Paraneoplastic Guillain-Barré Syndrome in Small Cell Lung Cancer

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Key Words

Guillain-Barré syndrome · Small cell lung cancer · Paraneoplastic syndrome

Abstract

Guillain-Barré syndrome (GBS) is defined as an acute, autoimmune polyradiculoneuropathy. It is a rare disease that occurs at a rate of 1.11 cases per 100,000 person-years. However, once infected, up to 20% of patients develop severe disability, and approximately 5% die. There have been reports of GBS in different cancers. Among them, there are 6 previous reports of GBS in small cell lung cancer. Here, we report a case of a 52-year-old man who was diagnosed with GBS in the setting of small cell lung cancer with chemotherapy.

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Introduction

Paraneoplastic syndromes are frequently found in lung cancer. Hypercalcemia, syndrome of inappropriate secretion of antidiuretic hormone, Cushing's syndrome, and skeletal-connective tissue syndromes are common in patients with lung cancer, especially those with small cell lung cancer (SCLC).

SCLC is a highly aggressive disease with rapid growth. Approximately two thirds of SCLC patients present with metastatic stage at the time of diagnosis. Lambert-Eaton syndrome occurs in 3% of SCLC patients as neurological paraneoplastic syndrome. However, the association of malignancy and Guillain-Barré syndrome (GBS) is not well known.

GBS is an acute, autoimmune polyradiculoneuropathy. It is a rare disease that occurs at a rate of 1.11 cases per 100,000 person-years. However, once infected, up to 20% of patients develop severe disability, and approximately 5% die [1]. There have been reports of parane-

oplastic GBS in different cancers. To the best of the present authors' knowledge, there are 6 published reports of GBS in SCLC [2–7]. Here, we report a case of a 52-year-old man who was diagnosed with GBS in SCLC with chemotherapy.

Case Report

A 52-year-old man presented with lower-limb weakness and was admitted. He was diagnosed with SCLC, limited disease, at another hospital 5 years ago. He had been recommended concurrent chemoradiotherapy at that time but had wanted to be treated with chemotherapy only. Thus, he was started on irinotecan and carboplatin. After 6 cycles, complete remission was noted, and prophylactic cranial irradiation was given. A year later, he had relocated residence and visited our hospital, presenting with relapsed lung cancer but refusing treatment. After 7 months, further disease progression and pancreatic metastasis was noted on computed tomography (CT) scanning. The patient received 6 cycles of a combination of etoposide and cisplatin. Meanwhile, superior vena cava syndrome occurred, and radiation therapy was delivered in the middle of chemotherapy. A CT scan for the response showed disease progression. He was started on cisplatin, doxorubicin, and cyclophosphamide (CAP) and also received palliative brain radiotherapy due to brain metastasis during the chemotherapy.

After 6 cycles of CAP, the cancer remained stable. However, in his fifth year of cancer diagnosis, he presented with lower-limb weakness and was admitted. He noticed weakness in both legs 2 weeks prior to admission and developed numbness throughout the lower extremities. After admission, he developed weakness in both arms. A neurological examination revealed no nuchal rigidity or Kernig's sign as well as absence of deep tendon reflexes. Magnetic resonance imaging (MRI) of the brain showed some unidentified bright objects (fig. 1). However, there was little possibility of brain metastasis or embolic infarction when comparing the patient's symptoms and physical examination with the MRI lesions. To evaluate neurologic problems, spinal cord MRI was performed. It revealed a fracture of the second lumbar vertebra that seemed to be benign (fig. 2). However, the ascending paralysis, from the lower extremities to the upper extremities, did not correlate with the cord compression lesion either. Nerve conduction studies showed decreased amplitudes and slow velocities of compound muscle action potential and sensory nerve action potential in the extremities. The results were consistent with sensorimotor polyneuropathy. A lumbar puncture yielded cerebrospinal fluid protein 94 mg/dl, albumin 61.3 mg/dl, glucose 173 mg/dl, and white blood cells 1/μl. These were assessed as being due to albuminocytological dissociation, and there were no signs of meningitis. Antiganglioside antibodies were not tested.

