Guillain-Barré Syndrome as a paraneoplastic neurological disease of pulmonary adenocarcinoma and squamous cell carcinoma: A case report

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Running title: Guillain-Barré Syndrome and lung cancaer

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Abstract

We present the case of a 69-year-old male who presented with profound weakness in the extremities. Remarkably, he lacked any identifiable precipitating factors preceding the onset of his illness. However, a diagnosis of Guillain-Barré Syndrome (GBS) was established based on typical clinical symptoms, cerebrospinal fluid analysis, and neurological examination. During his hospitalization, an incidental discovery of lung cancer was made, with subsequent pathological confirmation of both adenocarcinoma and squamous cell carcinoma in the lungs. This case report serves to underscore the exceptional rarity of the simultaneous occurrence of lung cancer and Guillain-Barré syndrome, renewing interest in investigating GBS as a potential paraneoplastic neurological syndrome.

Key words: Guillain-Barré Syndrome, paraneoplastic neurological disease, pulmonary adenocarcinoma, squamous cell carcinoma

Introduction

Paraneoplastic neurological syndrome is considered a neurological disorder caused by cancer. The underlying mechanism remains unclear; however, the prevailing view suggests it is immune-related and not attributable to metastasis, infection, metabolic abnormalities, coagulopathy, or the side effects of cancer treatment[1]. Previously, there have been numerous reported cases suggesting a possible association between lung cancer and Guillain-Barré Syndrome (GBS) [2]. Among these cases, small cell lung cancer has been the most frequently reported, with only one documented case of GBS as a paraneoplastic syndrome in lung adenocarcinoma[3], and a few cases involving squamous cell carcinoma[4]. We report a patient admitted for GBS and diagnosed with both adenocarcinoma of the lung and squamous cell carcinoma during hospitalization.

Case report

A 69-year-old male presented with a two-week history of progressive weakness initially involving both lower extremities and subsequently extending to both upper extremities. The patient had a medical history of type II diabetes mellitus, hypertension, chronic kidney disease stage 5, and gouty arthritis. There were no documented episodes of upper respiratory tract infection or fever preceding the onset of this illness.

During the two-week period, the patient's weakness progressively worsened, ultimately affecting both upper limbs. Upon arrival at the emergency room, he had lost the ability to walk.

Upon presentation to the emergency room, a physical examination revealed weakness in all four extremities, graded as Medical Research Council (MRC) grade 3, and loss of deep tendon reflexes (DTR) in both lower extremities. Pinprick sensation testing of the left limb indicated numbness. Routine laboratory tests indicated impaired renal function (BUN: 55 mg/dL, Cr: 2.66 mg/dL) and mild anemia (Hb: 9.6 g/dL). A lumbar puncture revealed an isolated elevation in protein content (87 mg/L), with white blood cell count and glucose levels within normal ranges.

Electrodiagnostic studies disclosed slowed nerve conduction velocity and reduced compound muscle action potential amplitude in all four limbs. Sensory nerve conduction studies yielded no response, and prolonged F-wave latency was observed in all four limbs.

The H-reflex study was not conducted due to the patient's condition. Based on these findings, a diagnosis of demyelinating sensorimotor polyneuropathy was suspected.

Furthermore, a chest radiograph identified a mass lesion in the left upper lobe of the lung. Consequently, a chest computed tomography (CT) scan was arranged and revealed a 4.6 x 4.1 cm mass in the left upper lobe, exhibiting imaging characteristics consistent with lung cancer. Subsequent whole-body bone scan and brain magnetic resonance imaging (MRI) did not reveal significant metastases. In summary, based on the imaging findings, the diagnosis was established as lung cancer, stage IB (cT2bN0M0).

The mass was confirmed as adenocarcinoma through a CT-guided biopsy. Microscopic examination revealed solid nests and irregular, incomplete glands composed of non-small neoplastic epithelial cells with hyperchromatic nuclei and prominent nucleoli. Immunohistochemical staining demonstrated that the tumor cells were positive for TTF-1 and negative for p40.

