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A case of MOGAD with rectal adenocarcinoma: Comorbidity or paraneoplastic neurological syndrome?

Yiyi Luo [a], Gang Peng [a], Jiahua Liang [a], Xuwei Song [a], Jiayu Tang [a,b,*]

[a] The School of Clinical Medicine, Hunan University of Chinese Medicine, No. 300, Bachelor Road, Hanpu Science and Education Park, Yuelu District, Changsha, Hunan Province, 410208, China
[b] Department of Neurology, Brain Hospital of Hunan Province, 427 Furong Middle Road, Changsha, 410007, Hunan, China

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ABSTRACT

Background: Myelin-oligodendrocyte glycoprotein antibody-associated disease (MOGAD) is a rare autoimmune disease characterized primarily by central nervous system demyelination. We report a rare case of MOGAD coexisting with rectal adenocarcinoma.
Case report: A 59-year-old female presented with fever and bilateral lower limb weakness. MRI of the brain revealed abnormal signals in multiple regions of the cerebrum, brainstem, and spinal cord. Both serum and cerebrospinal fluid tested positive for MOG antibodies. The symptoms improved after steroid therapy. During hospitalization, colonoscopy and pathological examination revealed rectal cancer, which was subsequently treated surgically. After six months of follow-up, neither the tumor nor MOGAD recurred.
Conclusion: Paraneoplastic etiologies may also contribute to the development of MOGAD. To date, no cases of MOGAD associated with rectal cancer have been reported. It remains uncertain whether paraneoplastic neurologic syndrome (PNS) is involved in this patient.

1. Introduction

Neuromyelitis optica spectrum disorder (NMOSD) is an inflammatory demyelinating disease of the central nervous system, with aquaporin-4 (AQP4) as the primary target antigen located on astrocytic end-feet. It primarily affects the optic nerve, spinal cord, and certain brain regions (Lorefice and Cortese, 2024). Some patients exhibit clinical features of NMOSD but test negative for AQP4-IgG, while showing positive serum autoantibodies against myelin-oligodendrocyte glycoprotein (MOG), leading to a diagnosis of MOG antibody-associated disease (MOGAD) (Banwell et al., 2023). The phenotypic spectrum of MOGAD includes acute disseminated encephalomyelitis (ADEM), optic neuritis, transverse myelitis, cortical encephalitis, encephalopathy, and brainstem or cerebellar syndromes (Moseley et al., 2024). The pathological features of MOGAD involve ADEM-like perivenous demyelination, characterized by MOG-dominant myelin loss, oligodendrocyte injury, and activated complement and IgG deposition within white matter lesions (Cho et al., 2024).

The etiology of MOGAD remains unclear, and the potential association between tumors and MOGAD has not been sufficiently described or studied.

Here, we report the clinical and laboratory characteristics of a patient with MOGAD associated with rectal cancer. Additionally, we review the relevant literature on the relationship between tumors and MOGAD, summarizing clinical features to aid in better research, diagnosis, and treatment of the condition.

2. Case presentation

A 59-year-old female was admitted with a 1-day history of fever accompanied by bilateral lower limb weakness. She had developed fever with a maximum temperature of 38.8 °C, generalized fatigue, unsteady standing and walking, bilateral vision loss with orbital pain, but no dizziness, diplopia, cough, sputum production, nausea, vomiting, dysphagia, choking on liquids, seizures, or consciousness disturbances. Her medical history was unremarkable for autoimmune diseases or tumors, and there was no significant personal, travel, or family history.

2.1. Admission examination

On admission, her temperature was 38.8 °C. Cardiac, pulmonary, and abdominal examinations were unremarkable, and no palpable

* Corresponding author. Department of Neurology, Brain Hospital of Hunan Province, 427 Furong Middle Road, Changsha, 410007, China.
E-mail address: Tangjiayu123QAZ@163.com (J. Tang).

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superficial lymph nodes were found. Neurological examination showed the following: clear consciousness, intact higher cortical functions, vision loss on optic nerve examination, normal findings for other cranial nerves, normal muscle strength in the upper limbs, grade 3 muscle strength in the lower limbs, increased muscle tone in all four limbs, diminished sensory function, and bilateral positive Babinski's signs. Reflex testing revealed negative deep and superficial reflexes, and other signs (meningismus, Kernig's sign, Hoffmann's sign) were negative.

