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RAPID PARALYSIS AND HIDDEN MALIGNANCY: ACUTE MOTOR AXONAL NEUROPATHY REVEALING PLEOMORPHIC LIPOSARCOMA

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ABSTRACT

Guillain-Barré syndrome is an immune-mediated neuropathy characterised by acute-onset of symmetric, ascending motor weakness and areflexia. Acute motor axonal neuropathy, a severe axonal variant, is distinguished by direct axonal injury and poor functional recovery. Although infections are recognised triggers for Guillain-Barré syndrome, it is notable that up to half of cases occur without a preceding infectious event, suggesting that other factors such as underlying malignancy may contribute to disease onset.

We present a rare and fatal case of acute motor axonal neuropathy in a 70-year-old woman, who was ultimately found to have an underlying pleomorphic liposarcoma. The patient presented with one week of progressive weakness, fatigue and encephalopathy. She required urgent mechanical ventilation due to respiratory failure; imaging identified multiple bilateral pulmonary nodules. Neurologic evaluation confirmed acute motor axonal neuropathy through nerve conduction studies and cerebrospinal fluid analysis, which showed albuminocytologic dissociation and positive anti-GM1 IgG antibodies. Despite standard treatment with intravenous immunoglobulin, the patient experienced no neurological recovery. Further imaging revealed a large pelvic mass, that was not present on a scan performed two months earlier. A biopsy confirmed pleomorphic liposarcoma, a rare and aggressive soft tissue sarcoma. Paraneoplastic panel testing was negative for onconeural antibodies, yet the clinical context raised suspicion for an immune-mediated, tumour-associated neuropathy.

Clinicians should maintain a high level of suspicion of underlying malignancy in patients with Guillain-Barré syndrome, especially in the absence of preceding infection and with rapid neurological decline.

KEYWORDS

Guillain-Barré syndrome, pleomorphic liposarcoma, acute motor axonal neuropathy, liposarcoma, paraneoplastic GBS, paraneoplastic neurologic syndrome

LEARNING POINTS

- Although infection is a well-established trigger for Guillain-Barré syndrome, patients presenting with Guillain-Barré syndrome may also have an increased risk of underlying malignancy.
- Clinicians should remain vigilant for the possibility of occult malignancy in patients hospitalised with Guillain-Barré syndrome, especially in those without a preceding infectious event.

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INTRODUCTION

Guillain-Barré syndrome (GBS) is an acute and immune-mediated polyradiculoneuropathy, which is characterised by rapidly progressive muscle weakness in an ascending pattern with diminished or absent deep tendon reflexes, and variable sensory or autonomic dysfunction. Its syndrome encompasses several clinical variants, including the more severe axonal forms acute motor axonal neuropathy (AMAN) and acute motor-sensory axonal neuropathy (AMSAN), which are distinguished by direct axonal injury rather than demyelination. First described during a *Campylobacter jejuni* outbreak in northern China, AMAN is most prevalent in East Asia and Latin America, although global cases are increasingly reported[1]. Worldwide incidence of GBS ranges from 0.8 to 1.9 per 100,000 person-years with higher rates in older adults and males. AMAN accounts for approximately 5–10% of GBS cases in Western countries but may comprise up to 30–65% in certain regions of China and Central America[2]. Aetiologically, AMAN is strongly linked to antecedent infections with *C. jejuni*, which is associated with the presence of anti-ganglioside antibodies such as anti-GM1, known to initiate complement-mediated axonal injury[3].

It is postulated that malignancy may elevate the risk of developing GBS through mechanisms such as molecular mimicry or cancer-related immunosuppression; however, the exact pathophysiological nature of this relationship remains unclear. Findings have also shown that incident cancer is significantly associated with an increased risk of subsequent GBS[4]. The temporal association between cancer and GBS, especially within one year of diagnosis, suggests a potential paraneoplastic mechanism[5]. However, current diagnostic frameworks do not recognise GBS as a classical paraneoplastic syndrome unless onconeural antibodies are detected. This limitation may contribute to under-recognition of atypical associations, especially with rare tumours such as sarcomas, underscoring the need for heightened clinical vigilance in unexplained GBS presentations.

