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Case Report

Internal Medicine Section

Ulcerative Colitis and Guillain-Barré Syndrome: Co-existence or Complication

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ABSTRACT

Ulcerative Colitis (UC) is a chronic recurring inflammatory illness of the gut, whereas Guillain-Barré Syndrome (GBS) is a sudden onset of muscular weakness produced by the immune system attacking the peripheral nerve system. Both UC and GBS can be caused by immune system dysfunction and can co-exist. There are just a few case reports in the literature of GBS occurring in UC patients. However, present case (52-year-old Indian female) is an unusual instance of UC that developed during GBS on Intravenous Immunoglobulin (IVIG) treatment.

Keywords: Inflammatory illness, Intravenous immunoglobulin, Muscular weakness

CASE REPORT

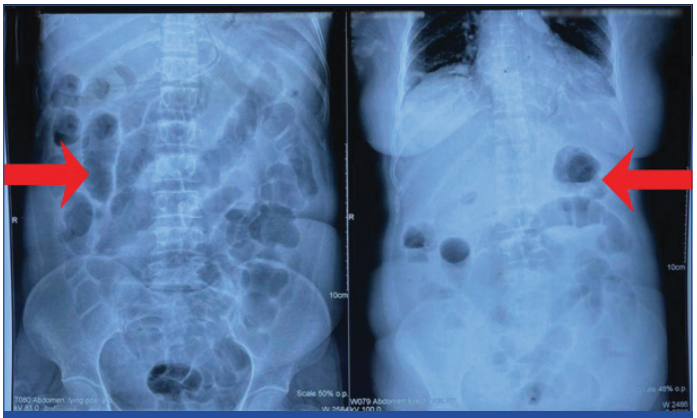
A 52-year-old Indian female, diabetic and hypertensive for two years, presented to emergency with complaints of progressive weakness of all the limbs (lower limbs followed by upper limbs) which developed over two days, which was associated with difficulty in holding the head up. The quadriparesis was acute onset, symmetrical, flaccid, and associated with tingling sensations in hands but without any bladder bowel involvement. The patient noticed the difficulty in keeping her head up, which was acute in onset and progressed to the extent that she was not able to lift the head from bed while being supine. Coinciding with the limb weakness, she noticed difficulty in pronouncing certain words, associated with difficulty in swallowing, both for solids and liquids. There were no complaints of drooping of eyelids, double vision, or facial weakness. There was no history of diurnal variation of weakness or exercise induced weakness. Subsequently, patient developed difficulty in breathing 10-12 hours prior to presentation to the centre. It was acute onset, progressive, present even at rest, not associated with palpitations or chest pain. She denied history of any vaccinations or animal bite in the recent past. There was no history suggestive of passing dark or reddish-brown urine.She never had complaints of joint pains, oral ulcers, hair loss, rashes, and photosensitivity in the past. Approximately a fortnight before the onset of these symptoms, she had history of low-grade intermittent fever, documenting up to 101°F, associated with loose stools and vomiting which was relieved with medications.

The physical examination revealed an increased respiratory rate of 28 and single-breath count of 12, while the rest of the vitals were normal. On neurological examination, the patient was conscious and oriented. The bilateral pupils were equal in size and sensitive to the light reflex, eye movements were normal, and nystagmus was not observed. Bilateral nasolabial grooves were symmetrical. Gag reflex was absent. There was no contraction observed in bilateral palatopharyngeal folds with uvula being central. There was no tongue deviation during tongue protrusion. The muscle strength of bilateral upper limbs was 2/5, and it was at 3/5 in bilateral lower extremities. There was weakness in neck flexion. Superficial and deep sensory modalities of limbs could not be evaluated in view of immediate intubation on presentation. Absence of biceps reflex, triceps reflex, knee reflex, and ankle reflex was observed. The finger-to-nose test and Romberg test could not be assessed due to weakness. Meningeal signs and pyramidal signs were negative. Abdomen was distended but soft, no organomegaly was palpable and bowel sounds were sluggish.

