Case Report

Repeated episodes of visual disturbances associated with subclinical coeliac disease and cerebral calcifications in a Chinese patient: a case report and review of the literature

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Abstract: Coeliac disease (CD), epilepsy, and cerebral calcifications (CEC) are manifested as a rare neurological syndrome reported most commonly in Italian, Argentinian, and Spanish people. In this study, a case of a 27-year-old Chinese woman with visual disturbances, unilateral occipitoparietal calcifications, and subclinical CD is reported. She had been suffering from repetitive episodes of “dizziness” for 18 years, which was finally diagnosed as occipital epilepsy via EEG. Cerebral CT and MRI showed asymmetrical right occipital calcifications and excluded vascular malformations. Although denying having diarrhea or flatulence, she still underwent endoscopy of the upper digestive tract and biopsy, of which the findings indicated CD. The patient began a strict gluten-free diet and had no clinical recurrence. Furthermore, to explain the cause of the related symptoms, existing literature was found to illustrate the importance of screening patients with epilepsy and cerebral calcifications for CD, regardless of any gastrointestinal symptoms.

Keywords: Coeliac disease, epilepsy, cerebral calcification, visual hallucination

Introduction

Coeliac disease (CD) is a chronic small intestinal, immune-mediated enteropathy precipitated by exposure to dietary gluten in genetically predisposed people [1]. The clinical manifestations of CD vary from asymptomatic to a wide spectrum of symptoms. Though gastrointestinal complaints are the most predominant symptom in CD patients, neurological manifestations, such as cerebellar ataxia, peripheral neuropathy, dementia and epilepsy have also been reported in 10-22% of patients [2].

Since Visakorpi et al. first described the syndrome of “CD, epilepsy, and cerebral calcifications” (CEC) in 1970 [3], less than 200 cases have been reported and these were found in geographically limited regions (i.e., mainly Italy, Spain, Argentina) [1, 4]. Here, a Chinese patient with CEC is described, where disease is manifested as subclinical CD, paroxysmal visual manifestations, and unilateral occipital calcifications.

Case report

A 27-year-old Chinese female with an 18-year history of repetitive episodes of “dizziness” was admitted to the neurology department of Wuhan University Renmin Hospital (Wuhan, China) on April 22, 2017. She had no relevant family history except a history of seizures at the age of 3 and had received antiepileptic drugs until she was 5 years-old without recurrence. She had been suffering from repetitive episodes of “dizziness”, unstable walking and vomiting for 18 years, but denied having diarrhea, flatulence, tinnitus, and limb twitching. She suffered from attacks of “dizziness” 2-4 times a year that always lasted 2-3 days and underwent treatment for dizziness for several years before admission to our hospital. While in the hospital, an episode of “dizziness” occurred, in which she described as multi-colored lights for few seconds. Her height, weight, and intelligence were normal and no intestinal or neuropsychiatric symptoms were present.
Initial clinical investigations at our hospital included cerebral CT, MRI, EEG and laboratory examination. Cerebral CT (Figure 1A) showed convoluted superficial right occipitoparietal calcifications. MRI (Figure 1B-E) also revealed asymmetrical right subcortical occipital calcifications, absence of vascular anomaly, contrast enhancement, microbleeds, and brain atrophy. EEG detected a large number of low-amplitude fast waves in the right occipital region and asymmetry on both sides without abnormal interparoxysmal signs (Figure 2). Laboratory tests showed a low serum hemoglobin level (Hb, 86 g/L; normal: 115-150 g/L), a low iron level (3.2 μmol/L, normal: 9.0-30.4 μmol/L), a low ferritin level (4.5 ng/mL; normal: 10-219 ng/mL), and a low vitamin D level (5.10 ng/mL; normal: 20-30 ng/mL) levels, normal thyroid hormone, parathyroid hormone, humoral and cellular immunity, folic acid, vitamin B12, calcium, phosphorus, total protein, albumin, and serum homocysteine levels.
In view of a special type of epilepsy with occipital paroxysms she suffered, digital subtraction angiography (DSA) and endoscopy of the upper digestive tract was performed and a biopsy was obtained from the descending part of the duodenum. The DSA imaging was normal, without vascular malformations. Pathology showed mild chronic inflammatory cell infiltration in the lamina propria of the mucosa associated with an increased number of intraepithelial lymphocytes, partial crypt hyperplasia, and villous atrophy (Figure 3), which were compatible with CD. Finally, CEC was diagnosed and a strict gluten-free diet was introduced. The patient was invited for a check-up three months after the introduction of a gluten-free diet, and symptoms of occipital paroxysms and abnormal EEG were absent. However, it was still observed that serum iron, Hb, and ferritin concentrations remained low. Therefore, iron supplementation was continued, and the follow-up after 6 months showed that blood iron and serum Hb levels tended to rise gradually.

