Concomitant Guillain–Barré Syndrome in a young Sri Lankan male with severe ulcerative colitis

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Abstract

Background: Guillain–Barré Syndrome is an immune mediated polyneuropathy. Ulcerative Colitis is an immune mediated chronic inflammatory condition mainly of the large intestine. Guillain–Barré Syndrome can present as a rare extraintestinal manifestation of Ulcerative Colitis when in remission or in a relapse. However, the concomitant presentation of Guillain–Barré Syndrome during a relapse of Ulcerative Colitis is very rare and only a few cases are reported to date.

Case presentation: A 24 year old young male diagnosed of Ulcerative Colitis presented with bloody diarrhea of frequency more than six times a day. He had been in clinical remission even after defaulting treatment for more than a year. He had also noted difficulty in walking prior to admission to the hospital. He was managed as for a severe relapse of Ulcerative Colitis and Guillain–Barré Syndrome. Appropriate management of both the illnesses helped him to recover.

Conclusion: Immune mediated diseases can have rare coexisting presentations. We report a case of Ulcerative Colitis with concomitant Guillain–Barré Syndrome. It is essential to be open minded and timely, appropriate treatment led to successful management of both the illnesses.

Keywords: Ulcerative colitis, Guillain–Barré Syndrome, Acute Motor Axonal Neuropathy, Inflammatory bowel disease, Case report

Background

Ulcerative colitis is a chronic inflammatory disease of the colon with relapses and remissions. Its incidence and prevalence are increasing globally including Asia [1]. Neurologic complications of inflammatory bowel disease are not very common [2]. Guillain–Barré Syndrome is considered as one of the rare extraintestinal manifestations of inflammatory bowel disease [3]. Guillain–Barré Syndrome is an immune mediated, monophasic acute paralyzing illness usually provoked by a preceding infection. Out of the different variants of Guillain–Barré Syndrome, Acute Motor Axonal Neuropathy (AMAN) is a primary axonal form of Guillain–Barré Syndrome. It is thought that genetic susceptibility, aberrant self-recognition and immunopathogenic autoantibodies against organ-specific cellular antigens shared by the colon and extra-colonic organs play a role in contributing to the pathogenesis and development of the extra intestinal manifestations [4]. The first documentation is in 1985 by Zimmerman where Guillain–Barré Syndrome had occurred in patients who were in remission [5]. To date, only about 9 cases are reported in patients who were in remission [5]. To date, only about 9 cases are reported according to the best of our knowledge. We present a young patient who...
had not received any TNF alpha therapy previously pre-
senting with Acute Motor Axonal Neuropathy (AMAN) 
variant of Guillain–Barré Syndrome along with a relapse 
of Ulcerative Colitis, a combination which has not been 
reported in literature.

Case presentation
Our patient is a young, 24 year old male, diagnosed with 
estensive colitis of Ulcerative Colitis in mid-2020. He 
had defaulted treatment and not attended to the rou-
tine clinic after three months following the diagnosis. 
However, he had been in clinical remission for almost a 
year. He was initially treated with oral prednisolone, sul-
fasalazine and azathioprine. This time he presented with 
clinical features suggestive of a relapse of severe ulcera-
tive colitis. There was no evidence of toxic megacolon or 
other detrimental complications. Cessation of smoking 
was identified as a potential precipitating factor in addi-
tion to the poor compliance. He did not have any con-
comitant extra intestinal manifestations. He had marked a 
unintentional weight loss of about 31% from his 
baseline body weight within a month. One week prior to 
admission he had noted difficulty in walking but was able 
to mobilize with support.

He had marked bilateral lower limb edema with general 
unwellness. He was afebrile and did not have tachycardia, 
hypotension or a tender abdomen. Lower limb examina-
tion revealed bilateral symmetrical proximal more than 
distal weakness with diminished reflexes and preserved 
sensation without sphincter involvement. There was no 
significant muscle wasting or fasciculations. Also, he had 
symmetrical proximal more than distal upper limb weak-
ness with diminished reflexes and all sensory modalities 
were intact. His cranial nerves, higher functions and cer-
ebellar examinations were normal. He had a weak neck 
muscle power and cough effort but was not in respira-
tory distress. He maintained his vital parameters with 
no desaturation or fluctuation of blood pressure or pulse 
rate.