Based on the aforementioned findings, the patient's clinical condition, and medical history, a diagnosis of 'pulmonary adenocarcinoma with concomitant GBS as a paraneoplastic syndrome' was established. In response, the patient underwent two rounds of emergency plasma exchange for GBS. Subsequently, there was a transient improvement in limb weakness and numbness, with an enhancement in muscle power (Medical Research Council grade improved from 3 to 4).

However, four weeks post-plasma exchange, the limb weakness and numbness relapsed, with the muscle power decreasing (Medical Research Council grade reduced from 4 to 3). By this point, more than 8 weeks had elapsed since the initial onset of the disease. Consequently, the patient initiated treatment with prednisolone at a daily dose of 40 mg and, one week later, underwent thoracoscopic segmentectomy as the standard treatment for lung cancer.

Pathological examination of the excised masses revealed micropapillary adenocarcinoma, poorly differentiated, and squamous cell carcinoma in situ with microinvasion. According to the eighth edition of TNM classification for lung cancer, the pTNM stage was determined as Adenocarcinoma pT2bN0M0 and Microinvasive squamous cell carcinoma pT1aN0M0.

Following the successful removal of the tumor, the patient's overall condition exhibited gradual improvement, accompanied by a progressive enhancement in muscle strength and a reduction in numbness. One week post-surgery, the prednisolone dosage was reduced to 60 mg once daily, and the patient was placed in a rehabilitation program to commence standing exercises. Following hospital discharge, the patient remained on a regimen of low-dose steroids. At a follow-up clinic visit one month later, there was a modest improvement in upper extremity muscle strength to a level of 4 out of 5, while lower extremity muscle strength had improved to 3 out of 5. Regrettably, due to

challenges with the patient's adherence to medication, further follow-up could not be conducted.

Discussion

Guillain-Barre syndrome (GBS) is characterized as an acute immune-mediated polyneuropathy. Its primary diagnostic criteria include an acute onset, the absence or weakness of deep tendon reflexes, and progressive, mostly symmetrical muscle weakness[5]. Following the exclusion of other atypical symptoms, the diagnosis of GBS can be further supported by isolated elevated protein levels in cerebrospinal fluid (CSF) in conjunction with typical electrodiagnostic study findings. Typical electrodiagnostic study findings comprise low-amplitude or absent sensory nerve action potentials (SNAPs), reduced motor conduction velocity, the disappearance of the H reflex, and prolongation or disappearance of the F wave[6]. Severe cases of GBS may not only involve the limbs but can also affect respiratory muscles[7] and even the autonomic nerves[8] , elevating the risk of mortality and disability. Available evidence suggests that the primary triggers for GBS are respiratory and gastrointestinal infections[9]. Other reported triggers include vaccinations[10], surgery[11], other episodic events[12-14], and cancer[15].

Paraneoplastic neurological syndromes (PNSs) represent remote effects of cancer and are generally recognized as immune-mediated disorders, although the precise underlying mechanism remains elusive. Graus et al. [16]and Graus F, et al. [17] have made notable contributions to the development of diagnostic criteria for PNSs. Nonetheless, Graus F, et al. concluded that individuals diagnosed with both cancer and Guillain-Barré Syndrome

(GBS) or Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) should not be categorized as having PNSs unless they exhibit high-risk antibodies[17]. Nevertheless, recent population-based studies have suggested a discernible association between cancer and GBS. Moreover, the diagnosis of GBS serves as a poor prognostic indicator for survival following a cancer diagnosis[15,18,19]. Consequently, we propose that in this patient, GBS should be considered as a PNS secondary to lung cancer, even in the absence of specific antibody testing.

An extensive review of the literature was conducted to identify reports indicating the potential occurrence of Guillain-Barré Syndrome (GBS) as an adverse effect of drugs administered in the treatment of lung cancer[20,21] . However, the literature pertaining to GBS being considered as Paraneoplastic Neurological Syndromes (PNSs) remains relatively limited, with only one case report documenting the diagnosis of GBS in conjunction with lung adenocarcinoma[3] and another case report describing a patient with concurrent GBS and squamous cell carcinoma of the lung[4]. Here, we present an exceedingly rare case of a patient diagnosed with both GBS and two distinct types of lung cancer. Following plasma exchange, steroid therapy, and surgical removal of the lung cancers, the patient experienced a successful recovery. Drawing lessons from this case, we recommend that clinicians maintain heightened awareness regarding the potential presence of cancer in elderly patients with GBS who lack discernible preceding infections or other triggering factors. Additionally, we advocate for the inclusion of early cancer

evaluation, particularly when GBS treatment proves ineffective.

