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# Paraneoplastic motor neuron disease in a patient with sigmoid colon adenocarcinoma - a case report

Keesari Sai Sandeep REDDY, Subbiah SENTHILNATHAN, T. VIVEKANANDAN, Priyadarshini VARADARAJ, N. GUNASEKARAN

General Medicine, Saveetha Medical College and Hospital, Chennai, Tamilnadu, India

## ABSTRACT

***Background.*** *Paraneoplastic neurological syndromes (PNS) are a rare and diverse group of disorders caused by immune-mediated effects of malignancies. Affecting less than 1% of all cancer patients, these syndromes often present diagnostic and therapeutic challenges. Motor Neuron Disease as a paraneoplastic condition is particularly uncommon, especially in association with gastrointestinal malignancies like sigmoid colon adenocarcinoma.*

***Case report.*** *A 62-year-old male with Type 2 Diabetes Mellitus (T2DM) presented with chronic diarrhea and a three-year history of progressive bilateral limb weakness. Initial symptoms were attributed to diabetic neuropathy, but the rapid progression and severity warranted further investigation. Neurological examination revealed hypotonia, muscle wasting, and absent reflexes in all four limbs. Diagnostic tests, including electromyography (EMG) and nerve conduction studies, confirmed motor sensory axonal neuropathy. Colonoscopy revealed a mass in the sigmoid colon, and biopsy confirmed adenocarcinoma. The patient was managed with surgical resection of the tumor, adjuvant chemotherapy, and immunomodulatory treatments, resulting in stabilization of neurological symptoms.*

***Conclusions.*** *This case highlights the importance of considering paraneoplastic syndromes in patients with unexplained neurological symptoms, particularly when a malignancy is suspected or known. Early recognition and a multidisciplinary approach are crucial for improving patient outcomes. Further research is needed to understand the pathophysiological mechanisms and develop sensitive biomarkers for early detection.*

**Keywords:** paraneoplastic neurological syndromes, lower motor neuron disease, sigmoid colon adenocarcinoma, autoimmune response, multidisciplinary approach, early detection, neurological symptoms, type 2 diabetes mellitus

**Abbreviations:**
EMG – Electromyography
PNS – Paraneoplastic neurological syndromes
T2DM – Type 2 diabetes mellitus

## INTRODUCTION

Paraneoplastic neurological syndromes (PNS) represent a heterogeneous group of disorders caused by the immune-mediated effects of malignancies rather than direct tumor invasion, metastasis, or compression. These syndromes, affecting less than 1% of all cancer patients, pose significant diagnostic and therapeutic

*Corresponding author:*
Keesari Sai Sandeep Reddy
*E-mail:* sandyreddy2221@gmail.com

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challenges due to their rarity and the broad spectrum of clinical manifestations [1]. PNS can affect any part of the nervous system, with manifestations potentially involving the central, peripheral, or autonomic nervous systems. Notably, these neurological symptoms can precede the diagnosis of the underlying malignancy, often leading to delays in recognition and management [2,3].

The clinical presentation of paraneoplastic Motor Neuron Disease can mimic that of more common neurodegenerative diseases, making the differential diagnosis challenging. Symptoms typically include progressive weakness, muscle wasting, and fasciculations, which are not confined to the distribution of a single nerve or root, distinguishing them from more localized neurological disorders [4]. The association between Motor Neuron Disease and malignancies like sigmoid colon adenocarcinoma is particularly rare, and literature documenting such cases is sparse.This rarity and the often-subtle initial presentations can complicate timely diagnosis and appropriate management [5].The need for a multidisciplinary approach is paramount, involving neurologists, oncologists, and other specialists to manage the complex interplay of symptoms and treatment responses. Given the potential for neurological symptoms to precede cancer diagnosis, awareness and understanding of PNS are crucial for clinicians across specialties. This facilitates early diagnostic interventions and the initiation of both tumor-directed therapies and immunomodulatory treatments aimed at mitigating the immune response, thereby potentially stabilizing or improving the neurological outcomes [6,7].

This case report seeks to highlight a rare instance of paraneoplastic LMN disease associated with sigmoid colon adenocarcinoma, emphasizing the importance of considering PNS in patients presenting with unexplained neurological symptoms, particularly when a malignancy is known or suspected.

## CASE REPORT

A 62-year-old male with a four-year history of Type 2 Diabetes Mellitus (T2DM) presented to the neurology clinic with chronic diarrhea and a three-year history of progressive bilateral limb weakness. Initially attributed to potential diabetic neuropathy, the severity and progression of his symptoms prompted further evaluation.