Full blood count revealed a moderate hypochromic 
microcytic anemia of 9.9 g/dl (reference value 12–15 g/
dl). His inflammatory markers such as CRP was 115 mg/L 
(reference value 0–5 mg/L) and ESR was 45 mm/hr (ref-
tence value 1–13 mm/hr). The albumin level was very 
low of 1.3 g/dl (reference value 3.5–5.5 g/dl). His renal 
functions were normal and urine full report did not 
reveal albuminuria. He had a mild hypocalemia and thy-
roid functions were normal. Stool cultures excluded other 
enteric infections and Clostridium difficile toxins were not detected. Flexible 
sigmoidoscopy revealed severe mucosal inflammation 
(Mayo score of 3 on endoscopic appearance as shown in 
Fig. 1) and histology excluded concomitant CMV colitis 
and confirmed Ulcerative Colitis flare. Nerve conduction 
study as in Table 1 revealed Acute Motor Axonal Neu-
ropathy type of Guillain–Barré Syndrome. CSF analy-
sis confirmed protein cell dissociation with absent cells 
and protein of 62 mg/dl. Covid 19 infection was safely 
excluded as well as other viral aetiologies as CMV, EBV, 
HIV.

The relapse of Ulcerative Colitis was managed with 
intravenous hydrocortisone of 100 mg every 6 hourly, 
subcutaneous enoxaparin as for DVT prophylaxis, intra-
venous fluids and albumin. He showed a significant clinical 
improvement by day 3 along with a rapid decline of 
CRP being less than 45. Subsequently, he was managed 
with oral prednisolone and later on with sulfasalazine 1 g 
bd and azathioprine 50 mg daily. Since he had many poor 
prognostic factors such as young age of onset, extensive 
colitis requiring hospitalization, low albumin, high CRP, 
Tofacitinib 10 mg twice a day was commenced as he was 
not a suitable candidate for TNF alpha blockers due to 
concomitant GBS and other biological agents as vedoli-
zumab or ustekinumab were not available.

Guillain–Barré Syndrome was managed with IV 
immunoglobulin 0.4 g/kg for five days by which his 
lower limb proximal muscle weakness improved. 
His vital capacity and other vital parameters were 
monitored daily. He received regular chest and limb

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Fig. 1 Endoscopic appearance of severe ulcerative colitis
physiotherapy. By day five there was an improvement in the proximal lower limb weakness. His hematological and biochemical test results too improved as depicted in the following Table 2. He was followed up at the clinic and Ulcerative Colitis was in remission with Tofacitinib, prednisolone tapering regime, sulfasalazine and azathioprine.

### Discussion and conclusions
We present a young male who presented with a relapse of Ulcerative Colitis subsequently developing Guillain–Barré Syndrome. Also he had a significant weight loss and generalized body weakness. Timely, appropriate diagnosis and management aided in marked improvement and recovery. This case demonstrates a rare clinical

