Axonal and Demyelinating Polyneuropathy Associated With Celiac Disease

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Background: The involvement of the peripheral nervous system in children with celiac disease is rare. **Case characteristics**: A 15- year- old girl affected by celiac disease, who presented with an acute polyneuropathy after accidental reintroduction of gluten in her diet. **Observation**: Neurological examination suggested asymmetric weakness of both legs distally. Anti-tissue transglutaminase antibodies were positive. Nerve conduction studies were consistent with a sensory-motor demyelinating peripheral neuropathy. **Outcome**: Symptoms improved spontaneously on a gluten-free diet. **Message**: Polyneuropathy may occur as a complication of celiac disease in childhood.

Keywords: *Acute flaccid paralysis, Gluten-sensitive disease, Neuropathy.*

Numerous celiac disease (CD) associated extra-intestinal conditions have been described, mostly in adults. Among the extra-intestinal manifestations, a wide spectrum of neurologic conditions have been classically associated with CD [1].

We present a girl with celiac disease, who experienced acute peripheral neuropathy at the age of 15 years on exposure to gluten in the diet.

CASE REPORT

A girl who was diagnosed to have celiac disease at the age of 9 months was on a strict gluten-free diet, and was asymptomatic. At the age of 15 years, she experienced acute weakness and pricking sensation confined to her legs; for the next two months she was occasionally consuming biscuits, mistaking them to be gluten free. She had no gastrointestinal symptoms.

Physical examination was unremarkable. Neurological examination revealed asymmetric (predominantly left) distal weakness of both legs. The knee jerks and ankle reflexes were depressed; plantar reflexes were flexor. Sensation of touch, pain and temperature on distal parts of both legs were decreased; tests for coordination were normal. Laboratory investigations showed a white cell count of 8900/mm^3, normal creatine kinase (98IU/L), alanine aminotransferase (16IU/L) and aspartate aminotransferase (35 IU/L) levels. Serum albumin, erythrocyte sedimentation rate, serum urea, electrolytes, creatinine, glucose, bilirubin, immunoglobulins, lead, iron and, copper were also normal. Blood levels of folic acid, and vitamins A, B_1, B_6, B_{12}, and E were also within normal limits. Analysis of urine did not reveal any porphyrins. Thyroid-stimulating hormone was 2.5 IU/mL, and free T4 was 1.2 ng/L. Antinuclear antibodies (ANA), cytoplasmic anti-neutrophil cytoplasmic antibodies and perinuclear antineutrophil cytoplasmic antibodies were negative. Antibodies to *Varicella zoster*, Epstein-Barr virus, cytomegalovirus, *Herpes simplex*, *Borrellia burgdorferi* and *Campylobacter jejuni* were negative. IgA antitissue transglutaminase antibodies (anti tTG) and IgG anti tTG levels were raised (120 IU/mL and 80IU/mL, respectively) Antibodies against gangliosides GM1 and GQ1b, myelin associated glycoprotein and myelin basic proteins were not tested. Nerve conduction studies were consistent with a sensory-motor demyelinating peripheral neuropathy. The parents refused consent for a lumbar puncture and nerve biopsy.

Her symptoms improved spontaneously on a strict gluten-free diet and she was discharged home after 2 weeks. Control electromyoneurography was not performed. She has been asymptomatic on a gluten-free diet for last one year.

DISCUSSION

The involvement of the peripheral nervous system in children with CD is particularly rare [1]. Peripheral neuropathy can be caused by a variety of systemic diseases, toxins, medications, infections, and hereditary disorders. The blood tests of our patient excluded most of the causes, such as diabetes, hypothyroidism, nutritional deficiencies, andvascular, toxic or infective etiology. Differential diagnosis also included Guillain-Barré syndrome. Our patient had non-progressive polyneuropathy and had spontaneous recovery on gluten-free diet.

There have been few previously reported cases of peripheral nervous system involvement in children with celiac disease. A chronic, progressive axonal

polyneuropathy with no improvement on gluten-free diet has been reported in two children [2,3]. Cacir, *et al.* [4] reported peripheral axonal polyneuropathy in 2 of the 27 children with CD. Ruggieri, *et al*. [5] reported a girl developing acute demyelinating neuropathy after accidental reintroduction of gluten in her diet, with rapid disappearance of symptoms on a gluten-free regimen. Unlike our case, she had negative serology for CD.

The exact cause of polyneuropathy in CD is not known. The suggested hypotheses include action of antibodies on extra-intestinal tissue transglutaminase proteins [6-9], pathogenic involvement of anti-ganglioside antibodies [8], direct toxic effects of gliadin, and associated vitamin deficiencies (B_6, B_{12} and E). The response to GFD in CD-associated peripheral neuropathy has been inconsistent. Some authors reported symptom regression and resolution of pathological electro-myoneurographic findings on gluten-free diet whereas others reported no benefit of gluten avoidance [10].

In conclusion, an acute polyneuropathy can rarely complicate celiac disease in childhood, and may resolve spontaneously on gluten-free diet.

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Tuberous Sclerosis Presenting with Hemorrhagic Stroke

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Background: Incidence of intracerebral hemorrhage in patients with tuberous sclerosis is rare, and in most of the cases it is associated with either underlying cerebrovascular malformation or hemorrhage into the subependymal giant cell astrocytoma. **Case characteristics:** A 2-year-old boy presented with a hemorrhagic stroke, and subsequently diagnosed as a case of tuberous sclerosis. **Observation:** Detailed work-up for stroke did not reveal any definite etiology. **Outcome:** Weakness gradually improved. Follow-up neuroimaging showed resolution of hemorrhage. **Message:** Clinician must be aware regarding this rare presentation of tuberous sclerosis.

Keywords: *Cerebral hemorrhage, Child, Stroke*.