestinal complications of DMD are most often seen in the late stages of the disease and are secondary to smooth muscle involvement and include gastroparesis, intestinal hypomotality, intestinal pseudo-obstruction, recurrent intussusceptions, and so on.[3] The association of CD and DMD in the index case may be due to interaction between different HLA subgroups as significant higher frequency of HLA-B*7:05 is associated with DMD[6] and

HLA-DQA1 and HLA-DQB1 with CD.[7] Or it may be a chance association in the index patient because of high prevalence of celiac diseases in North India. To conclude, CD in a boy with DMD is rare association and contributes to the disability. Gastrointestinal complications in a boy with DMD can be the part of the disease *per se* and seen in the late stage of the disease.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

Indar K. Sharawat, Shruti Sharma[1], Renu Suthar, Babu R. Thapa[1]

Departments of Pediatrics and [1]Gastroenterology, Postgraduate Institute of Medical Education and Research, Chandigarh, India

Address for correspondence: Dr. Renu Suthar, Department of Pediatrics, Postgraduate Institute of Medical Education and Research, Chandigarh - 160 012, India.
E-mail: drrenusuthar@gmail.com

References

1. Husby S, Koletzko S, Korponay-Szabó IR, Mearin ML, Phillips A, Shamir R, *et al*. European society for pediatric gastroenterology, hepatology, and nutrition guidelines for the diagnosis of coeliac disease. J Pediatr Gastroenterol Nutr 2012;54:136-60.
2. Campagna G, Pesce M, Tatangelo R, Rizzuto A, La Fratta I, Grilli A. The progression of coeliac disease: Its neurological and psychiatric implications. Nutr Res Rev 2017;30:25-35.
3. Suthar R, Sankhyan N. Duchenne muscular dystrophy: A practice update. Indian J Pediatr 2018;85:276-81.
4. Ravindra BS, Desai N, Deviprasad S, Bhede V, Ravat S, Sawant P. Myotonic dystrophy in a patient of celiac disease: A new association? Trop Gastroenterol Off J Dig Dis Found 2008;29:114-5.
5. Suthar R, Sankhyan N, Thapa BR, Singhi P. Proximal myopathy: A rare presentation of celiac disease. J Child Neurol 2013;28:1485-8.
6. Li H, Xiao L, Wang L, Lin J, Luo M, Chen M, *et al*. HLA Polymorphism affects risk of de novo mutation of dystrophingene and clinical severity of Duchenne muscular dystrophy in a southern Chinese population. Front Neurol 2018;9:970.
7. Megiorni F, Pizzuti A. HLA-DQA1 and HLA-DQB1 in Celiac disease predisposition: Practical implications of the HLA molecular typing. J Biomed Sci 2012;19:88.

Submitted: 24.01.2019 **Accepted:** 10.02.2019 **Published:** 08.12.2020

DOI: 10.4103/aian.AIAN_40_19