#### Table 1 Nerve conduction study

| Site                  | Latency (ms) | Amplitude (mV) | Area (Vms) | Segment                   | Distance (mm) | Interval (ms) | NCV (m/s) | NCV N D |
|-----------------------|--------------|----------------|------------|---------------------------|---------------|---------------|-----------|---------|
| **Motor Nerve Conduction Study** |              |                |            |                           |               |               |           |         |
| Ulnar R               |              |                |            |                           |               |               |           |         |
| Wrist                 | 2.37         | 2.86           | 25.54      | Wrist                     | 2.37          |               |           |         |
| Elbow                 | 6.69         | 2.82           | 23.01      | Wrist-Elbow               | 6.69          |               |           |         |
| Ulnar L               |              |                |            |                           |               |               |           |         |
| Wrist                 | 2.49         | 2.42           | 12.55      | Wrist                     | 2.49          |               |           |         |
| Elbow                 | 6.81         | 2.31           | 12.41      | Wrist-Elbow               | 6.81          |               |           |         |
| Peroneal R            |              |                |            |                           |               |               |           |         |
| Ankle                 | 2.85         | 900.00 uV      | 6.78       | Ankle                     | 2.85          |               |           |         |
| Head of Fibula        | 10.25        | 880.00 uV      | 7.92       | Ankle-Head of fibula      | 10.25         |               |           |         |
| Tibial R              |              |                |            |                           |               |               |           |         |
| Ankle                 | 6.95         | 2.92           | 11.65      | Ankle                     | 6.95          |               |           |         |
| Peroneal L            |              |                |            |                           |               |               |           |         |
| Ankle                 | 2.6          | 820.00         | 5.44       | Ankle                     | 2.6           |               |           |         |
| Head of Fibula        | 10.05        | 780.00         | 5.33       | Ankle-Head of fibula      | 10.05         |               |           |         |
| Tibial L              |              |                |            |                           |               |               |           |         |
| Ankle                 | 4.25         | 4.56           | 21.58      | Ankle                     | 4.25          |               |           |         |
| **Nerve Stim.site**   |              |                |            |                           |               |               |           |         |
| **F Wave Study**      |              |                |            |                           |               |               |           |         |
| Tibial R              | Ankle        | 47 ms          | 5.2 ms     | Absent                    |               |               |           |         |
| Tibial L              | Ankle        | 5.2 ms         | 5.2 ms     | Absent                    |               |               |           |         |
| Ulnar R               | Wrist        | 2.6 ms         | 2.6 ms     | 0/9.0% Repeaters          |               |               |           |         |
| Ulnar L               | Wrist        | 2.75 ms        | 2.7 ms     | 0/8.0% Repeaters          |               |               |           |         |
| **Sensory Nerve Conduction Study** |              |                |            |                           |               |               |           |         |
| Ulnar, R              | Wrist        | 1.56 ms        | 26.30 uV   | 1.33 uVms                 | 1.56 ms       |               |           |         |
| Ulnar, L              | Wrist        | 1.79 ms        | 31.10 uV   | 0.68 uVms                 | 1.79 ms       |               |           |         |
| Sural, R              | Sural        | 2.42 ms        | 7.40 uV    | 0.10 uVms                 | 2.42 ms       |               |           |         |
| Sural, L              | Sural        | 2.21 ms        | 9.40 uV    | 0.56 uVms                 | 2.21 ms       |               |           |         |
| Radial, R             | Forearm      | 1.15 ms        | 33.40 uV   | 0.75 uVms                 | 1.15 ms       |               |           |         |
presentation of coexistent Ulcerative Colitis with AMAN variant of Guillain–Barré Syndrome.

Extra intestinal manifestations occur in 5% to 50% of all patients with inflammatory bowel disease. The severity and occurrence of extra intestinal manifestations and their correlation with intestinal-inflammatory bowel disease activity vary, but most extra intestinal manifestations are directly associated with an ongoing intestinal flare [6].

The association of Ulcerative Colitis with neurologic involvement is rare and often controversial [7]. According to A. Lossos out of the IBD patients who developed neurologic manifestations; 74% had developed after a mean of 5.7 years following development of IBD and only 10% during an IBD exacerbation. The neurologic manifestations documented were in the form of myelopathy, myopathy, myasthenia gravis and cerebrovascular disorders [8]. Peripheral neuropathies related to IBD seems to be more frequent in Ulcerative Colitis, with a reported incidence of 1.9% but it seems that it is associated with a lower rate of demyelinating forms as compared to Crohn’s Disease [9].

Guillain–Barré Syndrome is one form of neurological manifestations which can occur both in remission or a relapse of Ulcerative Colitis [10]. The exact pathogenesis of Ulcerative Colitis with Guillain–Barré Syndrome is unclear. It may be related to the following factors: Ulcerative Colitis-associated vasculitis, post infection immunity, malnutrition, toxic metabolites, vitamin deficiency, and thrombotic disease [11]. It is also postulated that since both Ulcerative Colitis and Guillain–Barré Syndrome are autoimmune diseases there may be similar autoimmune mechanisms in the development of both these diseases. However, association of Guillain–Barré Syndrome and Ulcerative Colitis is extremely rare and only a few cases have been reported [12, 13]. There are different variants of Guillain–Barré Syndrome of which Acute Motor Axonal Neuropathy (AMAN) is one such type. Our case was an Acute Motor Axonal Neuropathy (AMAN) form of Guillain-Barré Syndrome with a relapse of Ulcerative Colitis which has not been reported up to date so far. Most cases have antecedent infection with Campylobacter jejuni and many have antibodies directed towards GM1 ganglioside-like epitopes. The mechanism of nerve-fiber injury has not been defined yet. Acute Motor Axonal Neuropathy (AMAN) is a novel disorder caused by an antibody- and complement-mediated attack on the axolemma of motor fibers [14]. The nerve conduction study was in favor of axonal injury in our patient.

