Landry-Guillaine-Barré syndrome a rare presentation of celiac disease

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Abstract: Celiac Disease (Gluten-Sensitive entropathy) is an immune-mediated systemic disorder elicited bygluten and related prolamines in genetically susceptible individualsand characterized by the presence of a variable combination of gluten dependentclinical manifestations**.** Celiac disease is associated with multiple extra intestinal presentations, including bone disease, endocrine disorders and neurological deficits**.** The disease has been associated with a variety of neurological illnesses, most frequently cerebellar ataxia, seizures, and peripheral neuropathy. We report a Landry-Guillaine-Barrésyndromesas apresentationof a 58 years old female patient with undiagnosed celiac disease throughout her entire life.
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1. Background:

Celiac disease is a permanent dietary disorder caused by an immunologic response to gluten that results in diffuse damage to the proximal small intestinal mucosa with mal-absorption of nutrients. It is estimated to affect 1 in 100 of people worldwide, suggesting that most cases are undiagnosed or asymptomatic, or manifested by intestinal (including diarrhea, steatorrhea, weight loss, abdominal distention), and/or extra intestinal symptoms (dermatitis herpetiformis, iron deficiency anemia, joint and bone pain, and seizures), tingling sensation in the legs (caused by nerve damage and low calcium). It is diagnosed by serologic tests and intestinal biopsy[1,2]. It is confirmed when symptoms resolve subsequently on a gluten-free diet. On the other hand, Guillain-Barré syndrome is an autoimmune disorder often considered a post infectious polyneuropathy involving mainly motor but also sensory and sometimes autonomic nerves. This syndrome affects people of all ages and is not hereditary[2]. he paralysis usually follows a nonspecific gastrointestinal or respiratory infection by approximately 10 days. Initial symptoms include numbness and paresthesia, followed by weakness which usually begins in the lowerextremities, then progressively involves the trunk, the upper limbs and the bulbar and respiratory muscles[1,3]. Patients in early stages of this acute disease should be admitted to the hospital for observation because the ascending paralysis canrapidly involve respiratory muscles during the next 24 hours. The association between long standing undiagnosed celiac disease and Guilian-Barré (or Guilian Barrélike-syndrome) as an extra intestinal manifestation had been recognized in few studies in the literature and the exact mechanisms that might explain this association is not established yet.

2. Case Report:

A 58 years old female patient referred to King Abdulaziz Hospital, Jeddah, complaining of insidious onset of urineretention andprogressive lowerlimbs weakness since 10 days. There was low grade low backache few days preceding the onset of the neurological symptoms. She was also known to havesome intermittent postprandial bloating with vague generalized mild abdominalpain, and used to experience intermittent greenish watery alternating with greasy diarrhea for more than 23 years which was diagnosed as irritable bowel syndrome with numerous lists of antispasmodic medications leading to partial relief of her Gastrointestinal symptoms. She also used to have some grade of iron deficiency anemia and low calcium level readings with no response toiron, calcium and vitamin D supplements for many years. On examination, weakness was ascending and progressive involving the calves, then thigh muscles up to the pelvic girdle, associated with hypotonia, hyporeflexia and flexor planters, superficial sensations were also diminished for pain and touch, as well as deep vibration sense. Cranial nerves and rest of CNS examination were intact. General, chest, cardiac and abdominal clinical examinations were unremarkable apart from pallor and marked generalized sweating not

