The many manifestations of a single disease: neuroborreliosis

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ABSTRACT
Lyme disease is a tick-borne illness that occurs in stages, multiple organs and tissue with highly variable clinical presentation. Most commonly, it presents with seventh cranial nerve palsy, often mimicking stroke and atypical rash (erythema migrans). Atypical presentations include abdominal pain, ileus/pseudo-obstruction and constipation thought to be due to autonomic dysfunction. Other less common presentations include Syndrome of Inappropriate Antidiuretic Hormones (SIADH). Lyme disease should be a differential when a patient presents from Lyme endemic areas with abdominal pain, constipation and SIADH in the setting of other causes of gastrointestinal and renal symptoms ruled out. Here we present a case of multisystem involvement in a single patient with Lyme Disease along with neuroborreliosis (neurological manifestation of Lyme disease).

1. Introduction
Lyme disease is a tick-borne illness caused by a spirochete, *Borrelia burgdorferi*. It is commonly found in North America and Europe. Clinically, the presentation is variable, most common being facial nerve paralysis. Other presentations include localized skin infection; erythema migrans, one of the first signs of Lyme disease. Early-disseminated disease can present as atrioventricular nodal blockade, carditis, neuritis (seventh nerve palsy or Bell’s palsy) and meningitis. Late Lyme disease can present as arthralgias, peripheral neuropathy and rarely, encephalopathy. Here, we present a case of a Lyme disease with classic seventh cranial nerve palsy ileus and SIADH.

2. Case presentation
A 65-year-old Caucasian female with a past medical history of estrogen receptor-positive breast cancer, on hormonal therapy presented to the Emergency Department with complaints of sudden right-sided ptosis with facial droop. Patient also complained of burning back pain radiating to the abdomen that started a week prior to presentation and was worsening over the past few days. She reported having constipation over the past few months which was partially relieved by stool softener. Patient did not have any other focal weaknesses, visual changes or slurred speech. She was admitted for a suspected stroke. She was started on valacyclovir for suspected herpes zoster infection which was discontinued shortly after. Later, she developed abdominal distension along with worsening constipation.

Vital signs were within normal limits except for mild hypertension. Initial complete blood count was normal. Complete metabolic panel showed sodium of 129 mEq/L (135–145 mEq/L) with serum osmolality of 267 mOsm/kg (227–297 mOsm/kg). Urine osmolality was 512 mOsm/kg (50–1200 mOsm/kg), urine creatinine 84.0 mg/dL and urine sodium of 106 mEq/L. Thyroid-stimulating hormone, uric acid and morning cortisol were not obtained. Initial stroke workup including Computerized Tomography (CT) scan of the head, Magnetic Resonance Imaging (MRI) of the head, carotid dopplers and echocardiogram were normal. Stroke was ruled out.

On further questioning, she reported regularly working in her backyard and exposure to wooded areas. She also recalled having a rash on her abdomen about 11 days ago that was poorly described but did not recall having a tick bite. Lyme serum antibody (IgG and IgM) was positive with confirmatory western blot resulting in multiband reactivity. She was subsequently scheduled for a lumbar puncture as her facial droop was now suspected to be due to the Lyme disease.

Cerebrospinal fluid (CSF) Lyme disease antibodies returned as more than one band detected for Lyme IgG and IgM consistent with intrathecal production; neuroborreliosis. CSF cell count showed 75% lymphocytes with high CSF protein (183.6 mg/dL) and normal glucose (57 mg/dL). CSF cytology showed ‘moderately cellular specimen consisting predominantly of polymorphic-appearing lymphocytes and monocytes and free admixed neutrophils, no metastatic carcinoma identified’ with findings suggestive...
of an aseptic meningitis. Patient was started on oral doxycycline for non-severe neuroborreliosis.

Along with the facial palsy, the patient continued to complain of diffuse abdominal pain with constipation. She had a bowel movement with enema but had persistent bloating and distension. An abdominal x-ray was obtained which showed mild ileus. CT abdomen with contrast was done which suggested constipation without obstruction or ‘significant’ ileus. Gastroenterology was consulted and recommended colonoscopy to rule out cancer (given her history of breast cancer, 13 lbs weight loss and poor appetite). Colonoscopy did not reveal any masses or identifiable cause of obstruction. At that point, clinical suspicion of a neurological disorder causing the dysmotility was suspected. She was treated with enema, laxatives and stool softener with improvement in abdominal pain and distension.

She also presented with hyponatremia and urine studies consistent with SIADH. She was treated as SIADH with fluid restriction. Sodium normalized during the hospital stay and remained normal upon discharge.