Conclusion

This case highlights the need for clinicians to consider cancer as a potential factor in GBS patients without apparent risk factors. Early recognition of this potential association can facilitate more timely cancer detection and improve patient outcomes.

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References

1. Honnorat J, Antoine JC. Paraneoplastic neurological syndromes. *Orphanet J Rare Dis* 2007; **2**: 22.

2. Kim MH, Hwang MS, Park YK, et al. Paraneoplastic Guillain-Barré Syndrome in Small Cell Lung Cancer. *Case Rep Oncol* 2015; **8**(2): 295-300.

3. Wang Y, Yang S, Fang L, et al. Pulmonary adenocarcinoma associated with Guillain-Barré syndrome: A case report. *Medicine (Baltimore)* 2018; **97**(21): e10737.

4. Wu D, Liu A, Baldinger E, Frontera AT. A Case of Paraneoplastic Guillain-Barré Syndrome Associated with Squamous Cell Carcinoma of the Lung. *Cureus* 2018; **10**(8): e3202.

5. Willison HJ, Jacobs BC, van Doorn PA. Guillain-Barré syndrome. *Lancet* 2016; **388**(10045): 717-27.

6. Gordon PH, Wilbourn AJ. Early electrodiagnostic findings in Guillain-Barré syndrome. *Arch Neurol* 2001; **58**(6): 913-7.

7. Alshekhlee A, Hussain Z, Sultan B, Katirji B. Guillain-Barré syndrome: incidence and mortality rates in US hospitals. *Neurology* 2008; **70**(18): 1608-13.

8. Chakraborty T, Kramer CL, Wijdicks EFM, Rabinstein AA. Dysautonomia in Guillain-Barré Syndrome: Prevalence, Clinical Spectrum, and Outcomes. *Neurocrit Care* 2020; **32**(1): 113-20.

9. Leonhard SE, van der Eijk AA, Andersen H, et al. An International Perspective on Preceding Infections in Guillain-Barré Syndrome: The IGOS-1000 Cohort. *Neurology* 2022; **99**(12): e1299-e313.

10. Woo EJ, Mba-Jonas A, Dimova RB, Alimchandani M, Zinderman CE, Nair N. Association of Receipt of the Ad26.COV2.S COVID-19 Vaccine With Presumptive Guillain-Barré Syndrome, February-July 2021. *Jama* 2021; **326**(16): 1606-13.

11. Rudant J, Dupont A, Mikaeloff Y, Bolgert F, Coste J, Weill A. Surgery and risk of Guillain-Barré syndrome: A French nationwide epidemiologic study. *Neurology* 2018; **91**(13): e1220-e7.

12. Bhusal A, Shrestha A, Muskan V, Bhattarai S, Subedi P, Yadav AK. Postpartum Guillain-Barré syndrome: a case report. *Ann Med Surg (Lond)* 2023; **85**(2): 191-4.

13. Tu WC, Chang ST, Huang CH, Cheng YY, Hsu CS. Guillain-Barré Syndrome with Respiratory Failure following Spine Surgery for Incomplete Cervical Cord Injury: A Case Report and Literature Review. *Medicina (Kaunas)* 2022; **58**(8).

14. Zhang Y, Huang C, Lu W, Hu Q. Case Report: Delayed Guillain-Barré syndrome following trauma: A case series and manage considerations. *Front Surg* 2022; **9**: 903334.

15. Levison LS, Thomsen RW, Sindrup SH, Andersen H. Association Between Incident Cancer and Guillain-Barré Syndrome Development: A Nationwide Case-Control Study. *Neurology* 2022; **98**(15): e1555-e61.

16. Graus F, Delattre JY, Antoine JC, et al. Recommended diagnostic criteria for paraneoplastic neurological syndromes. *J Neurol Neurosurg Psychiatry* 2004; **75**(8): 1135-40.

