Guillain-Barré Syndrome Following Lung Adenocarcinoma Surgery: A Case Report and Literature Review

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Patient: Male, 74-year-old
Final Diagnosis: Guillain-Barré syndrome (GBS)
Symptoms: Areflexia • ataxia • breathlessness • instability • paresthesia • swallowing difficulties • walking difficulties • weakness
Clinical Procedure: Lung tumor resection • uniportal video-assisted thoracoscopic surgery
Specialty: Immunology • Neurology • Oncology • Surgery

Objective: Unusual clinical course
Background: Guillain-Barré syndrome (GBS) is a rare immune-mediated peripheral nerve disorder. Among non-infectious factors, surgery has been identified as a potential trigger of the disease. This report presents the case of a 74-year-old man who developed GBS 15 days after a right lower lobectomy for lung adenocarcinoma.

Case Report: We present a case of a patient who was a former smoker who underwent uniportal video-assisted (U-VATS) right lower lobectomy for localized lung adenocarcinoma. Fifteen days after surgery, he exhibited bilateral lower-limb weakness, widespread paresthesia, and postural instability. Comprehensive diagnostic workup, including clinical assessment, serological tests, cerebrospinal fluid (CSF) analysis, and nerve conduction studies (NCS), confirmed the diagnosis. Notably, CSF analysis revealed albumin-cytological dissociation, with albumin 453.2 mg/L, protein 757 mg/L, glucose 67 mg/dl, 3 white blood cells (WBC)/uL, and polymorphonucleates (PMN) 33%. NCS demonstrated motor and sensory abnormalities. Prompt administration of intravenous immunoglobulins (IVIG) 2 g/kg daily for 5 days resulted in complete recovery within 3 months.

Conclusions: This case emphasizes the importance of prompt recognition and management of GBS as a postoperative complication. Neurological examination, neuroimaging, and electrophysiological studies are essential for accurate diagnosis. IVIG therapy remains a cornerstone in GBS management, with favorable outcomes observed in this case. Enhanced awareness among clinicians about the potential association between surgery and GBS is vital to prevent more serious complications and ensure optimal patient management. Further research is crucial to determine the precise pathogenesis and mechanisms of GBS following lung surgery.

Keywords: Carcinoma, Non-Small-Cell Lung • Guillain-Barré Syndrome • Thoracic Surgery, Video-Assisted

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Introduction

Guillain-Barré syndrome (GBS) presents as an acute inflammatory demyelinating polyneuropathy (AIDP), characterized by progressive muscle weakness and areflexia. Its incidence is approximately 1-2 cases per 100,000 person-years [1]. Alongside AIDP, GBS includes axonal forms like acute motor axonal neuropathy (AMAN) and acute motor and sensory axonal neuropathy (AMSAN) [1].

The exact pathogenesis of GBS remains elusive, but it is largely attributed to aberrant humoral and cellular immune responses [2]. GBS frequently follows infections, including Campylobacter jejuni, Cytomegalovirus, Epstein-Barr virus, Zika virus, and Mycoplasma pneumoniae [2]. Antecedent respiratory or gastrointestinal tract infection may elicit an autoimmune assault on peripheral nerve gangliosides [3].

Non-infectious factors are also implicated as potential triggers of GBS. The administration of general or locoregional anesthesia preceding surgery may influence the natural course of GBS [4]. Notably, certain surgeries, particularly cardiothoracic, spine, and abdominal surgeries, have been associated with AIDP development [5-7]. Surgery may weaken the immune system, increasing susceptibility to infections and potentially triggering GBS through mechanisms such as autoimmunity or molecular mimicry [2,8].

This report describes a 74-year-old man who was a former smoker with GBS 15 days following right lower lobectomy for adenocarcinoma of the lung.

Case Report

We report the case of a 74-year-old man, a former smoker until the age of 55 (120 pack-years) with history of ischemic heart disease, arterial hypertension, and dyslipidemia. A contrast computed tomography (CT) scan of the chest revealed a significant increase in size of a 22-mm pseudo-nodular formation in the superior segment of the right lower lung (Figure 1).