He reported chronic diarrhea lasting two months, characterized by 1-2 watery, non-bloody, non-foul-smelling episodes per day, and progressive weakness in both upper and lower limbs over the past three years, significantly impairing his daily activities and mobility. The weakness started insidiously in the lower limbs and gradually progressed to the upper limbs, accompanied by mild, non-specific abdominal pain, discomfort, involuntary facial twitching, and a burning sensation with numbness in the lower limbs, worsening over the past year.

The patient's medical history included a diagnosis of T2DM managed with oral hypoglycemics, with no history of hypertension, tuberculosis, or asthma. He had previously undergone surgical management for a diabetic foot ulcer. He had a history of occasional alcohol consumption, ceased three years prior, followed a mixed diet, reported normal sleep, and experienced altered bowel habits due to his current complaint.

Physical examination revealed the patient to be alert and oriented with stable vital signs: temperature 98.6°F, pulse 85 bpm, blood pressure 110/70 mmHg, respiratory rate 16 breaths/min, and oxygen saturation 99% on room air. Neurological examination showed hy-

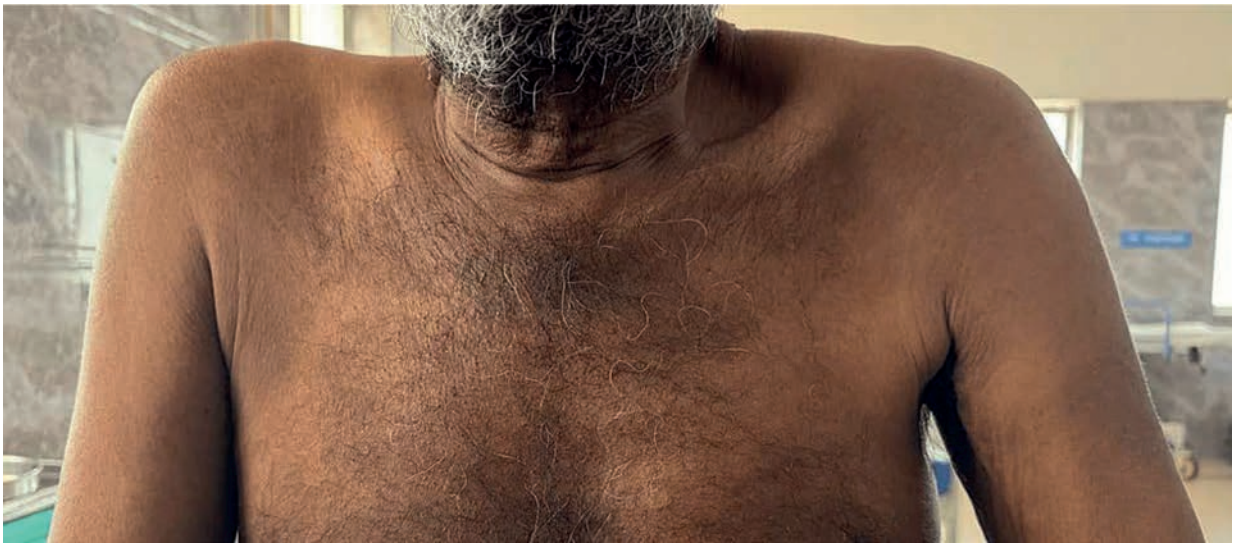

***FIGURE 1.*** *Generalised muscle wasting*

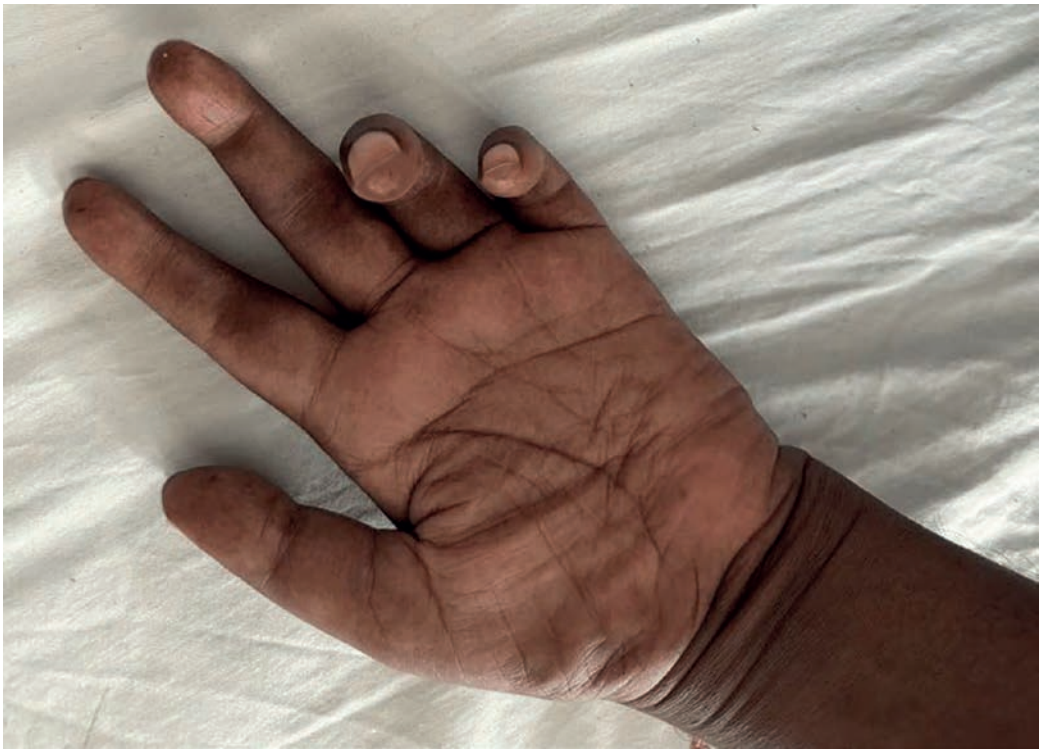

***FIGURE 2.*** *Muscle wasting in hand*

potonia in all four limbs, muscle wasting (Figure1 and 2) in both upper and lower limbs, and muscle strength graded as upper limb flexors 4/5, extensors 2/5, and lower limb flexors 2/5, extensors 4/5. Deep tendon and plantar reflexes were absent, and sensory examination demonstrated a glove-and-stocking pattern of sensory loss, more pronounced in the lower limbs, involving both small and large fibers.