Infliximab, a Tumor Necrosis Factor (TNF) alpha blocker, is known to be an effective treatment for Ulcerative Colitis. There are many cases documented in the literature mainly by the US Food and Drug Administration where Guillain–Barré Syndrome had developed after the initiation of anti-Tumor Necrosis Factor (TNF) alpha therapy [15, 16]. Interestingly, our patient had not received infliximab therapy at any time.

Vedolizumab is an anti integrin, a humanized IgG1 monoclonal antibody against a4b7 integrin that inhibits leukocyte adhesion of MAdCAM-1 specific to the bowel. It is recommended for the treatment of moderate to severe ulcerative colitis for those who have failed to recover from conventional and/or biological therapies. It acts by blocking the p40 subunit of IL-12 and IL-23 and can be used in naïve subjects or patients previously exposed to biologics [17]. The adverse effects of ustekinumab on the nervous system are very minor. However, both these agents are scarce and very costly in a developing country as ours. Our next choice was Tofacitinib which is an orally administered small molecule and a Janus kinase inhibitor. Tofacitinib is one of the drugs emerging into the limelight for the management of moderate to severe Ulcerative Colitis. It is known to be cost effective and also effective in achieving endoscopic response, endoscopic remission, and mucosal healing [18].

It is important to exclude other causes of weakness in a patient presenting with diarrhea; mainly electrolyte

| Table 2 | Comparison of investigations before & after treatment of severe UC |
|-------------------|--------------------------|
|                   | Pre Treatment | Post Treatment |
| WBC (x 10^9/L)    | 24           | 13            |
| Hb (g/dL)         | 9.9          | 10.9          |
| Pt (x 10^9/L)     | 571          | 437           |
| CRP (mg/L)        | 115          | 43            |
| ESR (mm/hr)       | 45           | 22            |
| Na (mmol/L)       | 127          | 134           |
| K (mmol/L)        | 3.1          | 3.8           |
| Albumin (g/dL)    | 1.3          | 3.6           |
| Globulin (g/dL)   | 3.2          | 3             |
| ALP (mg/dL)       | 91           | 98            |
| SGPT (U/L)        | 34           | 33            |
| SGOT (U/L)        | 22           | 22            |
| GGT               | 39           | 36            |
| Cr (mg/dL)        | 0.8          | 0.7           |

It is important to exclude other causes of weakness in a patient presenting with diarrhea; mainly electrolyte
imbalances, endocrine disorders as hypothyroidism, thyrotoxicosis and iatrogenic Cushing’s syndrome. Finally, the clinical picture and the relevant investigations directed us for appropriate and timely management of our patient. Thus, our case highlights the importance of thorough clinical examination and being keen on the rare manifestations of common illnesses.

Abbreviations
DVT: Deep vein thrombosis; CSF: Cerebro spinal fluid; IBD: Inflammatory bowel disease; CRP: C reactive protein.

Acknowledgements
Not applicable.

Author contributions
JMHDJ VT TA DA were involved in managing the patient and gathering of data. JMHDJ and VT did the literature review and writing of the initial manuscript was done by JMHDJ. RP finalized the manuscript and gave expert opinion in management issues. All authors read and approved the final manuscript.

Funding
None.

Availability of data and materials
Not applicable.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Informed written consent for the publication of details and pictures was obtained from the patient. Consent form can be made available to the editor on request.

Competing interests
The authors declare that they have no competing interests.

Received: 21 August 2021   Accepted: 20 July 2022
Published online: 05 September 2022

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