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Case Report

Peripheral Neuropathy in Ulcerative Colitis: A Case Report

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ABSTRACT

Inflammatory bowel diseases (IBD) were systemic disorders involving many organ systems. Besides intestinal manifestations, extra intestinal manifestations (EIMs) including neurologic complications have been reported among 6%-40% of IBD patients.
Ulcerative colitis (UC) was a subtype of IBD only affecting the colonic mucosa and sub mucosa. Although the EIMs of UC could affect any organ system, central and peripheral neurological manifestations were relatively rare.
Here, we described a case of UC and concurrent primary sclerosing cholangitis (PSC) who complained about paresthesia and weakness of his upper and lower limbs for the past two months. Through physical examination revealed decreased muscle tone in his legs and arms. Electrophysiological studies were compatible with the diagnosis of chronic mixed polyneuropathy which improved after administration of intravenous immunoglobulin (IVIG) and the patient was discharged in good general condition.
Although both immunologic and non-immunologic mechanisms we considered to play a role in development of neuropathies, further investigations were still required to accurately understand the underlying mechanism.

Keywords: Inflammatory bowel disease; Ulcerative colitis; Primary sclerosing cholangitis; Neurologic manifestations

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INTRODUCTION

Inflammatory bowel diseases (IBDs) were systemic disorders involving many organ systems and were considered as one of the most common etiologies of gastrointestinal morbidities in western countries. This category was comprised of ulcerative colitis (UC) and Crohn's disease (CD) which can be differentiated according to intestinal localization, features of inflammation and complications(1-6).

Besides intestinal manifestations, extra intestinal manifestations (EIMs) have been reported among 6%-40% of IBD patients-predominantly in CD subtype- and were of importance since they might occur prior to onset of the main disorder and their treatment has essential in preventing main morbidities(4,5,7-9).

Among various types of EIMs, neurologic complications were reported in 0.2%–47.5%

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patients with IBD-predominantly male gender-that usually appear after establishment of main diagnosis. The observed diversity could be attributed to the differences of the characteristics of study populations and admittance criteria. Moreover, neurologic complications might aggravate during flare-ups of the primary disorder or might have a progress independent of intestinal presentations.(4,9,10).

Although one of the most frequently reported neurological complications of IBD were peripheral neuropathy(PN), the underlying mechanism was weakly understood.(2,3,11) However, diverse mechanisms are hypothesized to be responsible for development of neuropathy including malabsorption, nutritional deficiencies, infections, medications, immunological abnormalities and prothrombotic states(2, 3,12,13).

Among IBD patients, UC only affects the colonic mucosa and sub mucosa in form of remissions and exacerbations and demonstrates a wide spectrum of gastrointestinal and non-gastrointestinal manifestations(2,4,14). Although the extra intestinal manifestations(EIMs) of UC could affect any organ system, central and peripheral neurological manifestations were relatively rare(1).

Here, we would like to report a case of UC and PSC who developed Chronic Inflammatory Polyneuropathy.

CASE REPORT

A 37- year -old gentleman who was a known case of UC and PSC for the last 10years presented to our clinic complaining paresthesia and weakness of his lower limbs for the past two months.

His ulcerative colitis was diagnosed in 2004 after he developed rectal bleeding, tenesmus, abdominal pain, and arthralgia and weight loss. Colonoscopy and colonic biopsy established UC confined to the recto sigmoid. Firstly in 2004, he went under treatment with Sulfasalazine (2 gr/day), and folic acid (1mg/day).Moreover, he received metronidazole (1g/day) for a one month period. During the course of his treatment, his therapeutic regimen was discontinued and changed into Mesalazine due to infertility caused by sulfasalazine.

Further paraclinical works up including blood chemistry analysis, hormonal panel, urine analysis,viral and immunologic markers during follow ups revealed high levels of liver transaminases and alkaline phosphatase. An abdominal spiral computed tomography and endoscopic retrograde cholangiopancreatograsphy (ERCP) had been performed and the diagnosis of concurrent PSC was also confirmed. Hence, a stent was placed and his laboratory tests were normalized. The stent was removed two years after placement. Moreover, two subsequent stents were placed with 4year intervals during the last 6 years and his last stent was removed four months prior to his current presentation.

Medications on admission on 2014 included: Mesalazine 2gr PO daily and Ursodeoxycholic acid BD. He had no known drug allergies.

At presentation the C Reactive protein (CRP) was 60 mg/l, Erythrocyte sedimentation rate (ESR) and D-dimer were 34mm/h and 343 ng/ml, subsequently. Other blood test results were demonstrated on table 1.

He complained about weakness of arms and legs. On examination, respiratory and cardiovascular systems were normal. On the neurologic examination, mental status and cranial nerve functions were normal, as were ocular fundus copy and cerebellar tests. Weakness and decreased muscle tone were determined in his legs and arms. Muscle strength was 3+ to 4+ in the arms and 2+ to 3+ in the legs by manual muscle testing. Perceptions of temperature, touch and vibration were normal. Deep tendon reflexes were decreased and no pathologic reflex was detected.