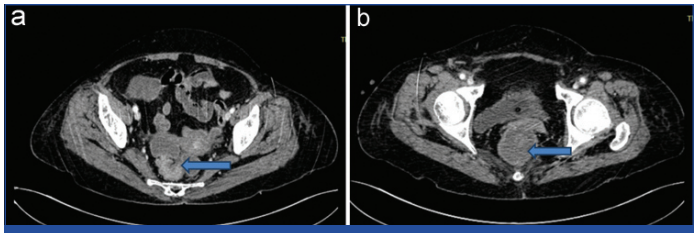
Complete blood count, kidney and liver function tests and arterial blood gas analysis were within normal limits at presentation. Urine routine microscopy showed no abnormality. Cerebrospinal fluid (CSF) analysis showed no cells but protein of 112 mg/dL. The acid-fast staining, ink negative staining, and CSF culture were all negative.

In view of severe respiratory weakness patient was intubated and mechanically ventilated. Patient was immediately started on IVIG at 2g/kg over five days in view of clinical diagnosis of GBS. Despite the above treatment, patient's paresis worsened. Nerve conduction study was done which showed decreased sensory and motor amplitudes suggestive of Acute Motor Sensory Axonal Neuropathy (AMSAN) variant of GBS confirming the clinical diagnosis. Hence, IVIG was continued.

On day four of admission patient had an episode of massive per rectal fresh bleeding. On proctoscopy, no haemorrhoids were seen. Adrenaline-soaked gauze packing was done for control of bleeding. However, the patient continued to bleed profusely. Multiple packed cell transfusions were done to maintain volume, while an urgent Contrast Enhanced Computed Tomography (CECT) abdomen with angiography and X-ray was done which showed hypodense mural thickening of rectum, sigmoid colon, and descending colon with loss of haustra. Mild enhancing circumferential mural thickening in descending colon and distal half of transverse colon with surrounding mesenteric fat stranding and heterogeneity. Homogenously enhancing circumferential mural thickening of sigmoid colon was also noted [Table/Fig-1,2]. Findings represented inflammatory bowel disease-ulcerative colitis but no active bleeding was found on angiography.



[Table/Fig-1]: X-ray abdomen erect and supine showing dilated bowel loops (red arrows).



[Table/Fig-2]: CECT abdomen axial section showing mural thickening of the sigmoid colon (a) and rectum (b).

Stool cultures for bacterial pathogens and serologic tests for amoebiasis were negative. Colonoscopy was contemplated but could not be done because of the poor general condition of the patient. The tumour markers (CEA, CA 19-9, alpha fetoprotein) came out to be negative. Hence, she was started on intravenous methylprednisolone pulse therapy along with 5-aminosalicylic acid (5-ASA) via Ryle's tube. An autoimmune profile was sent which showed elevated Perinuclear Antineutrophil Cytoplasmic Antibodies (p-ANCA) levels (34 U/mL). Serum calprotectin levels were elevated in index patient (617 µg/g). The patient continued to bleed profusely and developed hypovolemic shock. An emergency laparotomy was planned while the patient was managed with fluid bolus, Packed Red Blood Cells (PRBC) transfusions, inotropes and antifibrinolytics. The patient could not be taken up for surgery and finally succumbed to her illness.

DISCUSSION

The GBS is an acute, usually fulminant polyradiculopathy of autoimmune aetiology which manifests as rapidly progressive and are flexic motor paresis with or without sensory impairment. The event is usually preceded by an antecedent respiratory or gastrointestinal infection in approximately 70% of cases [Table/Fig-3] [1,2].

Guillain-Barre Syndrome	
Aetiology	Infection- *Campylobacter jejuni*, Cytomegalovirus, Ebstein Barr Virus Vaccinations- H1N1,
Clinical Manifestations	Rapidly evolving are flexic motor paralysis with or without sensory disturbance, with bladder involvement
Investigations	Nerve conduction studies
Treatment	i.v. Immunoglobulin

[Table/Fig-3]: Aetiology, clinical manifestations, investigations, treatment of Guillain-Barre syndrome.