2.2. Laboratory findings

Blood work revealed: WBC 7.62 $\times$ 10^9/L, neutrophil ratio 75.8 %. Inflammatory markers: PCT <0.020 ng/mL, IL-6 9.700 pg/mL, CRP <2.0 mg/L. Cerebrospinal fluid (CSF) analysis showed total cell count 44 $\times$ 10^6/L (monocytes 8 %, polymorphonuclear cells 92 %), total protein 1221.9 mg/L, glucose 4.35 mmol/L, chloride 124.9 mmol/L. CSF smear tests for tuberculosis, bacteria, and India ink staining were negative. Blood and CSF cultures were also negative. Oligoclonal bands were absent. CSF antibody testing revealed MOG antibody positivity (1:1), with serum MOG antibody at 1:32. Tests for NMDAR, AMPH, Yo, AQP4, and antinuclear antibodies were negative.

2.3. Electrophysiology

Visual evoked potentials showed normal P2 latency in bilateral visual pathways, but poor P2 waveform differentiation, indicating visual pathway involvement. Brainstem auditory evoked potentials suggested bilateral auditory pathway impairment. Somatosensory evoked potentials indicated abnormal conduction in the bilateral tibial nerve pathways of the lower limbs.

2.4. Imaging findings

Enhanced MRI of the brain revealed patchy T1-and T2-weighted signal abnormalities in the pons and medulla, with slightly high T2-FLAIR signals. DWI showed no high signal, and mild enhancement was observed on contrast scans. Patchy high T2-FLAIR signals were seen around the anterior and posterior horns of the lateral ventricles, with slightly high DWI signals but no enhancement on contrast. Lesions in the basal ganglia, thalamus, periventricular white matter, and centrum semiovale appeared as patchy T1-and T2-weighted signal abnormalities, with some T2-FLAIR signal attenuation and slightly high DWI signals but no enhancement. No abnormalities were seen in the skull. These findings suggested NMOSD (Fig. 1).

2.5. Diagnosis and treatment

Based on the clinical history and auxiliary examinations, the patient was diagnosed with MOGAD. High-dose intravenous methylprednisolone (1000 mg) was administered for 10 days, followed by oral prednisone (60 mg/day) maintenance therapy. The patient's condition improved.

2.6. Additional findings

During hospitalization, the patient reported over a month of vague abdominal pain and hematochezia. Enhanced abdominal CT revealed an abnormal enhancement in the left posterior wall of the rectum. Colonoscopy and biopsy confirmed a rectal villotubular adenoma with high-grade intraepithelial neoplasia and local carcinoma, ruling out gastrointestinal bleeding caused by steroid therapy. Further evaluations, including enhanced chest, abdominal, and pelvic CT and whole-body bone scans, excluded tumor metastasis.

The patient underwent radical rectal cancer surgery under general anesthesia. Postoperative pathology confirmed a moderately to highly differentiated adenocarcinoma of the rectum, invading the superficial muscular layer, with no lymph node metastasis (0/22) or tumor involvement at the proximal or distal resection margins (Fig. 2).

2.7. Follow-up

The patient was closely monitored due to the possibility of MOGAD recurrence. After six months, follow-up brain MRI showed no recurrence (Fig. 1). The patient remained disease-free one year later, suggesting a monophasic course.

3. Discussion

The concept of neuromyelitis optica spectrum disorders (NMOSD) is evolving to encompass a spectrum of diseases, including AQP4-IgG-positive NMOSD, MOGAD, and double-seronegative NMOSD (Uzawa et al., 2024). A multicenter observational study on MOGAD reported clinical syndromes such as decreased consciousness, seizures, fever, abnormal behavior, and movement disorders (Armangue et al., 2020a).