CASE DESCRIPTION

A 70-year-old woman was presented with a one-week history of generalised weakness, profound fatigue and increasing confusion. According to her family, she had become bed-bound and unable to maintain head control. Until the onset of symptoms, she had been functionally independent in all activities of daily living. She denied fever, cough, rhinorrhoea or gastrointestinal symptoms. Her medical history included well-controlled primary hypertension, major depressive disorder and fibromyalgia. Approximately two months earlier, she had been evaluated in the emergency department for left upper quadrant abdominal pain. At that time, a computed tomography (CT) scan of the abdomen and pelvis revealed no significant findings. She had no other recent healthcare encounters.

On presentation, she was found to be encephalopathic with a Glasgow Coma Scale score of 5. Arterial blood gas analysis revealed a pH of 7.18 and pCO_2 of 87 mmHg, indicative of acute hypercapnic respiratory failure. She was emergently intubated and initiated on mechanical ventilation. Initial imaging included a non-contrast CT of the head which was unremarkable, and a CT pulmonary angiogram that ruled out pulmonary embolism but revealed multiple bilateral pulmonary nodules *(Fig. 1)*. Empiric broad-spectrum

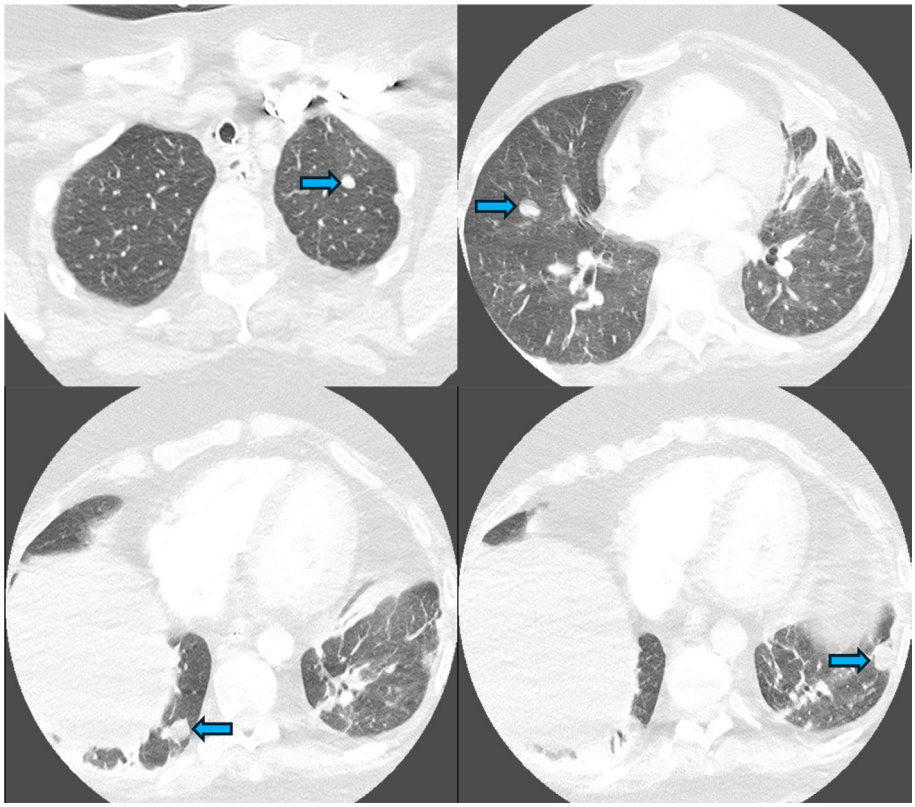


Figure 1. Axial sections of CT chest showing bilateral pulmonary nodules (blue arrows).

