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CASE REPORT

Co-existent ulcerative colitis and Guillain–Barré syndrome: a case report and literature review

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Abstract
Ulcerative colitis (UC) is a chronic and recurrent inflammatory disease involving the intestine, and Guillain–Barré Syndrome (GBS) is rapid-onset muscle weakness caused by the immune system damaging the peripheral nervous system. UC and GBS can be caused by immune system abnormalities and can co-exist. To date, there are 7 reported cases of GBS in patients with UC. However, only one patient developed UC after GBS treatment. We report a rare case of UC that appeared after intravenous immunoglobulin therapy for GBS. This case report and literature review will allow accurate and prompt diagnosis of co-existent GBS and UC.

Keywords Ulcerative colitis · Guillain–Barré syndrome · Extraintestinal manifestation · Intravenous immunoglobulin

Introduction

Ulcerative colitis (UC) is a chronic and recurrent inflammatory disease involving the intestine [1]. Guillain–Barré syndrome (GBS) is an acquired inflammatory peripheral neuropathy characterized by acute onset, cerebrospinal fluid (CSF) albumin cytological dissociation, and a clinical monophasic course with partial or total recovery. The pathogenesis of GBS is related to opportunistic infections, such as respiratory viral and campylobacter infections. In 60% of GBS cases, the onset is preceded by acute respiratory or gastrointestinal tract infection, such as *Mycoplasma pneumoniae* or *Campylobacter jejuni* infections, but in most of the cases, it is not possible to know the causative agent [2]. Most evidence supports a hypothesis of an autoimmune origin [3]. There may be similar immunological mechanisms between UC and GBC. It is reported that about 40% of patients with UC have extraintestinal manifestations [4]. Peripheral neuropathy is not a rare phenomenon in patients with UC and it is reported that neurological involvement can occur in 1.9–19.6% of UC patients [5, 6]; however, there are few reports on GBS as an extraintestinal manifestation. In 1985, Zimmerman first reported on GBS as an extraintestinal manifestation of UC [7]. To date, there are 8 reported cases of GBS as an extraintestinal manifestation of UC. Here, we report a rare case of UC that appeared after intravenous immunoglobulin treatment for GBS. Further, we summarize cases of co-existent GBS and UC that have been reported previously.

Case presentation

A 39-year-old male patient was admitted to the Department of Neurology of our hospital for numbness in the upper extremities, weakness of limbs, and aggravation and progression of symptoms from the distal to the proximal limbs. The patient had begun to show inability to hold things in his hands and showed loss of abduction and gradual opposition of fingers. At the time or presentation, he had no gastrointestinal symptoms, such as bloody and mucopurulent diarrhea or abdominal pain. The patient denied other previous diseases, such as hypertension, diabetes, hepatitis B, tuberculosis, and so on. He had no history of gastrointestinal diseases. Physical examination showed that his vital signs were normal.

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Laboratory findings on admission were as follows: total protein, 7.1 g/dL; albumin, 3.2 g/dL; hemoglobin, 13.3 g/dL; white blood cells, 10,880/mm^3; mild neutrophilic leukocytosis, 72.8%; thrombocytosis, platelets, $58.7 \times 10^4/\mu L$; and C-reactive protein level, 16.43 mg/dL (increased). Urine routine, stool routine, and stool cultures revealed normal results and tumor markers, vitamin B_{12}, and rheumatoid factor (RF) were all in the normal range. Tests for varicella zoster virus, herpes simplex virus, cytomegalovirus, and Epstein–Barr virus-DNA were all negative. Test for anti-ganglioside antibody was also negative. There were no obvious abnormalities on CT examination.

On neurological examination, the patient was fully conscious. No speech or articulation disorders were detected. Right peripheral facial paralysis and eye abduction failure were detected. There was no tongue deviation during tongue protrusion. The muscle strength was at level IV (manual muscle testing) and symmetrical in the bilateral upper limbs, at level IV in the bilateral proximal lower extremity, and at level III in the bilateral distal lower extremity. Moderate impairment of the radioperiosteal reflex, knee reflex, and ankle reflex was observed. The patient could not complete the finger-to-nose test and Romberg test. Meningeal irritation and pyramidal signs were negative. Physical examination showed a well-nourished patient with a normal abdomen.