## Investigations

The patient underwent a series of diagnostic tests, which are summarized in the following Table 1, Figures 2 and 3.

## Differential Diagnosis

1. Paraneoplastic Motor neuron disease secondary to sigmoid colon adenocarcinoma.
2. Diabetic neuropathy.

## Management

The patient was managed with a multidisciplinary approach involving neurology, oncology, and gastroenterology. Treatment included surgical resection of the sigmoid tumor, initiation of adjuvant chemotherapy, and supportive care for neurological symptoms, including high-dose corticosteroids.

***TABLE 1.*** *Investigations and interpretations*

| Investigation | Results | Interpretation |
|---|---|---|
| CBC | Hb:9.7g/dL,<br>TLC:12690 /µL,<br>Platelets: 7.51 L/µL,<br>ESR: 120mm/hr | Microcytic hypochromic anemia, leukocytosis |
| Electrolytes | Within normal limits | - |
| Renal Function Tests | Within normal limits | - |
| Liver Function Tests | ALP: 103 U/L | Mild elevation |
| HbA1c | 9.90% | Indicative of poorly controlled diabetes |
| Fasting Blood Sugar | 190 mg/dL | Elevated |
| MRI Brain and Spine | Cervical spinal cord thinning, diffuse brain atrophy (Figure 3) | Suggestive of chronic ischemic changes and myelopathy |
| EMG and Nerve Conduction Study | Motor sensory axonal neuropathy | Suggestive of Motor Neuron disease |
| Colonoscopy | Mass in sigmoid colon (Figure 4) | Biopsy confirmed adenocarcinoma |
| Stool Occult Blood Test | Positive | Suggestive of gastrointestinal bleeding |