In accordance with multidisciplinary evaluation, the patient underwent right lower uniportal video-assisted thoracoscopic lobectomy (U-VATS) followed by systematic mediastinal lymphadenectomy, without complications [9]. Intraoperative and definitive histological analyses confirmed lung adenocarcinoma with a micropapillary growth pattern. The conclusive report confirmed total resection, dismissing lymph node involvement (Stage Ila, pT2aN0M0R0). The patient was discharged on the fourth postoperative day with no reported major adverse events. Fifteen days later, he presented to the Emergency Department (ED) with bilateral muscle weakness of the lower limbs and widespread paresthesia throughout the body, along with postural instability. His gait was wide-based and ataxic, as evidenced by a positive Romberg test. Examination of the patient revealed an overall decrease in muscle strength (grade 3/5 in the lower extremities according to Medical Research Council scale). Deep tendon reflexes were abolished in the lower limbs. Autonomic involvement was excluded. Brain and spinal MRI showed no evidence of spinal cord compression or disease recurrence.

The patient was then admitted to the Neurology Unit, where a significant neurological worsening with mild difficulty in

Figure 1. Preoperative imaging findings. Transverse (A) and Coronal (B) computed tomography (CT) scans, highlighting primary lesion in the right lower lobe (black arrows).
swallowing and breathing was observed. However, these difficulties did not necessitate intubation or nasogastric tube feeding. Immediately, specific therapy with 2 g/kg daily for 5 days intravenous immunoglobulins (IVIG) was administered, in accordance with the suspicion of AIDP. He had no adverse effects to this therapy, which was well tolerated. Cerebrospinal fluid (CSF) biochemistry showed albumin-cytological dissociation (albumin 453.2 mg/L, protein 757 mg/L, glucose 67 mg/dl, 3 WBC/μl, PMN 33%), with no oligoclonal bands detected. Serologic testing for autoimmune and infectious diseases, as well as anti-ganglioside antibodies (GM1-IgM, GM2, GD1α, GD1b, GT1b, GQ1b), were all negative. Anti-onconeural antibodies against Hu, Yo, Ri, CV2, Ma2, SOX-1, and Amp were negative. This effectively ruled out the possibility of a paraneoplastic neurological syndrome (PNS). After 20 days, needle electromyography (EMG) of selected muscles demonstrated rare fibrillations and normal motor unit potentials. Sensory nerve conduction study (NCS) of the left ulnar nerve revealed absent evoked responses. Motor NCS displayed a decreased compound muscle action potentials (CMAPs) amplitude of the left ulnar, left tibial, and bilateral common peroneal nerves, along with an extended distal motor latency. The F-wave of the left tibial nerve was prolonged (31.5 ms). Thus, the electrophysiological examination demonstrated motor and sensory abnormalities. NCS findings are reported in Table 1.

The patient gradually recovered after 25 days of hospitalization. Subsequently, he was discharged and transferred to a rehabilitation center, where his weakness was totally resolved within 3 months. No disease recurrence was noted during the follow-up visit.

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration. Written informed consent was obtained from the patient for publication of this case report.

### Table 1

<table>
<thead>
<tr>
<th>Nerve</th>
<th>Nerve conduction velocity (m/s) (40-60 m/s)</th>
<th>Distal motor latency (ms)</th>
<th>CMAPs amplitude (mV) (&gt;6 mV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>L Ulnar nerve</td>
<td>55.0</td>
<td>4.02</td>
<td>1.94</td>
</tr>
<tr>
<td>L Tibial nerve</td>
<td>39.2</td>
<td>7.0</td>
<td>0.83</td>
</tr>
<tr>
<td>R Common Peroneal nerve</td>
<td>47.8</td>
<td>10.8</td>
<td>1.57</td>
</tr>
<tr>
<td>L Common Peroneal nerve</td>
<td>48.3</td>
<td>9.1</td>
<td>0.73</td>
</tr>
</tbody>
</table>

L – left; R – right.

## Discussion

GBS is a rare potentially life-threatening immune-mediated disease of the peripheral nerves, typically triggered by infections [1]. This case report underscores the importance of considering GBS as a potential complication after pulmonary lobectomy.

Antecedent surgery, particularly cardiac and spinal surgery, is a major contributor to trauma-related GBS, with a risk of 4.1 per 100 000 surgical operations. GBS in cardiac surgery is more frequently observed following coronary artery bypass grafting (CABG) and valve replacements [7]. CABG has been linked to complement activation, release of both inflammatory and anti-inflammatory cytokines (IL-8, IL-10), tumor necrosis factor (TNF-α), and neutrophil stimulation [6].

Gensicke et al. found an unexpected high incidence of post-surgical GBS cases, with a risk of developing GBS within 6 weeks after surgery 13.1 times higher than the usual incidence [8]. The primary mechanisms are based on a surgery-related involvement of the cellular and humoral immune systems [10].