Electromyography (EMG) showed that the ulnar nerve conduction velocity was low, with a low amplitude. CSF examination showed no findings of cell number increase, malignant cells, and protein cell dissociation. GBS was diagnosed on the basis of the patient's symptoms (weakness of limbs that aggravated and progressed from the distal limbs to the proximal limbs, peripheral facial paralysis, and eye abduction failure) and electromyographic evidence of neurogenic injury (Asbury Criteria for GBS).

The patient consented to the treatment program, involving neural protection, administration of folic acid and B12, and other supportive treatments. Concomitantly, he was treated with 2 g/day intravenous immunoglobulin (IVIG). After treatment with two courses of IVIG for 5 days (4-week interval), his limb weakness was relieved, muscle strength improved to level V, and the feeling of numbness also relieved.

Two weeks after the final administration of IVIG, diarrhea and mucous in stools were observed. Two weeks after diarrhea appeared, bloody stools started. Five days after the appearance of bloody stools, colonoscopy was performed. We detected a diffuse mucosal pattern in the total colon, which included mucosal friability, loss of vascular pattern, erythema, and edema with a purulent white spot (Fig. 1). Fecal culture test was negative. Two weeks after colonoscopy until the pathological results were obtained, the diarrhea (with occasional blood) continued. Pathological findings indicated moderate chronic active inflammatory cell infiltration and cryptitis and crypt abscess; moreover, a decline in goblet cell mucus was observed, compatible with UC pathological findings (Fig. 2). These clinical findings indicated that UC was more likely than infectious colitis. Thus, he was treated with 800 mg of 5-aminosalicylate (5-ASA) (oral administration [PO]) three times a day. After 2 weeks of 5-ASA treatment, bloody stool disappeared and the number of episodes of diarrhea was relieved from 6 times/day to 4 times/day. He was discharged as soon as his clinical condition was relieved. However, diarrhea (about 3–4 times/day) and mucous in stools continued. After 2 months of 5-ASA treatment, clinical remission occurred. After 9 months, he continued to be in the remission stage

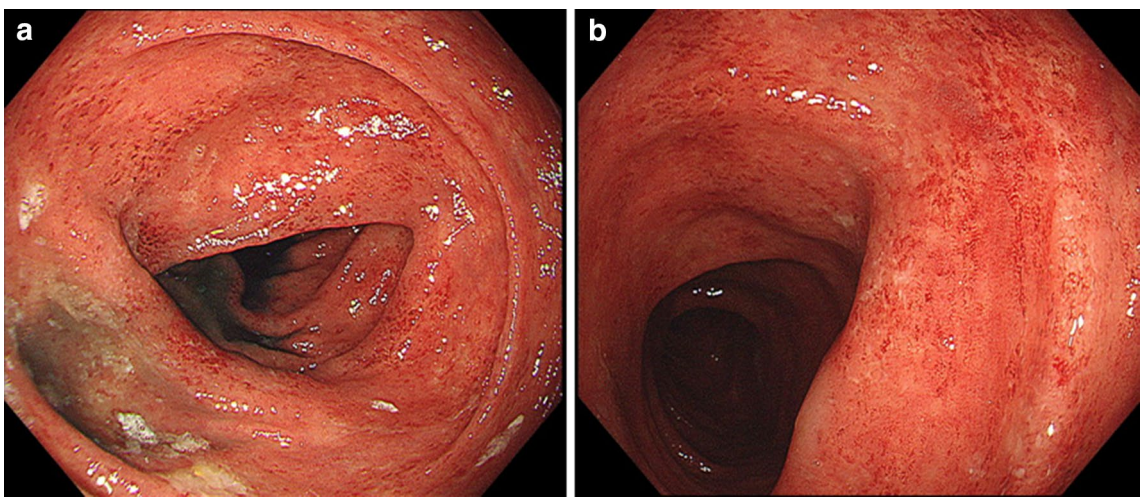

Fig. 1 Findings of colonoscopy. **a** Ascending colon and **b** sigmoid colon (black arrows indicate abnormal mucosal vascular pattern, friability, and granular changes)