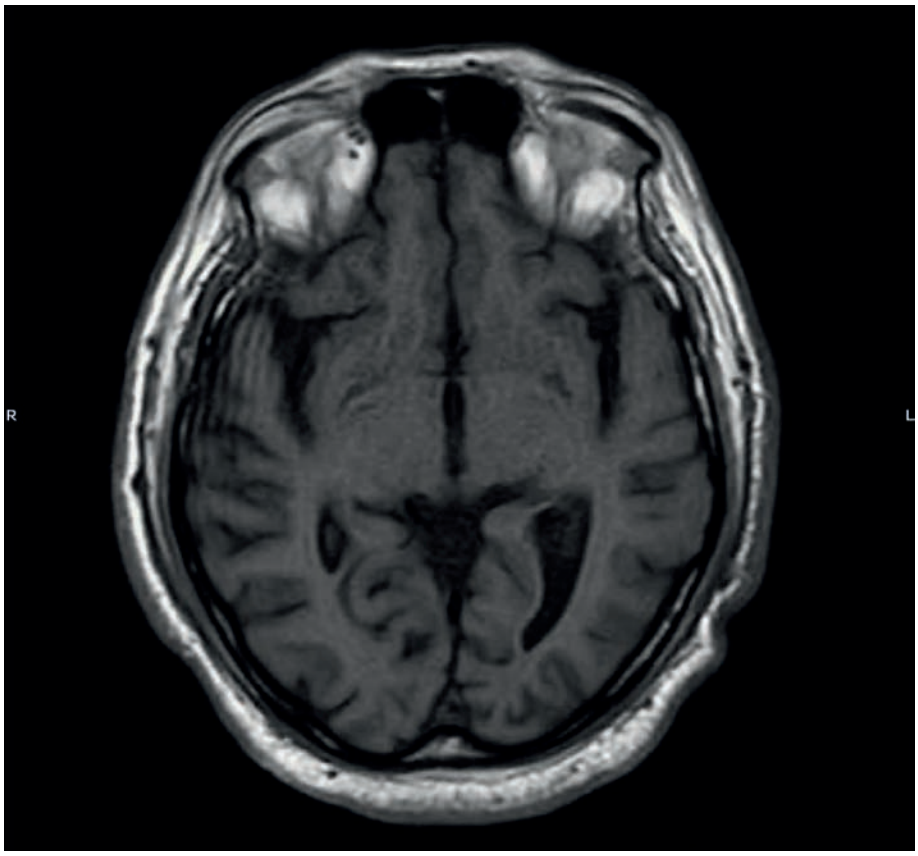


***FIGURE 3.*** *MRI Brain showing diffuse brain parenchymal atrophy*

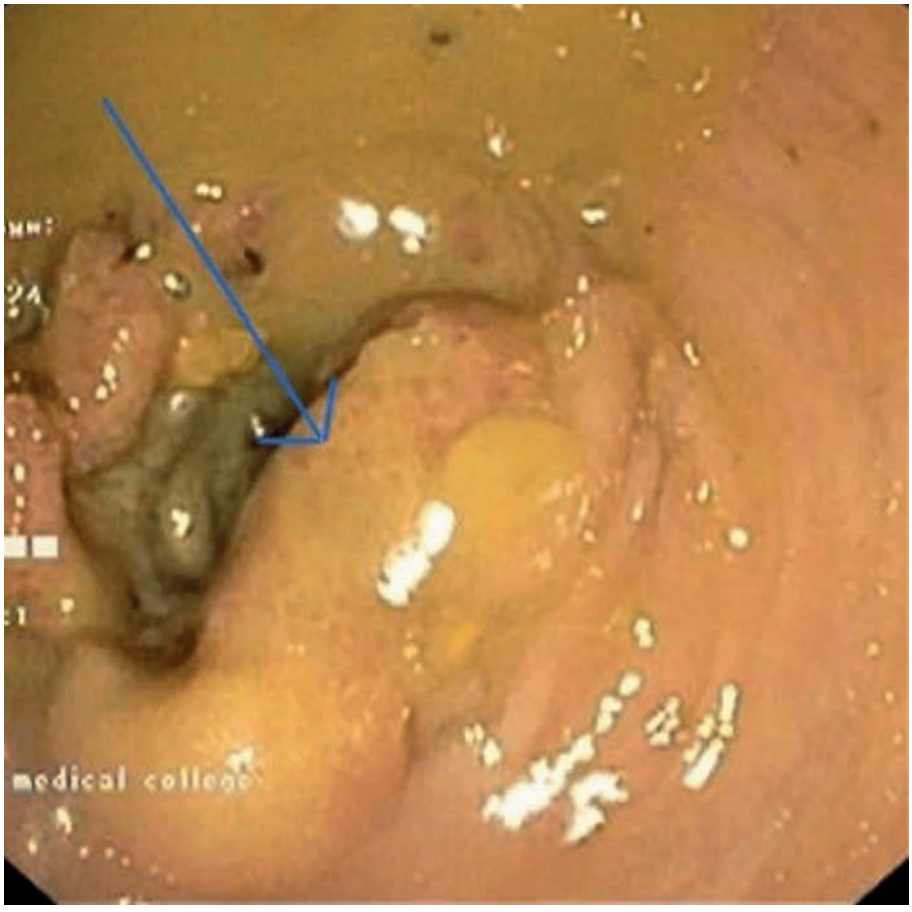


***FIGURE 4.*** *Colonoscopy showing mass in sigmoid colon*

### Outcome

Post-operative recovery was uneventful, and the patient showed some stabilization of neurological symptoms, although significant recovery was limited due to the chronic nature of the neurological damage.