3. Discussion

Our patient had early disseminated Lyme disease based on her history, clinical presentation and serum studies. The patient met all the criteria for neuroborreliosis [1]. She lived in an endemic area, lymphocytic meningitis, immunological evidence of exposure to *Borrelia burgdorferi* with intrathecal antibody production (CSF positive for IgG and IgM Lyme antibodies). She had seventh cranial nerve palsy on presentation as well. Difference between the presentation of early vs late Lyme neuroborreliosis is discussed in Table 1. Percentage of neurological symptoms in patients of Lyme neuroborreliosis is shown in Table 2.

### Table 1. Difference in presentation of early vs late Lyme neuroborreliosis [2].

| Parameter          | Early Lyme neuroborreliosis | Late Lyme neuroborreliosis |
|--------------------|-----------------------------|-----------------------------|
| Percentage of cases | 98%                         | 2%                          |
| Appearance of neurological symptoms | Weeks to months |                           |
| Months to years    |                             |                             |
| Typical Manifestations | Bannwarth's syndrome: painful meningopolyradiculitis of the spinal nerves with unilateral or bilateral facial paresis |                           |
| Pain               | Radicular pain               | Rarely any pain             |

### Table 2. Percentage of symptoms in Lyme neuroborreliosis.

| Percentage of symptoms in Lyme neuroborreliosis | Percentage of symptoms in Lyme neuroborreliosis |
|-------------------------------------------------|-------------------------------------------------|
| Radiculitis of the spinal nerves                 | 70–75%                                          |
| Radiculitis of the cranial nerves II–XII          | 47–56%                                          |
| facial nerve paresis                             | 83–92%                                          |
| ocular muscle paresis                            | 4–9%                                            |
| Encephalitis                                     | 4–5%                                            |
| Meningitis                                       | children 30%                                     |
|                                                  | Adults 4–5%                                      |

There have been many case reports in the past highlighting the atypical presentation of Lyme disease including, but not limited to pseudo-obstruction, constipation, back pain radiating to abdomen (radiculo-neuritis) known as Bannwarth Syndrome [1,3] as a manifestation of autonomic dysfunction related to neuroborreliosis [4]. There have been case reports of radiculo-neuritis causing abdominal pain as being misdiagnosed as herpes zoster [5] as seen in our case. Our patient was also misdiagnosed initially and started on valacyclovir for suspected herpes zoster as her burning lower back pain radiating to abdomen was suggestive of it. Figures (1 and 2) showed dilated bowel loops containing fecal matter, suggestive of ileus. She also had other features of gastrointestinal manifestation such as anorexia, evident in 23% of patients per study of 314 patients with early Lyme disease [6]. Shamim et al. [7] reported two cases of patients who presented with severe constipation and hyponatremia in addition to other features of Lyme disease. Although more commonly reported cases of intestinal pseudo-obstruction and constipation are reported as acute Lyme neuroborreliosis (LNB), there has been a case report for chronic LNB as the culprit of chronic intestinal pseudo-obstruction (CIP) with a previously reported case of acute LNB causing CIP [4]. The patients can develop worsening constipation and obstipation as diagnosis and treatment is delayed, leading to diffuse bowel dilation in the absence of mechanical obstruction [8].

There have been a few case reports of SIADH associated with neuroborreliosis. SIADH has multiple etiologies including malignancy (most common), medication-induced, non-malignant pulmonary disease and less commonly, infection of the central nervous system [9]. There is thought to be an elevation of interleukin-6 (inflammatory cytokine) in CSF of patients with LNB [10] inducing the release of antidiuretic hormone (ADH). Our patient had lymphocytic pleocytosis and elevated CSF proteins in the setting of positive Lyme serology, pointing towards neuroborreliosis as the driving force behind SIADH. Although she was treated with fluid restriction, treatment for neuroborreliosis was also started which seemed to help with resolution of hyponatremia. Some case reports have reported an association between LNB and SIADH [7]. As a well-known fact, the treatment of SIADH is to identify and treat the
Figure 1. Supine view of abdominal x-ray showing significant bowel dilatation.

Figure 2. Transverse view of CT abdomen and pelvis with contrast showing dilated bowel loops and large amount of colonic fecal matter.
underlying cause. Although our patient did not present with signs of meningeal irritation, her CSF analysis was consistent with aseptic meningitis suggesting inflammation and, therefore, release of ADH causing SIADH. Therefore, Lyme disease should be suspected in patients who are from Lyme endemic areas and present with ileus and SIADH with or without cranial nerve palsy. A careful history and examination can clue clinicians into the diagnosis and appropriate treatment.

**Disclosure statement**

No potential conflict of interest was reported by the authors.

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