17. Graus F, Vogrig A, Muñiz-Castrillo S, et al. Updated Diagnostic Criteria for Paraneoplastic Neurologic Syndromes. *Neurol Neuroimmunol Neuroinflamm* 2021; **8**(4).

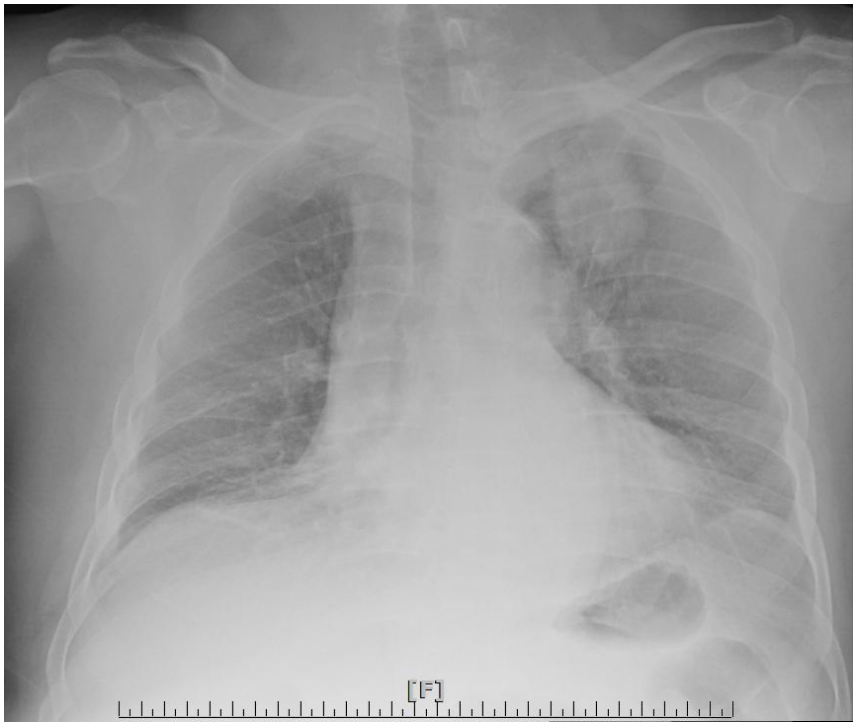
18. Girma B, Farkas DK, Laugesen K, et al. Cancer Diagnosis and Prognosis After Guillain-Barré Syndrome: A Population-Based Cohort Study. *Clin Epidemiol* 2022; **14**: 871-8.

19. Vigliani MC, Magistrello M, Polo P, Mutani R, Chiò A. Risk of cancer in patients with Guillain-Barré syndrome (GBS). A population-based study. *J Neurol* 2004; **251**(3): 321-6.

20. Cheng K, Wang Y, Zhou Y, Xia R, Tang L, Liu J. Neurological Adverse Events Induced by Immune Checkpoint Inhibitors in Non-Small Cell Lung Cancer: Current Perspectives and New Development. *Clin Med Insights Oncol* 2021; **15**: 11795549211056261.

21. Ding M, Deng C, Liu X, et al. Case Report: ICIs-induced Guillain-Barré syndrome recovered from mycophenolate mofetil. *Front Immunol* 2023; **14**: 1132692.

Summary: Patients with GBS in the absence of other triggers should be alerted to the possibility of an underlying cancer.