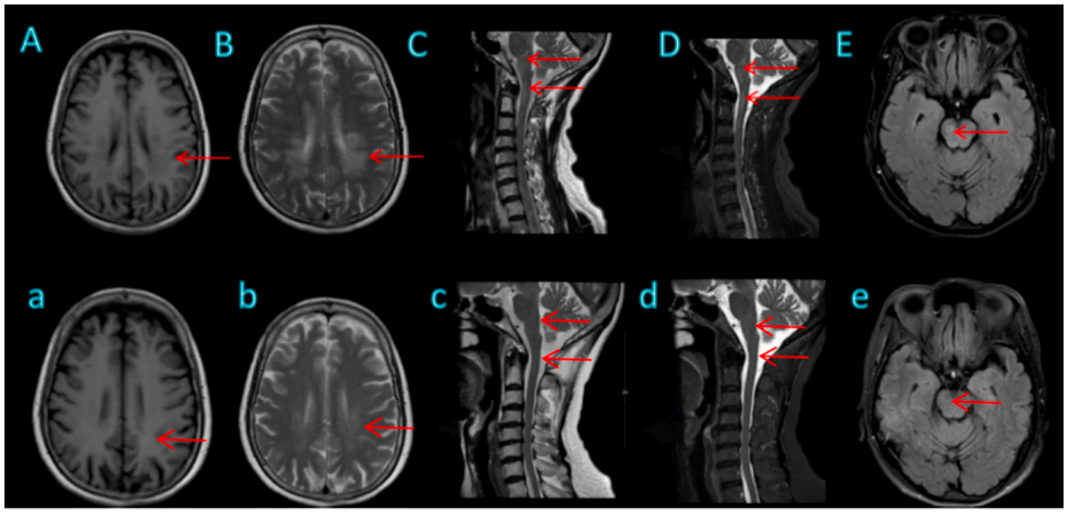

Fig. 1. Brain MRI Findings
UPPERCASE annotations indicate imaging during the onset of the disease, while **lowercase** annotations indicate imaging during the follow-up period after treatment.

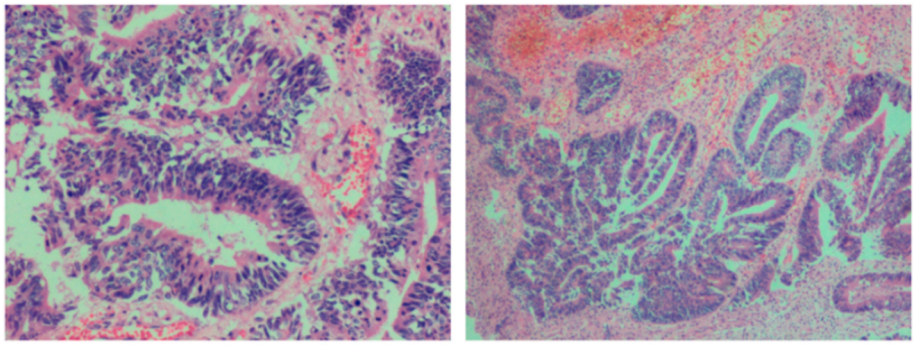

Fig. 2. Postoperative Histopathological Examination The histopathology revealed a moderately to well-differentiated adenocarcinoma of the rectum, invading the superficial muscularis layer. No cancer metastasis was detected in the perirectal lymph nodes (0/22). Both proximal and distal surgical margins were free of carcinoma.

MOGAD manifestations include isolated optic neuritis or transverse myelitis, acute disseminated encephalomyelitis (ADEM), brainstem or cerebellar syndromes, or cortical encephalitis (Du et al., 2022). According to diagnostic criteria published by an international expert group in *The Lancet* in 2023, MOGAD diagnosis requires three criteria: (A) clinical or imaging features indicative of demyelinating disease; (B) positive MOG-IgG detection; and (C) exclusion of multiple sclerosis and other conditions (Banwell et al., 2023). A hallmark of AQP4-IgG-positive NMOSD is recurrent disease with multiple clinical relapses, whereas MOGAD can present as monophasic or relapsing (Hegen and Reindl, 2020). The clinical symptoms, imaging findings, and serological antibody testing in our case align with these MOGAD criteria.

MOG is located on the external surface of oligodendrocytes, potentially allowing antibodies to access this target antigen. However, the triggers initiating MOGAD remain unclear. Studies by Jyh Yung Hor (Hor and Fujihara, 2023) suggest that infections, antecedent infections, COVID-19 vaccination, other vaccinations, autoimmune diseases, and genetic factors such as HLA associations may play a role in MOGAD. Our patient exhibited no signs of preceding infection, and despite the fever, infection markers were low, and blood and CSF cultures were negative, ruling out infectious causes.