Variable	Patient value	Reference range
Colour/appearance	Clear	Clear
Red blood cell count (/µl)	0	<2
White blood cell count (/µl)	1	<6
Glucose (mg/dl)	68	40–70
Protein (mg/dl)	282	12–60
Meningitis-encephalitis panel	Negative	Negative
Bacterial/fungal cultures	Negative	Negative

Table 1. Cerebrospinal fluid analysis.

antibiotics were initiated for presumed sepsis-associated encephalopathy, but infectious workup returned negative. On hospital day 2, during a spontaneous awakening trial, the patient was able to interact non-verbally while indicating intact cognitive function. Neurological examination revealed symmetric flaccid quadriparesis: strength was 1/5 in the lower limbs and 2/5 in the upper limbs. Deep tendon reflexes were absent throughout; sensory examination was preserved. She became tachypnoeic during spontaneous breathing trials, further suggesting neuromuscular respiratory insufficiency. An MRI of the brain and cervical spine revealed no structural abnormalities.

Electromyography and nerve conduction studies confirmed a diagnosis of AMAN, with findings more pronounced in the upper limbs. A lumbar puncture was performed, and cerebrospinal fluid analysis revealed albuminocytologic dissociation with markedly elevated protein levels and normal cell count *(Table 1)*. Anti-GM1 IgG antibodies were positive, supporting the diagnosis of the axonal variant of GBS. The patient was promptly initiated on intravenous immunoglobulin therapy for AMAN. Given the presence of multiple pulmonary nodules, a paraneoplastic aetiology was suspected. A CT-guided biopsy attempt was unsuccessful. Further imaging with CT abdomen and pelvis revealed a 19 cm heterogeneous mass medial and lateral to the left iliac crest, along with multiple enlarged pelvic lymph nodes *(Fig. 2)*. Ultrasound-guided biopsy of the pelvic mass confirmed the diagnosis of pleomorphic liposarcoma *(Fig. 3)*.

Both serum and cerebrospinal fluid paraneoplastic panels, including anti-Hu and onconeural antibodies, were negative. Despite completion of intravenous immunoglobulin infusions, the patient's motor function showed no improvement, and she remained ventilator-dependent by day 14 of hospitalisation. In view of her poor prognosis and wishes, she declined a tracheostomy and opted for comfort-focused care. She passed away in the hospital surrounded by her family.

DISCUSSION

This case presents a rare and compelling intersection between AMAN – a variant of GBS – and pleomorphic liposarcoma, the rarest and most aggressive subtype of soft tissue sarcomas. The temporal relationship between tumour development and the onset of GBS, alongside absence of recognised triggers, suggests a potential paraneoplastic and immune-mediated mechanism, despite the absence of classical onconeural antibodies[3]. Axonal variants of GBS such as AMAN are less common, more severe and frequently associated with anti-ganglioside antibodies such as GM1, which are known to mediate peripheral nerve injury via complement activation and macrophage-induced axonal

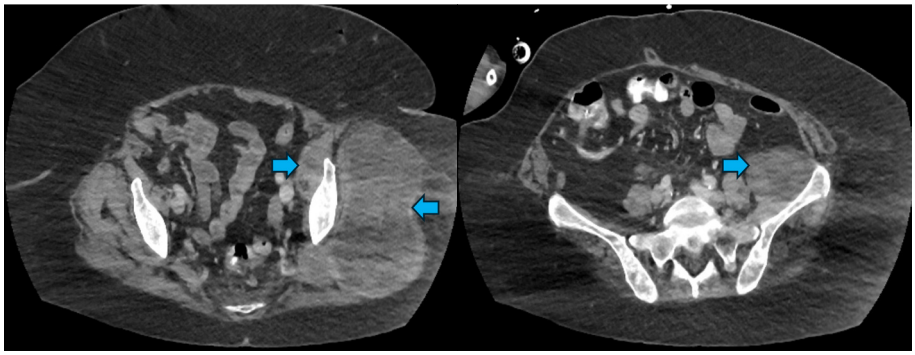


Figure 2. Axial sections of CT pelvis illustrating a large soft tissue mass medial and lateral aspect of left iliac crest (blue arrows).