Discussion

CEC is a genetic, non-inherited, ethnically and geographically restricted syndrome associated with environmental factors that is mostly restricted to Mediterranean areas and Argentina [1]. Most previous reports have indicated that gastrointestinal symptoms are mostly subclinical or silent in CEC patients [4, 5]. In the current report, the patient denied any history of gastrointestinal symptoms but had low serum Hb and iron levels, which suggested she was suffering from iron deficiency anemia, and a lack of vitamin D, supporting the diagnosis of malabsorption. Thereafter, she was confirmed as having subclinical CD by duodenal biopsy, the “gold standard” criteria for this diagnosis.

Sturge Weber Syndrome (SWS) should also be considered in this case, of which the main clinical manifestations are epilepsy and occipital calcifications. It is known as a rare neurocutaneous syndrome with encephalotrigeminal or meningiofacial angiomatosis, due to early embryonic vascular malformation. Manifestation with a unilateral cutaneous nevus or with red wine stains on the face is a distinguishing feature [6]. The absence of cutaneous lesions and angiomatosis on DSA help us to eliminate this diagnosis. Although other symptoms were very confusing, she was eventually diagnosed with occipital epilepsy via EEG. Visual hallucinations, the hallmark of occipital seizures, usually occur in the contralateral visual field, affect the visual cortex, and then spread to the entire visual field [7]. Visual seizures are always characterized by transient visual manifestations which may be either positive (flashes, phosphenes) or, less commonly, negative (scotoma, hemianopia, amaurosis) [7]. Occipital epilepsy is difficult to diagnose from a patient’s history, especially from children, and is not invariably present. Furthermore, epilepsy is not strictly associated with local deposits of calcium. Our patient suffered from a special type of “dizziness”, which presented as flashes of mobile, colorful light. These symptoms were complex visual hallucinations, indicating occipitotemporal cortex involvement, and originated from the right occipital region by scalp EEG. The patient’s other occipital seizure symptoms, such as recurrent dizziness, unstable walking, and ictal vomiting, presumably represented abnormal discharges spread to the posterior temporoparietal region from the occipital focus [7].

Cerebral calcifications are situated mainly in the unilateral or bilateral occipital regions in CEC patients. However, the actual pathophysiology has not yet been determined. As CD may present with malabsorption, especially chronic folic acid deficiency, Pfaender et al. demonstrated that calcifications might be related to
malabsorption and impairment of folic acid transport across the blood-brain barrier, reducing central nervous system folate concentrations [8]. However, folic acid deficiency is not always present in CEC patients, and can’t explain the pathophysiology successfully. Another possibility is that the cerebral calcifications are caused by autoimmune- or immune complex-related endothelial inflammation [7, 9]. In addition, some drugs and treatments, such as methotrexate, radiotherapy, and some antiepileptic drugs, like phenytoin, may induce calcifications [7].

To date, the association between cerebral calcifications and occipital epilepsy is still unknown. Since a very small percentage of patients with CD and cerebral calcifications do not have epileptic attacks, it has been hypothesized that calcifications merely represent an epiphenomenon of the underlying disease process. However, it remains controversial, as some researchers have confirmed that there may be a link between intractable seizures and calcifications through the resection of the calcification region [10].

Indeed, seizures can respond well to treatment or be drug resistant. Although there are currently no data on the correlation between epilepsy severity and age of seizure onset or extent of cerebral calcifications, most reports indicate that a gluten-free diet might help control the seizures if started soon after the onset of epilepsy and at an early age [2]. However, in those patients who develop drug resistant epilepsy, surgical intervention may be necessary. Nakken et al. suggested lesionectomy should be offered to patients with CD, unilateral occipital calcifications, and difficult to treat symptomatic occipital epilepsy [10].

In conclusion, the current case report describes a Chinese adult female patient with a history of visual disturbances from childhood, unilateral occipitoparietal calcifications, and subclinical CD. Visual symptoms representing occipital epilepsy and cerebral calcifications may be the first clue to the presence of asymptomatic CEC. Therefore, patients with occipital seizures and unexplained cerebral calcifications should be carefully screened for CD, even in the absence of gastrointestinal symptoms. Furthermore, early institution of a gluten-free diet in combination with anti-epileptic treatment results in more successful seizure control.

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Disclosure of conflict of interest

None.

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