The UC is a chronic, severe disease characterised by inflammation of the intestinal mucosa, mediated by autoimmune mechanisms. Commonly diagnosed in 3rd to 4th decade, it usually has a relapsing-remitting course with bloody diarrhoea and abdominal pain as the chief features during exacerbations [Table/Fig-4] [3,4].

Apart from the bowel involvement, UC is notorious for the extraintestinal manifestations seen in upto 40% of cases which commonly include joints, skin, eyes and liver. Neurologic manifestations in UC are even rarer [5].

Ulcerative colitis	
Aetiology	Genetics Defective immune regulation Commensal microbiota
Clinical Manifestations	Diarrhoea Rectal bleeding Tenesmus Passage of mucus Crampy abdominal pain.
Investigations	Colonoscopy Contrast CT Magnetic Resonance Imaging (MRI)
Treatment	5-aminosalicylic acid Steroids Azathioprine Methotrexate Cyclosporine

[Table/Fig-4]: Aetiology, clinical manifestations, investigations, treatment of ulcerative colitis.

The possibility of GBS and UC co-existing can be considered as both follow a similar immunological phenomenon [6,7]. However, concomitant GBS and UC remains a gray area till date.The probable mechanisms of GBS in UC elucidated are

- UC mediated vasculitis.
- Vitamin deficiencies- malabsorption leading to Vitamin B12 deficiency.
- Opportunistic infections due to immunosuppression-predisposes to infections by *Campylobacter*, Ebestein Barr Virus.
- Toxic metabolites.

Previously, GBS was considered as an extraintestinal manifestation of UC presenting in the remission phase, with limited case reports in the literature, however the theory was subsequently refuted [8-10].

Bouchra A et al., proposed the role of Tumour Necrosis Factor (TNF)-α blockers in the pathogenesis of GBS developing in patients of UC. TNF-α possesses immunoregulatory properties and its insufficiency results in the failure to regress myelin-specific T-cell activity and activated T-cells have a higher chance of survival. Endogenous TNF-α is suppressed by repeated injections of a TNF-α antagonist, which promotes T-cell proliferation and cytokine release. TNF-α antagonists are hypothesised to promote autoimmune responses by modifying antigen-presenting cell function, increasing T-cell receptor signalling, and lowering auto-reactive T-cell death [11]. This was further corroborated by the Adverse Events Reporting System of the United States (US) Food and Drug Administration, as 17 instances of GBS patients were attributed to the use of anti tumour necrosis factor-a monoclonal antibody [12].

As regards to UC developing after GBS, literature search revealed only a single case report till date. Tominaga K et al., reported a case of 39-year-old male who presented with GBS, with no previous history suggestive of gastrointestinal symptoms, and he was treated with IVIG. The patient developed bloody diarrhoea two weeks after the last administration of IVIG. He was labelled as a mild case and was treated with 5-ASA. The mechanism proposed by them was that certain type of viral modulation and immunomodulatory drug, such as IVIG, influenced the manifestation of a mild UC [13].

This patient also had no previous gastrointestinal symptoms, presented with symptoms and signs suggestive of GBS which was confirmed by nerve conduction studies. Peculiar features in this case were a fulminant presentation of initial episode of UC which seemed refractory to treatment and massive per rectal bleeding after IVIG administration. This paper postulate the hypothesis that IVIG administration incited the dormant autoimmune processes in the patient which resulted in manifestation of a florid UC.

CONCLUSION(S)

The GBS and UC share an immunopathophysiology, and the existence of GBS as an extraintestinal manifestation has been documented occasionally in the literature. However, in index case, the initial symptom of GBS preceded the first symptom of UC, raising the question of whether GBS and UC may co-exist. More research may be required to determine the probable processes behind the co-existence of the two autoimmune diseases. This case report and literature review will aid in the correct and timely diagnosis of co-existing GBS and UC.

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