associated with fever, vital signs were also within normal except for sinus tachycardia 115/min, sitting and standing blood pressure showed systolic decline of 20 mmHg. Initial management plan included a long list of laboratory and radiological investigations including full biochemistry study, Anti-gliadin, Anti TTG antibodies, MRI cervical, thoracic and lumbosacral spines. Lumbar puncture was also performed few hours after admission, and intravenous fluids plan were initiated together with neurology, neurosurgery, and Gastroenterology consultations. Her initial abnormal laboratory results were: Hemoglobin 8.7 g/dl, MCH 25.4 Pg/cell, MCV 78.1 FL, Potassium: 3.3 mmol/L. Calcium: 2.09 mmol/L, albumin: 19.7 U/L. Serum Iron 15 microgram /dl, TIBC 490, ferritin 15ng/mL. The rest of biochemistry, acute phase reactants, U&E, Thyroid function tests were within normal limits. Stool analysis: no Salmonella, no Shigella or any evidence bacterial growth. Abdominal X ray: dilated bowl loops were noted. Chest X-ray and Pelvic-abdominal ultrasound revealed normal studies. CSF Examination showed normal pressure with raised protein 120 mg/ dL, normal cells and glucose. MRI brain and spinesat all levels were normal. HRCT chest was also normal.

Twenty four hours after admission in the medical ward the patient started to be oxygen desaturated with fluctuations of oxygen saturation from 92, 88, down to 78% on room air,urgent spirometry revealed reduced Forced vital capacity to 12 mL/kg. ABG readings denoted respiratoryacidosis, progressive marked hypoxia down to 55mmhg, CO_2 45% and pH 7.20. D-Dimer was normal. ICU admission was urgently arranged with full ventilatory support. A provisional diagnosis of Guilian-Barré syndrome was estimated despite the absence of previous history or lab evidence of any neither recent infection nor vaccinations prior to the history of presentation, plasma-pheresis session was also urged plus IV corticosteroids, no remarkable improvement in ventilatory parameters and weaning trials throughout the following four days. Intensive chest physiotherapy, prophylactic antibiotics and anticoagulation were maintained, meanwhile, the patient was on nasogastric tube feeding (NGT) on conventionalfluid diet with no specific restrictions, until the fifth day of ICU admission when the autoantibody results received with positive serology for both Anti-Gliadin, and anti-tissue transglutaminase (Anti TTG) IgG test.

Dieting plan was commenced on gluten free dietary through the NGT, and that was followed by dramatic improvement in the requirements for ventilatory support, successful weaning and later on response to chest physiotherapy was rapid, regaining ability to swallow as well as the motor power at the lower limbs was also so fast that in one week after weaning the patient was able to move freely, however, urine retention and hence the need for continuous Folly's catheter insertion remained for 3 weeks together with postural hypotension manifested with mild dizzy spells on walking.

Eventually, the patient was discharged at 25th day of admission to the hospital with no special recommendations apart from maintaining some physiotherapy, and advise of Gluten free diet for the rest of her life.

3. Discussion:

Celiac disease (CD) is associated with multiple extra-intestinalpresentations, including bone disease, Endocrine disorders and neurological deficits [1,2]. Serologic screening studies have reported an increasing Incidenceof CD to the magnitude of two to fivefold over the past 50 years [3,4,5]. This increase is multifactorial either a true rise in disease incidence over time, increasing awareness of CD among clinicians and the general population, and/or greater utilization of serological tests identifying patients with either atypical presentations or who are asymptomatic. Yet, population studies suggest that the majority of patients with CD remain undiagnosed [3,6]. Microcytic anemia refractory to iron supplement, Intense symptoms of Irritable Bowel Syndrome (IBS) [8], negative serology positive response to gluten free diet are the commonest clinical scenarios suggesting diagnosis of CD [4]. On the other hand, false positive serology with absence of CD is usually related to sensitivity and specificity of CD antibodies that sometimes can be misleading in diagnosis[3], Making the main determinant of confirmed CD diagnosis relying on the dramatic improvement of intestinal (and to a lesser extent) extra intestinal symptoms in gluten free diet [6].