Zeng et al. reported a similar case of a hepatic cancer patient who experienced limb weakness 4 days following partial hepatectomy, consistent with a diagnosis of GBS. The authors concluded that cancer and surgery can trigger GBS [4].

Furthermore, the administration of anesthetics before surgery may also be responsible for the onset of GBS. Maldistribution of local anesthetics, surgical positioning, and pharmacologic agent neurotoxicity have been proposed to explain this phenomenon [11]. The anesthetic medications induce initiation of immunological cascades through the interaction between the lipid-soluble anesthetic agents and the myelin of the peripheral nerves [6,12].

Our patient underwent right lower uniportal video-assisted (UVATS) lobectomy for lung adenocarcinoma. Fifteen days later, he was diagnosed with GBS. In the literature, the only
documented case of GBS following lung lobectomy is reported by Plojoux and colleagues [13], in which GBS emerged on the 11th postoperative day following upper right video-assisted (VATS) lobectomy. Although the specific clinical contexts may differ, both cases underwent meticulous diagnostic evaluations and received IVIG therapy for treatment, illustrating similarities with our report. Progressive ascending four-limb paresis was observed in both cases, alongside preserved muscle strength and absent reflexes. Both cases involved NCS to assess nerve function. Negative infectious and autoimmune markers and normal CSF biochemistry were consistent findings. Rapid administration of IVIG led to gradual recovery and eventual symptoms resolution in both patients. In line with their findings, we support the hypothesis that immune suppression can facilitate bacterial airway colonization, and antigen exposure can trigger immune cross-reaction with myelin proteins, particularly in lung operations [13,14].

Moreover, the appearance of GBS after surgery underscores the intricate connection between surgical stressors, blood-brain barrier (BBB) breakdown, and underlying malignancy. First, psychological stress resulting from surgery has been associated with complex neuroendocrine and immune interactions, particularly Toll-like receptor 4 (TLR4) and tissue necrosis factor (TNF) polymorphism. Second, inflammatory responses may cause BBB breakdown after different surgeries [15]. There is accumulating evidence that an altered expression of heat shock protein (HSP), especially 70-kDa HSP70, and release of various cytokines may play a role in the pathogenesis, leading to myelin sheath and axon damage [2]. Finally, comorbid malignancy emerged as an independent risk factor for the onset of post-surgical GBS [16].

Wang et al described the first case of a patient who developed lung adenocarcinoma GBS [17]. Similar to our report, they emphasized the importance of a careful examination to exclude underlying systemic conditions, particularly PNS. However, the exact mechanism underlying PNS remains poorly understood. In our case, negative serologic tests for anti-onconeural antibodies, together with the exclusion of disease recurrence, ruled out a possible PNS.

AMAN is defined by rapidly progressing ascending muscle weakness, often involving the respiratory system, and necessitating mechanical ventilation. According to Bao et al, the electrodiagnosis of post-surgical GBS supports the presence of acute axonal neuropathy (AMAN and AMSAN) [10]. However, our electrophysiological findings were indicative of AIDP rather than the axonal form of neuropathy. AIDP progresses less rapidly than AMAN and is associated with a more favorable prognosis.

In general, patients who exhibit unexplainable symmetrical weakness within 20 days from surgery should be closely monitored for GBS. Timely recognition of neurological symptoms, coupled with neurophysiological evaluations and CSF analysis, is imperative for accurate diagnosis [8]. A literature review of 18 cases conducted by Kakehi et al revealed that unexplained atypical symptoms and abnormal NCS findings are useful for diagnosing GBS when CSF examination cannot be performed after spinal surgery [5]. In our case, NCS demonstrated a multifocal demyelinating process and CSF exhibited elevated protein levels.

Early initiation of high-dose IVIG, or plasma exchange is critically important. These treatments should ideally be started as soon as possible; in our case, a milder benefit was observed with treatment initiated up to 3 weeks after symptom onset [2]. We strongly emphasize the efficacy of immunomodulating therapies, highlighting their valuable role in mitigating disease progression and improving patient outcomes.

**Conclusions**

GBS following lung lobectomy for lung cancer is uncommon, likely attributable to immune-mediated processes and surgical stress. Clinicians should vigilantly monitor for sudden muscle weakness after surgery, enabling corresponding measures to minimize GBS-related disabilities and optimize healthcare resources. Further research is needed to discover the precise pathogenesis and mechanisms of GBS following lung surgery.

**Declaration of Figures’ Authenticity**

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