## DISCUSSION

Motor neuron disease (LMN type) is characterized by progressive weakness, muscle wasting, and absent reflexes, often with a distal predominance [4]. In the presented case, the patient's progressive bilateral limb weakness and associated muscle wasting were initially suggestive of a primary neurological disorder such as amyotrophic lateral sclerosis (ALS) or a severe form of diabetic neuropathy. However, the absence of upper motor neuron signs and the rapid progression beyond typical diabetic neuropathy patterns raised suspicions of an alternative diagnosis. Electromyography (EMG) and nerve conduction studies confirming a sensory and motor axonal neuropathy supported the hypothesis of LMN involvement. These findings emphasize the need for comprehensive neurophysiological testing in patients presenting with atypical neuromuscular symptoms [6].

The pathophysiology of paraneoplastic Motor Neuron Disease involves an autoimmune response where antibodies or cytotoxic T cells, initially targeting tumor antigens, cross-react with neuronal components, leading to neuronal degeneration [8]. This autoimmune hypothesis is supported by the finding of onconeural antibodies in some PNS patients, although such antibodies are often absent in LMN disease [9].

The patient's history of Type 2 Diabetes Mellitus and associated sensory neuropathy complicated the clinical picture. Diabetic neuropathy is a common complication of diabetes, characterized by distal symmetric polyneuropathy, which typically presents with sensory deficits, pain, and autonomic dysfunction [10]. In this case, the patient reported a burning sensation and numbness in the lower limbs consistent with diabetic neuropathy. However, the progressive motor weakness, muscle wasting, and rapid clinical deterioration were atypical for diabetic neuropathy alone, indicating an additional pathological process. This coexisting diabetic sensory neuropathy may have initially masked the Motor Neuron Disease, delaying diagnosis and appropriate management [11].

The association between colorectal cancer and paraneoplastic neurological syndromes is exceedingly rare, with few cases documented in the literature [2]. In this case, the temporal relationship between the onset of neurological symptoms and the diagnosis of sigmoid colon adenocarcinoma, coupled with the exclusion of other potential causes, strongly suggested a paraneoplastic etiology. The mechanisms underlying this association likely involve autoimmune responses where antigens shared between the tumor and nervous system components trigger an immunological attack on the neurons [3]. Management of paraneoplastic Motor Neuron Disease involves addressing both the underlying malignancy and the immune-mediated neurological damage. The mainstay of cancer treatment in this context included surgical resection followed by adjuvant chemotherapy, aimed at reducing tumor burden and potentially diminishing the driving force behind the autoimmune response [12]. Concurrently, immunomodulatory treatments such as corticosteroids and intravenous immunoglobulins were used to mitigate the immune response against neural tissues. Despite these interventions, neurological recovery in paraneoplastic syndromes is often limited and may not fully reverse the damage, highlighting the importance of early detection and intervention [13].

This case underscores the importance of considering paraneoplastic syndromes in patients with cancer who present with new, unexplained neurological symptoms. It also illustrates the need for a multidisciplinary approach involving neurology, oncology, and other specialties to optimize patient outcomes. Clinicians should maintain a high index of suspicion for Paraneoplastic syndromes in patients with known malignancies, especially when neurological symptoms are disproportionate to other explanations [6].

Further research is needed to better understand the pathophysiological mechanisms linking colorectal cancer to paraneoplastic neurological syndromes. Additionally, developing more sensitive and specific biomarkers for early detection of Paraneoplastic syndromes could significantly improve the prognosis for these patients by enabling earlier and more targeted interventions [9].

## CONCLUSION

In conclusion, paraneoplastic lower motor neuron disease, particularly in association with colorectal cancer, remains a rare and challenging diagnosis. This case underscores the critical role of a comprehensive, multidisciplinary approach in diagnosing and managing such complex presentations. Early recognition and targeted treatment of both the malignancy and the neurological syndrome are essential to improve patient outcomes and quality of life. Clinicians should remain vigilant for paraneoplastic syndromes in patients with unexplained neurological symptoms, ensuring a broad and thorough differential diagnosis to guide appropriate management strategies.

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