Wallenberg syndrome as a sole presentation of celiac disease

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ABSTRACT

مرض سبيور البطني هو اعتلال معوي حساس للجلوتين والذي يكون فيه ضمور زغابي في الأمعاء الدقيقة مصحوباً بأعراض معدية معوية وخارج الأمعاء. يصعب تحديد نسبة الانتشار الصحيحة بسبب أن العديد من المرضى لديهم أعراض لا نمطية أو ليس لديهم أعراض على الإطلاق. ظهر على عدد قليل من الأطفال أعراض على الجهاز العصبي المركزي مثل اعتلال عصبي محيطي و عدم الانتظام في المخيخ. لم يتم الإبلاغ عن السكتة الدماغية في القطاع الدائري الخلفي كحالة حاضرة للمرض البطني لتاريخه. لدينا وصف حالة لذكر يبلغ من العمر ١٥ عاماً والذي حضر الى المستشفى وهو يعاني من متلازمة والنبرج بدون أي تاريخ طبي إيجابي. أكدت نتيجة الأشعة بالرنين المغناطيسي للدماغ وجود الاحتشاء وأظهرت نتيجة التخطيط بالرنين المغناطيسي تضيق في الشريان الفقاري. كشفت نتائج المختبر الإصابة بالأنيميا ونتيجة فحص المصل كانت إيجابية بالإصابة بالمرض البطني. كما أكدت نتيجة العينة المأخوذة من الإثني عشر الإصابة بالمرض. أي طفل لديه أعراض عدم الكفاءة فقارية قاعدية: عند ذلك يجب الأخذ بعين الإعتبار الإصابة بالمرض البطني كسبب قابل للعلاج.

Celiac sprue is a gluten sensitive enteropathy in which there is a small bowel villous atrophy associated with gastrointestinal and extraintestinal symptoms. True prevalence is difficult to ascertain because many patients have atypical symptoms or none at all. Few children display CNS symptoms such as peripheral neuropathy and cerebellar ataxia. So far, stroke in posterior circulation territory as a presentation for celiac disease has not been reported. We report a 15-year-old male patient who presented as Wallenberg syndrome without any positive medical history. Brain MRI confirmed infarction, and magnetic resonance angiography showed vertebral artery stenosis. Laboratory findings revealed anemia and positive serologic tests for celiac disease, and duodenal biopsy confirmed the disease. In any children with symptoms of vertebrobasilar insufficiency, celiac disease as a treatable cause must be considered.

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Celiac disease (CD) is a digestive disease that is characterized by malabsorption resulting from inflammatory injury to the small intestine mucosa after the ingestion of wheat gluten or related rye and barely protein.[1] It may develop into a neurological disorder with unknown reason, but Wallenberg syndrome has not been reported so far in CD. Wallenberg syndrome (dorso-lateral medullary syndrome) is produced by infarction of a wedge of lateral medulla posterior to the inferior olivary nucleus and is usually caused by vertebral artery occlusion. The objectives of this report are to present an unusual presentation of CD as Wallenberg syndrome, and increase physician awareness to consider CD as a cause of obvious stroke.

Case Report. A 15-year-old male patient with a body mass index of 22 (healthy weight category) was admitted to our clinic with a sudden onset of true vertigo, oscillopsia, diplopia, ataxia with veering to the right. He reported a sudden vertigo and right side weakness on the day before admission. There was no history of any problem in the past. On his physical examination, upper limb blood pressure was equal. Right cerebellar hemiataxia and hemisensory loss with right Horner syndrome and right soft palate paralysis were detected. Routine laboratory investigations showed hypochrom microcytic anemia [(Hgb=10.9 gm/dL normal range (13.2-16.2 gm/dL)], with strongly positive antiendomysial (AEMA) and antigliadin antibodies (AGA). He did not report diarrhea, constipation, abdominal distention or weight loss in his medical history. His biochemical tests (including plasma lipids, albumin, and aminotransferase levels were within normal limits. Estimated sedimentation rate, C reactive protein, collagen vascular disease evaluation (antinuclear