The patient was diagnosed with GBS and was recommended treatment with intravenous immunoglobulin (IVIg), which he refused. He received supportive care, and his general weakness worsened. He died 18 days after diagnosis.

Discussion

Sensorimotor neuropathy is common in cancer patients [8]. It could be caused by adverse effects of chemotherapy or by other underlying diseases that have nothing to do with malignancies, such as diabetes. However, these sensorimotor neuropathies almost always result in mild to moderate dysfunction and usually do not affect patients' survival.

GBS is an acute, autoimmune polyradiculoneuropathy. It is characterized by both limbs and muscles innervated by cranial nerves being weakened. Approximately 70% of GBS cases are preceded by respiratory or gastrointestinal infection. Nearly 30% of cases are preceded by infection with *Campylobacter jejuni* [9]. Cytomegalovirus has been identified in up to 10% of cases [10].

The diagnosis is suspected based on its characteristic clinical features. A progressive bilateral, symmetric weakness of the extremities manifests over a period of 12 h to 28 days from disease onset [11]. The nerve conduction study result was consistent with acute peripheral neuropathy, a cerebrospinal fluid analysis demonstrating an elevated protein level and absence of leukocytosis due to albuminocytological dissociation will be helpful to confirm the GBS diagnosis [12].

A differential diagnosis of GBS is important. GBS should take into account various diseases, such as brain or leptomeningeal metastasis from cancer, and spinal cord compression. Meningitis and chemotherapy-induced peripheral neuropathy should also be considered. It is known that some anticancer drugs can cause peripheral neuropathy. Brouwers et al. [13] described neuropathy occurring after treatment with a combination of oxaliplatin and cisplatin; Nardone et al. [14] also reported 4 cases of acute peripheral neuropathy after completion of oxaliplatin treatment.

All patients should be monitored for cardiac and pulmonary dysfunction and require supportive care. In addition, when patients with GBS are not able to walk independently, immunotherapy is required. In immunotherapy, either IVIg or plasmapheresis can be used. These treatments have been observed to be effective when started within the first 2 weeks after disease onset [15].

This case is different from the existing 6 cases. In the present case, GBS occurred in a patient receiving long-term antineoplastic therapy, whereas GBS had occurred at the initial point of presentation in the 6 other cases [2–7]. This is the first reported case of paraneoplastic GBS that developed in an SCLC patient with long-term therapy.

To the present authors' knowledge, in the 5 cases of GBS with SCLC, there was no relationship between chemotherapy and GBS. In 4 of the 5 reports, patients received chemotherapy; however, in all 4 of these reports, the patients underwent chemotherapy after GBS had been diagnosed and IVIg had been given. In addition, in 3 of these 4 reports, a combination of etoposide and carboplatin was used, whereas the other report did not indicate the chemotherapy regimen [2–6].

The present patient was diagnosed with GBS 3 weeks after symptom onset. Immunotherapy was recommended at the time of diagnosis, but he refused the treatment because of his advanced cancer stage and poor general condition.

Patients with cancer are vulnerable to infection and can have problems with the immune system. As illustrated by this report, paraneoplastic GBS in SCLC is a life-threatening disease. Thus, it should be monitored and treated when acute progressive peripheral neuropathy occurs in patients with SCLC.

The authors submitted a waiver from their institutional review board stating that this case report does not require institutional review board approval or oversight.

Disclosure Statement

The authors report no conflicts of interest in connection with this work.

Statement of Ethics

The authors have no ethical conflicts to disclose.

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Fig. 1. Diffusion-weighted MRI showing some unidentified bright objects.

Fig. 2. MRI of the spinal cord showing second lumbar vertebra compression fracture.