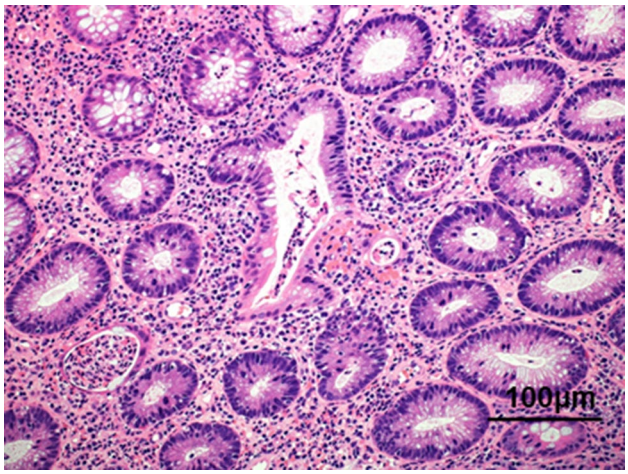

Fig. 2 Histological analysis. The hematoxylin and eosin staining of the biopsied tissue from the colon. **a** Lower magnification. **b** Higher magnification

clinically as well as endoscopically, and 5-ASA treatment was continued for maintenance; neurological symptoms have also not recurred.

Discussion

It was previously reported that GBS as an extraintestinal manifestations of UC often occurs in the remission period [4, 7–10]. Nowadays, it has been reported that GBS can also occur in the active phase of UC [11]. Moreover, only one case of a patient developing UC after GBS treatment has been reported until now [12].

We summarize the English literature on cases of UC with GBS, which include 9 cases, including our case (Table 1). The ages of the patients ranged from 31 to 74 years, and the ratio of men to women was 4:5. The period from UC onset to GBS onset was 0–30 years. Six cases of GBS occurred during UC remission; 1 case of GBS occurred in the active phase; and in 2 cases, including ours, UC onset followed commencement of GBS treatment [12]. The possible causes for GBS onset were presumed to be tapering of the steroid in 2 cases; anti-TNFα treatment in 1 case; and rubella, tuberculosis, and upper respiratory inflammation in the other cases. Of the cases of GBS, 5 were treated with immunoglobulin therapy; 2, with methylprednisolone; 2, with corticosteroids; and 1, with plasmapheresis. Upon treatment, 6 cases showed recovery and 3 cases showed improvement; only 1 case showed recurrence.

The pathogenesis of UC with GBS has not been elucidated, and there are several possible hypotheses. There is a view that the pathogenesis of GBS is related to opportunistic infections such as the respiratory viral and campylobacter