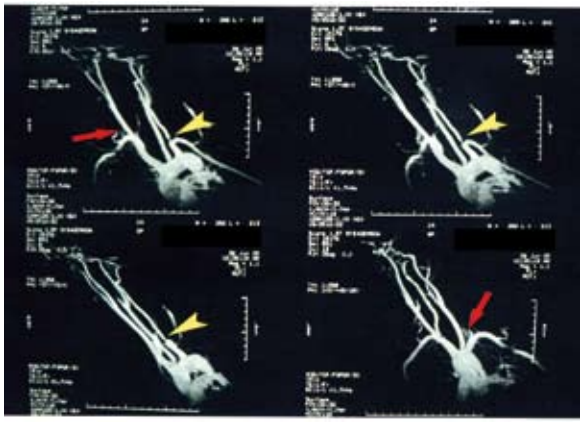

Figure 1 - Magnetic resonance angiography showing absence of flow in right vertebral artery and stenotic lesion proximal of the left vertebral artery.

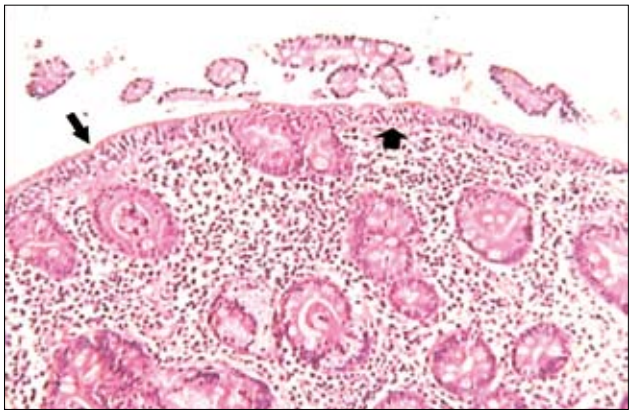

Figure 3 - Duodenal biopsy showed chronic inflammation, intraepithelial lymphocyte (short arrow) and subtotal villous atrophy that were compatible with celiac disease (arrow).

antibody, lupus anticoagulant, rheumatoid factor), homocysteine level, protein C and S, antithrombin III levels did not show any abnormality, echocardiography, and brain CT scan were normal. Magnetic resonance angiography revealed absence of flow in the right vertebral artery and stenotic lesion proximal of the left vertebral artery (**Figure 1**). Brain MRI showed signal abnormality in the right cerebellum and medulla showing low T1 and high T2 intensity (**Figure 2**). Duodenal biopsy, showed chronic inflammation, increased intraepithelial lymphocyte counts, and subtotal villous atrophy that was compatible with celiac disease (**Figure 3**). Gluten free diet and anticoagulation therapy was started and after 6 months follow up, he had only mild cerebellar ataxia.

Discussion. The incidence rate of CD in 22 European countries is one case every 1000 live births. Over 95% of patients with celiac express the HLA_DQ heterodimer. This specific heterodimer predispose T-cell mediated immune response against ingested gluten in genetically predisposed people. Patients with CD may develop a neurological disorder of unknown cause, while autoimmune mechanisms are suspected.[2] Infants with celiac show impaired growth, diarrhea, and abdominal distention, vomiting, pallor, and edema, however, in children diagnosed later in childhood (>2 years) extra intestinal symptoms often predominate. The possibility of CD should also be considered in patients with iron-deficiency anemia without demonstrable bleeding, unexplained folate deficiency, or unexplained osteopenic bone disease. Neurological manifestations are various and common in patients with refractory celiac. The most common neurological disorder includes cerebellar ataxia and peripheral neuropathy that progress slowly.[3] Stroke due to large vessel involvement in CD is rare and on literature review, we could find only one case of CD reported that presents a recurrent transient ischemic attack in