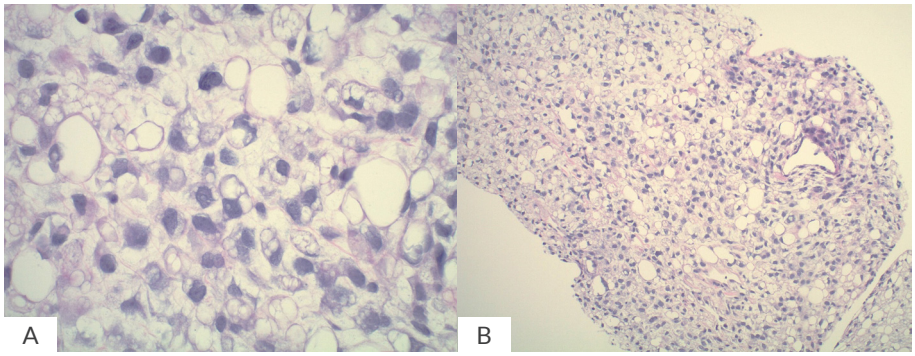


Figure 3. Histopathological images showing pleomorphic liposarcoma: A) proliferation of abundant lipoblasts with enlarged, hyperchromatic nuclei scalloped by cytoplasmic vacuoles, and B) lipoblasts, including scattered 'signet-ring' lipoblasts, characteristic of liposarcoma.

degeneration[6]. While GBS is not classically defined as a paraneoplastic syndrome, there is increasing recognition of its association with malignancy, particularly in the absence of typical infectious triggers[7].

Recent cancer diagnosis has been associated with a 3.6-fold increased risk of subsequent GBS, even after adjusting for comorbidities, surgery and infections, suggesting that unidentified cancer-related factors may contribute to this association. The link between cancer and peripheral neuropathy has been recognised since the earliest descriptions of paraneoplastic neuropathies in the 1940s; however, later studies have proposed that GBS associated with cancer may represent a distinct entity. Two main hypotheses prevail regarding this connection: first, specific onconeural antibodies may induce an immune response targeting peripheral nerves, resembling the molecular mimicry mechanism observed with *C. jejuni*; second, cancer may induce an immunosuppressive state, allowing autoantibodies to attack the peripheral nervous system[4].

A 2022 population-based study from the Clinical Epidemiology journal demonstrated an increased incidence of malignancy following GBS diagnosis, with standardised incidence ratios suggesting a statistically significant risk, especially within the first year of diagnosis (SIR 3.10; 95% CI: 2.28–4.09). Haematologic, pulmonary and neurological malignancies were most frequently associated, while sarcomas were exceedingly rare[7]. In addition, GBS appears to be an adverse prognostic marker for cancer survival. Patients with a recent GBS diagnosis had a 1.6-fold higher all-cause mortality risk following cancer diagnosis compared to those without GBS, even after controlling for cancer stage and comorbidities. This case illustrates a novel association with pleomorphic liposarcoma, a tumour with aggressive growth kinetics as illustrated by the absence of detectable masses just two months prior.

The diagnostic workup revealed multiple bilateral pulmonary nodules and a rapidly enlarging pelvic mass, suggesting metastatic disease. While biopsy confirmed pleomorphic liposarcoma, both serum and cerebrospinal fluid paraneoplastic panels were negative, including anti-Hu and other classical onconeural antibodies. The pathophysiological possibility of molecular mimicry remains valid. Shared antigens between tumour tissue and peripheral nerves including gangliosides may trigger a cross-reactive autoimmune response. Anti-GM1 antibodies have been implicated in paraneoplastic neuropathies despite the absence of other serological markers, suggesting an alternative pathway for immune-mediated nerve injury.

Current guidelines by the 2021 International Panel on Paraneoplastic Neurological Syndromes recommend that GBS is not categorised as paraneoplastic unless onconeural antibodies are detected[8]. Studies have demonstrated that malignancy risk in GBS is elevated with advancing age, and cases have been documented where GBS occurred in the context of malignancy without detectable onconeural antibodies. Furthermore, commercially available immunodot assays used to screen for paraneoplastic neurological syndrome have limitations in sensitivity and diagnostic yield[9].

CONCLUSION

This case highlights a rare association between GBS and pleomorphic liposarcoma, which is an aggressive soft tissue sarcoma. It emphasises the need for heightened clinical vigilance for malignancy in patients with GBS, particularly in the absence of antecedent infections. Furthermore, the absence of onconeural antibodies should not preclude the consideration of malignancy in patients with GBS. This case also underscores the need for further research to clarify the complex interplay between malignancy and GBS.

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