The magnetic resonance imaging (MRI) of brain and cervical spine show normal findings, subsequently a lumbar puncture was performed which yielded into drainage of a clear colorless fluid with following characteristics: RBC=0, WBC=0, glucose=65 mg/dl and protein=105mg/dl.

Additionally, nerve conduction velocities (NCVs) and Electromyography (EMG) of motor and sensory nerves in upper and lower extremities were performed. The findings were compatible with the diagnosis of chronic mixed mainly axonal polyneuropathy with conduction block in left common proneal nerve.

Considering the aforementioned data, the patient was diagnosed to suffer chronic progressive distal polyneuropathy due to UC and treatment with intravenous immunoglobulin (IVIG) 25gr daily was administered for 5 days. Consequently, the patient was discharged with improvement of symptoms.

DISCUSSION

The most common form of IBD worldwide is UC which only involves mucosa and has less susceptibility for developing complications. Most frequently involved organs outside the alimentary tract were the hepatobiliary system, eye, skin and joints thus UC was known to be

Table 1: **Complementary laboratory evaluations.**

Biochemistry		**Viral markers**		**Immunologic markers**	
Fasting blood glucose(FBS,mg/dl)	92	Hepatitis C virus (HCV) Antibody	Negative		
Urea(mg/dl)	27	Human immunodeficiency virus (HIV) test	Negative		
Creatinine(mg/dl)	1.07	Hepatitis B virus surface antigen(HBs Ag)	Negative		
Uric acid (mg/dl)	2.6	**CSF analysis**			
Cholestrol(mg/dl)	142	appearance	clear		
LDL- cholesterol(mg/dl)	76	color	colorless		
HDL-cholestrol(mg/dl)	32	Glucose(mg/dl)	65		
Calcium (mg/dl)	9.9	Protein(mg/dl)	105		
Phosphorus(mg/dl)	4.6	Total cell count	zero		
Na(mEq/L)	139.5	RBC	zero		
K(mEq/L)	4.21	WBC	zero		
Alkaline phosphatase(IU/L)	175				
Alanine transaminase(ALT,IU/L)	15				
Aspartate transaminase (ASL,IU/l)	20				
Partial thromboplastin time (second)	35				
Hormonal panel		**Urine Analysis**		**Stool exam**	
Thyroid stimulating hormone (TSH,mIU/ml)	0.4	White blood cell (WBC,number/high power field)	0-1	Occult blood(OB)	Negative
T4(mIU/ml)	10.3	Red blood cell (RBC,number /high power field)	0-1	White blood cell(WBC)	Negative
T3(ng/ml)	1.7	Cast	none	Red blood cell(RBC)	Negative

a systemic disorder. The EIMs may occur prior to or parallel with the intestinal manifestations.(14)

While, EIMs have been reported in 42% of UC patients neurologic involvement was rarer than that of other systems.(15,16) One of the most frequently reported neurologic complications related to IBD is PN which can be demonstrated as acute or chronic demyelinating neuropathies or non-demyelinating pure sensory, motor or mixed axonal neuropathies(10, 14).

Although, immunologic mechanisms play a major role in development of neuropathies, several non-immunologic mechanisms also contribute in advance of aforementioned condition.(10,17) As an illustration to mentioned fact, administration of metronidazole, sulfasalazine and tumor necrosis factor-alpha antagonists has been associated with development of neurological manifestations.(18,19) Additionally, deficiency of micronutrients including Vitamin B12 due to mal absorption and colectomy are demonstrated to be capable of inducing neurologic complications(4,9).

Various therapeutic options including immunosuppressive and immunomodulatory therapies in addition to plasmapheresis have been proposed to be effective on PN associated with IBD(14, 20).

Review of literature in this regard has demonstrated the following facts. In a large study performed by Bernstein et al on 8072 patients with IBD (3879 with UC and 4193 with CD), PN was reported in 2.4 and 2.34% of UC and CD patients, respectively(21).

In another study performed by Larrode et al.(22), among four patients suffering from sensorimotor neuropathy parallel to the course of IBD, were found to suffer from vitamin B-12 deficiency and metronidazole neurotoxicity while activity of IBD f was found to be responsible in the other two patients itself.

In another study performed by Greco et al, axonal sensorimotor polyneuropathy was reported in a six-year-old girl with recovery after administration of three-month period steroids(19).

In another study performed by Gondim et al., PN was reported as a spontaneous extra intestinal manifestation of IBD in 33 patients, 15 of whom had UC. Additionally, a long lag period was reported between the diagnosis of IBD and the development of neurological symptoms(13).

Our patient was found to have mixed axonal polyneuropathy in the absence of gastrointestinal symptoms of UC considering the clinical findings and nerve conduction studies. He only had sulfasalazine and metronidazole for one month about ten years ago which rules out their probable association to his recent

condition and on admission he was taking TNF-alpha antagonist and was receiving requisite supplements. His blood level of Vitamin B12 was in normal range. For these reasons, we conclude that our patient's neuropathic manifestations were associated with UC.

To summarize d their frequency, neurologic complications are usually poorly recognized. It is important for gastroenterologists to be familiar with the different presentations, differential diagnosis and therapeutic possibilities of neurological manifestations. Moreover, they should lower their threshold for detailed neurologic evaluation in patients with new symptoms.

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