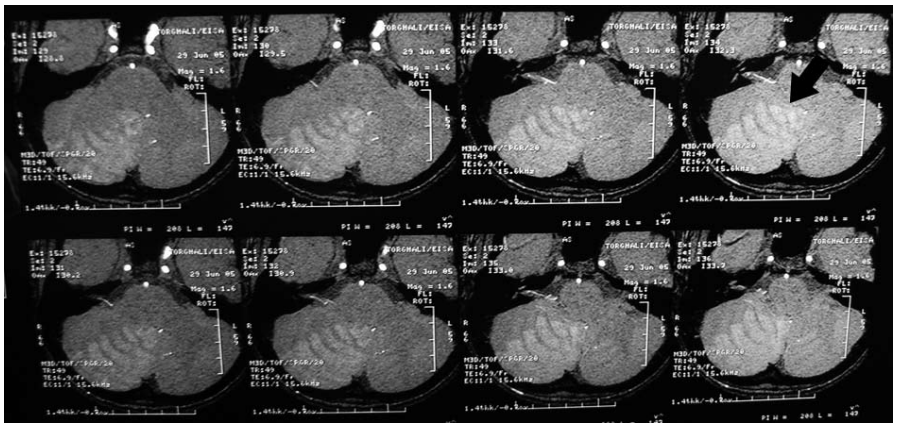

Figure 2 - T2 weighted axial brain MRI at the level of medulla; there is a right posterior inferior cerebellar artery territory infarct (arrow).

the carotid territory.[4] Acute ischemic stroke attributable to occlusion of the basilar and vertebral artery carries an extremely poor prognosis and is rarely encountered in children. Cerebrovascular disorders are among the top 10 causes of death in children.[5] Current estimates of incidences are: cardiac disease (25%), coagulopathy (protein C, protein S, antithrombin III deficiency), antiphospholipid syndrome (25%), sickle cell disease (the common risk factor in black child), moyamoya (10-20%), varicella zoster infection, anabolic steroid use, inflammatory vasculitis, and spontaneous dissection. A recent report emphasized that common factors of pediatric posterior circulation stroke were male gender and vertebral artery dissection.[6,7] A possible explanation for the male preponderance is the increased potential for trauma and more frequent structural abnormalities of the cervical spine in boys. The most common segment is V3 (at C1-C2) and V1 (they are transverse by facial bands and skeletal muscle).[8,9] Celiac is associated with vasculitis in various tissues. Severe cutaneous vasculitis has no relation with severity of gut disease and does not necessarily respond to dietary restrictions. Rush et al,[10] reported biopsy to proven CNS vasculitis in association with celiac disease, and Ozge et al,[11] described patients with recurrent stroke and CD have evidence of CNS vasculitis.[11] Arslan et al[12] describe Takayasu and CD in a 12-year-old girl with gastrointestinal symptoms and fever of unknown origin continued from 3 years old. The posterior cerebral circulation has selective vulnerability to CD and occipital calcification has been reported with CD. Patients with CD may develop a neurological disorder with unknown reasons, although autoimmune mechanisms are suspected. Tissue transglutaminase is the major auto antigen in CD, and is thought to maintain vascular endothelial integrity. Antiendomysial immunoglobulin A antibodies, demonstrated to be the same autoantibody as anti transglutaminase, react with cerebral vasculature, suggesting an autoimmune mechanism for CD associated vasculopathy. As CD is a potentially treatable cause of cerebral vasculopathy, serology-specifically anti tissue transglutaminase antibodies should be included in the evaluation for cryptogenic stroke in childhood, even with no typical gut symptoms.

Laboratory data suggest a role for tissue transglutaminase in blood- brain barrier mechanisms. Thus, tissue transglutaminase could interfere with blood-brain barrier integrity, facilitating activation of autoimmune mechanisms in the CNS. Neuronal degeneration might be result of transglutaminase apoptotic function. Tissue transglutaminase change was demonstrated in atherosclerosis.[13,14] Goodwin et al[4] report a 3-year-old girl with a recurrent transient hemiplegia. Although there were virtually no gastrointestinal symptoms and she had normal thriving, celiac serology was strongly positive and a duodenal biopsy confirmed the disease.

In conclusion, our case report represents an association between large vessel vasculopathy and cryptic gluten sensitivity, and illustrates that CD must be considered in the diagnosis of stroke with obscure etiology. As CD becomes more commonly diagnosed, it is likely that some associated diseases may merely be the result of chance and due to a higher prevalence of vertebral malformation in the male gender. So this anomaly is either incidental or due to vulnerability of posterior circulation to celiac? Further research to answer this question must be carried out.

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