In rare instances, malignancy has been reported in association with MOGAD, suggesting that paraneoplastic mechanisms may contribute to its pathogenesis (Moseley et al., 2024). A single-center cohort study by Milena Trentinaglia (Trentinaglia et al., 2023) indicated a potential link between tumors and MOGAD. It is noteworthy that Cohn et al. reported a case involving a patient with advanced colon adenocarcinoma and ADEM (Cohn et al., 2020). This case highlights the overlap between MOGAD and other demyelinating diseases. The similarities between this case and our patient further support the possibility of a paraneoplastic association between colorectal malignancies and MOGAD. Paraneoplastic syndromes (PS) associated with MOG antibodies have been documented in cases of breast cancer, ovarian cancer, and teratomas (Armangue et al., 2020b; Cherian et al., 2022). The mechanisms underlying these triggers—whether molecular mimicry, CNS damage-induced immunogenic MOG exposure, or MOG-specific lymphocyte activation mediated by bystander pro-inflammatory cytokines—remain uncertain.

PS in rectal cancer have been reported in conditions such as idiopathic pulmonary fibrosis, dermatomyositis, Lambert-Eaton myasthenic syndrome (LEMS), and chronic inflammatory demyelinating polyneuropathy (CIDP) (Trentinaglia et al., 2023; Haviv et al., 1998; Oliveira Santos et al., 2024; Chen et al., 2024). Although there is currently no direct evidence establishing a definitive link between PS and the immune mechanisms of early-stage CRC, studies suggest that immune escape, cytokine secretion, and molecular mimicry may potentially contribute to the development of colorectal cancer-associated PS (Goto et al., 2024; Li et al., 2025). For instance, during the early stages of colorectal cancer, activation of the SOX17 gene enables precancerous cells to become “invisible” to the immune system, evading immune surveillance. This immune evasion mechanism may also induce systemic immune instability (Goto et al., 2024). Additionally, most tumors produce cytokines, growth factors, chemokines, and proteases, which can influence or induce systemic inflammation. In murine models of localized colorectal cancer, the release of multiple inflammatory mediators in the tumor microenvironment, such as CXCL10, may alter cytokine signaling and activate related pathways, leading to sensory neuronal dysfunction (Balogh et al., 2022). Furthermore, tumor-expressed onconeural antigens (e.g., Hu and Yo proteins) exhibit molecular mimicry with peripheral nerve myelin proteins. The resulting IgG autoantibodies may attack neural structures through complement-dependent cytotoxicity. Adnan et al. proposed that colorectal cancer might produce antigens resembling or cross-reacting with surface molecules on Schwann cells, thereby triggering immune responses that damage Schwann cells and contribute to CIDP (Malik et al., 2023).

We hypothesize that the mechanism underlying MOGAD in our reported case might involve a paraneoplastic syndrome. Early stage rectal cancer may already have micrometastases or systemic changes which, despite the small tumour load, result in an early immune system response that may be sufficient to indirectly and non-specifically trigger MOG antibody production. However, since the patient declined MOG antibody testing after tumor resection, a definitive diagnosis of PNS could not be established.

To our knowledge, this is the first reported case of concurrent MOGAD and rectal adenocarcinoma. It remains challenging to distinguish between MOGAD coexisting with rectal adenocarcinoma and PNS. Long-term follow-up of this patient will continue. Further studies are needed to investigate the risk and incidence of malignancies in larger MOGAD cohorts.

4. Conclusion

This case report describes the coexistence of MOGAD and rectal adenocarcinoma as an initial clinical presentation, as well as subsequent treatment and follow-up. However, a paraneoplastic association between these diseases cannot be definitively established. For patients with a history of malignancy and suspected PNS, prompt detection of onconeural antibodies in serum and CSF is crucial for timely diagnosis and treatment to avoid delays.

CRediT authorship contribution statement

Yiyi Luo: Writing – original draft. **Gang Peng:** Writing – review & editing. **Jiahua Liang:** Writing – review & editing. **Xuwei Song:** Writing

– review & editing. **Jiayu Tang:** Writing – review & editing.

Informed consent

Written informed consent was obtained from the patient.

Declaration of competing interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Abbreviations:

MOG	Myelin oligodendrocyte glycoprotein
MOGAD	Myelin Oligodendrocyte Glycoprotein Antibody-associated Disease
PNS	Paraneoplastic Neurologic Syndrome
CNS	Central Nervous System
ON	Optic Neuritis
NMOSD	Neuromyelitis Optica Spectrum Disorders
CSF	Cerebrospinal Fluid
PS	Paraneoplastic Syndromes
CIDP	Chronic Inflammatory Demyelinating Polyneuropathy
LEMS	Lambert-Eaton myasthenic syndrome
ADEM	Acute Disseminated Encephalomyelitis
CRC	Colorectal Cancer

Data availability

No data was used for the research described in the article.

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