CD can present at any age, as typically presented in our case study,the peak period for diagnosis in adults is still in the fifth decade, with a female preponderance [7]. Many patients are wrongly diagnosed with irritable bowel syndrome for many years[9]. Stillthe most common presentation of celiac disease is iron-deficiency anemia unresponsive to iron therapy [10]. But CD is also associated with low calcium, high phosphate and hypoalbuminaemia[3].The only treatment for CD remains lifelong strict adherence to a gluten free diet [11,12]. CDhas long been associated with a wide range of neuromuscular diseases and may be the presenting feature especially with long term undiagnosed cases who are not on gluten free diet regimen, neurologic and psychiatric disorders include: cerebellar ataxia, peripheral neuropathy, epilepsy, dementia, and depression[13]. Earlier reports mainly have documented the involvement of the nervous system as a complication

of pre-diagnosed CD. However, more recent studies have emphasized that a wider spectrum of neurologic syndromes may be the presenting extra intestinal manifestation of gluten sensitivity with or without intestinal pathology. These include migraine, encephalopathy, chorea, brain stem dysfunction, myelopathy, mono-neuritis multiplex, Guillain-Barré-like syndrome, and neuropathy with positive antiganglioside antibodies. The association between most neurologic syndromes described and gluten sensitivity remains to be confirmed by larger epidemiologic studies[14].

It further has been suggested that gluten sensitivity (as evidenced by high antigliadin antibodies) is a common cause of neurologic syndromes (notably cerebellar ataxia) of otherwise unknown cause. Additional studies showed high prevalence of gluten sensitivity in genetic neurodegenerative disorders such as hereditary spino-cerebellar ataxia and Huntington's disease[14]. It remains unclear whether gluten sensitivity contributes to the pathogenesis of these disorders or whether it represents an epiphenomenon. Studies of gluten-free diet in patients with gluten sensitivity and neurologic syndromes have shown variable results[14]. Diet trials also have been inconclusive in autism and schizophrenia, the two diseases in which sensitivity to dietary gluten has been implicated [14].In our case presentation, a dramatic improvement had been observed in biochemical profile of serum iron, calcium, phosphorus, total protein, albumin levels as well as the lower limbs weakness, and sensations, but autonomic symptoms like urine retention, sweating and postural hypotension remained for several weeks after motor power recovery, Early at presentation, the low backache was of mild intensity and remained only for few days and resolved spontaneously without analgesics contrary to the severe backache classically described in typical GBS. All these atypical features in the course of GBS and its recovery makes the term GBS-like syndrome more appropriate term to our case report description as well as in the few case reports with similar conditions[15]. Further studies clearly are needed to assess the efficacy of gluten-free diet and to address the underlying mechanisms of nervous system pathology in gluten sensitivity[14].In one large study, Guillaine - Barré syndrome (GBS) acute paralysis develops, in 70% of patients 1-4 weeks after respiratory infection or diarrhea particularly campylobacter, distal Paresthesia and limb pains (often severe) precede a rapidly ascending muscle weakness from lower to upper limbs, more marked proximally than distally [15,16]. Respiratory weakness requiring ventilatory support occurs in 20% of cases. In most patients, weakness progresses for 1-3 weeks but rapid deterioration to respiratory failure can develop within hours as seen in our case study. On examination, there is diffuse weakness with widespread loss of reflexes [17]. The CSF protein is elevated at some stage of the illness but may be normal in the first 10 days [15].Treatment of GBS includes plasma pheresis and/or intravenous Immunoglobulins, which can shorten the course of the disease and reduces the need for long ventilatory support[15]. In our patient, plasmapheresis and steroids did not give any response regarding the respiratory failure and the motor weakness in daily follow up, but the dramatic improvement few days after commencing gluten free diet might explain the strong correlation between gluten sensitivity immune response and the neurological symptoms.

Conclusion:

Extra-intestinal manifestations of celiac disease are related to long standing mal-absorption of essential nutrients mainly iron, calcium and proteins, one of those neurological manifestations can be typical or atypical Guilian-Barré like syndrome, early recognition of this complication and starting Gluten free diet regimen can reverse the course of this serious complication. Further immune-pathological studies are recommended to explain the exact correlation between Gluten sensitivity and its associated neurological manifestations.

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