Table 1 Summary of cases reported

Clinical data of patients with UC before GBS													
Case (No.)	Ref (No)	Authors	Reporting year	Age (yrs)	Sex	Duration of UC	UC phase	Type	UC treatment	Other factors predisposing to GBS	GBS symptoms	GBS treatment	Outcome of GBS
1	7	Zimmerman J and Steiner I	1985, 1986	65	F	1.5 years	Remission	Distal	PSL, SASP +steroid enemas	Tapering of corticosteroid dose	Weakness and hypoesthesia of her legs, and within a week she became quadriparetic with urinary and rectal incontinence.	Corticosteroids	Improvement and relapse
2	7	Zimmerman J	1985	58	M	12 years	Remission	Left side	SASP→ACTH, PSL	-	Paresthesia of the legs appeared and involved the arms in a "glove and stocking" distribution.	Corticosteroids	Recovery
3	8	Masaaki Saito	1994	56	F	27 years	Remission	N/A	PSL, 5ASA	Rubella, tapering of corticosteroid dose	Weakness and hypoesthesia of her hands and lower limbs	Plasmapheresis	Recovery
4	9	Roca B	1999	69	F	30 years	Remission	N/A	5ASA	Adenocarcinoma of the colon, upper respiratory infection	Interscapular pain and lower limb paresthesia	Immunoglobulin	Improvement
5	4	Bouchra A	2009	47	F	10 years	Remission	N/A	anti-TNFα, 5ASA	Use of anti-TNFα (after 3rd dose)	Paresthesia of her hands and lower limbs	Intravenous gamma globulin	Recovery
6	11	Krystallis CS	2010	59	M	5 years	Active	N/A	PSL,5ASA,AZA	Relapse of UC	Deep tendon reflexes of upper and lower extremities were reduced bilaterally, the muscle weakness of the lower extremities was more profound proximally than distally.	IgG Immunoglobulin 2 g/kg IV, methylprednisolone	Recovery
7	10	Zhengru Liu	2017	31	F	3 months	Remission	Total	5ASA,	-	Numbness of upper extremities, weakness of limbs, and the symptoms aggravated and progressed from distal limbs to proximal limbs.	Supplying folic acid and B12, intravenous methylprednisolone	Recovery
Clinical data of patients with UC after GBS													
Case (No.)	Ref (No)	Authors	Reporting year	Age (yrs)	Sex	Duration of UC	UC phase	Type	UC treatment	Other factors predisposing to GBS	GBS symptoms	GBS treatment	Outcome of GBS
8	12	de la Torre RG	2010	74	M	Outbreak after GBS treatment	Active	Total	5ASA	Tuberculosis (treated with isoniazid, rifampicin, and pyrazinamide), IVIG	The patient suffered acute and progressive legs weakness that ascended to the arms in the first 24 hours, without sensory loss	Immunoglobulin	Recovery
9	-	our case	2018	39	M	Outbreak after GBS treatment	Active	Total	5ASA	Some infection prior to GBS, IVIG	Weakness of limbs, and the symptoms aggravated and progressed from distal limbs to proximal limbs.	Immunoglobulin	Improvement

N/A: data not available

infections [13]. Bouchra reported that the reason for the co-existence of UC with GBS is that TNFa mAb increases the risk for opportunistic infections in patients with UC [4, 14]. Moreover, the US Food and Drug Administration's Adverse Events Reporting System reported that GBS was associated with the use of anti-TNF-a mAb in 17 cases [15].

The exact pathogenesis of UC with GBS is unclear, and it may be related to the following other factors: UC-associated vasculitis, postinfection immunity, malnutrition, toxic metabolites, vitamin deficiency, and thrombotic disease [4, 9].

In this report, it is possible that GBS may be related to the extraintestinal manifestation of chronic asymptomatic pre-existing UC. In addition, there was only case showing GBS followed by UC; thus, we compared our case with this previous case (case 8 in Table 1) to check the validity of our case. In case 8, after treatment of tuberculosis, the symptom of GBS appeared. The GBS was treated by intravenous administration of immunoglobulin (IVIG; 0.4 g/kg over 5 days) therapy. Two months after IVIG therapy, the patient suffered diarrhea with bloody stool, which is not typical of infectious colitis and is consistent with UC from endoscopic and pathological findings. The UC was relatively mild and could be controlled by 5-ASA. Our case also had some infection before GBS symptoms (CRP; 16.43 mg/dL, WBC 10,800/mm^3) and GBS was treated by IVIG. Furthermore, the patient's UC symptom was relatively mild and was controlled by 5-ASA. From these points of view, our case and case 8 are quite similar and we speculate there may be some common underlying mechanism in case 8 and our case. We suspect that some infectious modulation and immunomodulatory agent like IVIG affected the occurrence of mild UC.

We believe that this case report and literature review will ensure accurate and prompt diagnosis of co-existent GBS and UC.

Compliance with ethical standards

Conflict of interest Kentaro Tominaga, Atsunori Tsuchiya, Hiroki Sato, Atsushi Kimura, Chiyumi Oda, Kazunori Hosaka, Yuzo Kawata, Naruhiro Kimura, Kazunao Hayashi, Junji Yokoyama and Shuji Terai declare that they have no conflict of interest. The authors declare that they have no current financial arrangement or affiliation with any organization that may have a direct influence on their work.

Human rights All procedures followed have been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

Informed consent Informed consent was obtained from all patients for being included in the study.

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