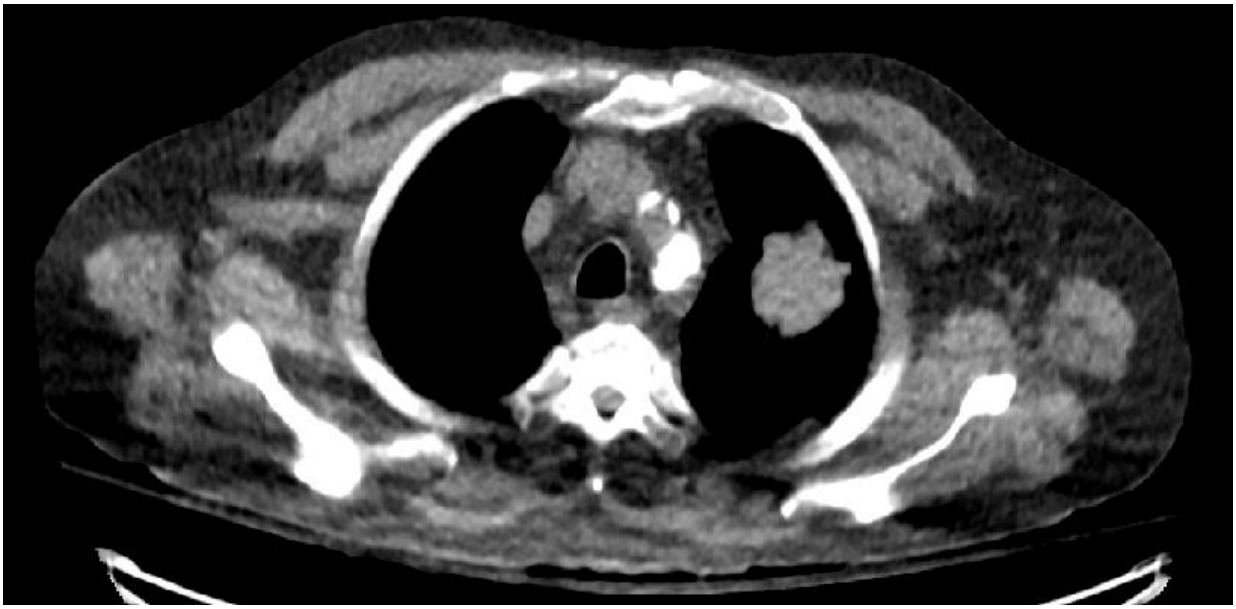


Figure 1. Chest x ray: 5.3~5.7CM mass lesion over left upper lobe

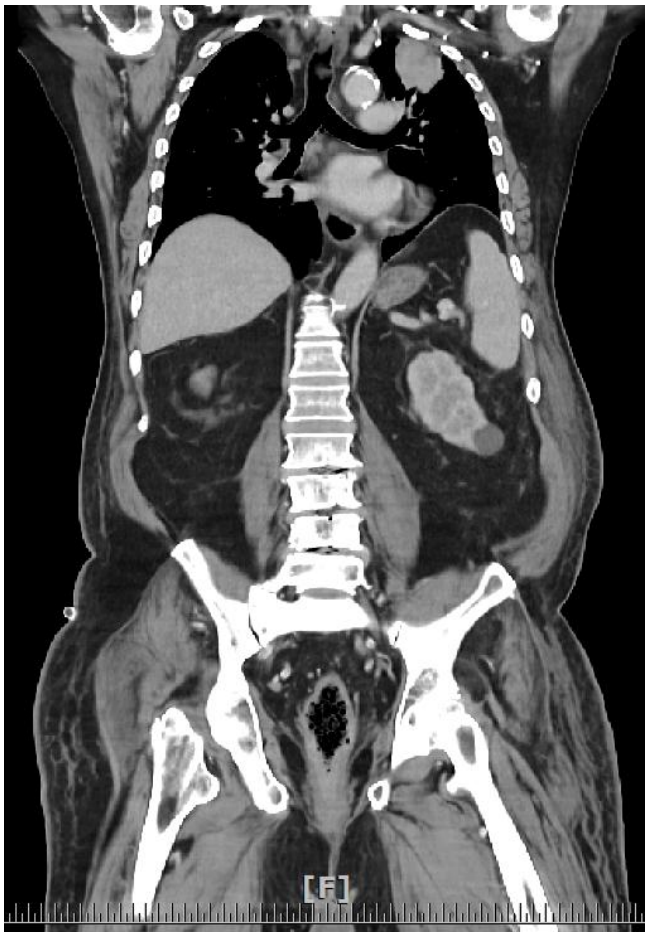


Figure 2,3. Chest computed tomography: a lung mass in the left upper lobe, measuring 4.6 cm in width and 4.1 cm in depth. This is indicative of stage IB lung cancer (T2bN0M0), with no lymph node or distant metastasis.