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Case Report

Pembrolizumab-induced Guillain–Barré Syndrome in Early-stage Triple-negative Metaplastic Breast Cancer Responded to Intravenous Immunoglobulin and Steroids: A Case Report

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Abstract

Pembrolizumab is an immune checkpoint inhibitor that blocks the PD-1 pathway on T-cells. It has been associated with a variety of immune-related adverse events, including Guillain–Barré syndrome (GBS), a rare but critical event. We report the case of a patient with early-stage metaplastic breast cancer who developed Grade 4 pembrolizumab-induced GBS early in the treatment course and had a remarkable response to intravenous immunoglobulins and steroids.

Keywords: Case report, guillain–Barré syndrome, intravenous immunoglobulin, pembrolizumab, steroid, triple-negative breast cancer

Introduction

Pembrolizumab is an immune checkpoint inhibitor (ICI) that blocks the PD-1 pathway on T-cells and is widely used in the treatment of several types of cancers.[1] The use of pembrolizumab has allowed for novel combination strategies to fight cancer but has also led to various degrees and presentations of immune-related adverse events (irAEs). The KEYNOTE 522 study randomly assigned patients with untreated stage II or stage III triple-negative breast cancer (TNBC) to receive neoadjuvant therapy with four cycles of pembrolizumab or placebo plus paclitaxel and carboplatin followed by the four cycles of pembrolizumab or placebo plus doxorubicin or epirubicin plus cyclophosphamide. The study was the first to demonstrate that adding pembrolizumab to neoadjuvant chemotherapy followed by continued adjuvant pembrolizumab significantly improved pathological complete response (pCR) rate, event-free survival, and overall survival in patients

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with early-stage TNBC.[2] Consequently, pembrolizumab in combination with cytotoxic chemotherapy has become a standard for early-stage TNBC patients.[2] However, the impact of irAEs on early-stage potentially curable cancer still requires meticulous vigilance. In this article, we report the case of a patient who developed Guillain–Barré syndrome (GBS) as a severe irAE after pembrolizumab in combination with carboplatin and paclitaxel who had a remarkable response because of early detection and adequate intervention.

Case Report

A 68-year-old postmenopausal woman presented with left breast metaplastic carcinoma with extensive squamous differentiation, hormone receptor-negative, human epidermal growth factor receptor 2 0/3+, Ki-67 50%, cT3N3M0, locally advanced to small lymph nodes in left axilla level I, and a small lymph node in the left supraclavicular region. She had no history of tobacco, alcohol, or betel nut use, and there was no relevant family medical history. She was initially treated with weekly carboplatin, paclitaxel and triweekly pembrolizumab.

She had limited side effects in the first 5 weeks of treatment and remained independent in activities of daily living. However, she developed an on and off fever with chills and upper respiratory symptoms in week eight. Progressive bilateral symmetric ascending dysesthesia with a tingling sensation in a socks and gloves pattern developed over the next 4 days, accompanied by proximal thigh weakness. On the following day, a neurological examination showed ascending hypoesthesia as well as ascending weakness from distal to proximal (4 + to 3) in both lower and upper extremities. She could barely hold a pen to sign her name. She had not received a vaccination in recent days and had no urinary symptoms, diarrhea, back pain, or abdominal pain. COVID-19 and influenza tests were negative. Cerebrospinal fluid (CSF) analysis revealed a significant elevation in protein level (118.9 mg/dL, normal: 15–45 mg/dL) and normal white cell count with no evidence of malignant cells. CSF cultures including cryptococcal antigen, fungus, Gram's stain, acid fast bacilli, and anaerobic pathogens were all negative. Serological tests included rheumatoid factor; immunoglobulins (IgG, IgA, and IgM); complement components C3, C4, and C1q; acetylcholine receptor antibody; anti-proteinase 3 antibody; anti-β2-glycoprotein I antibody; anti-Sjögren's syndrome A (SS-A/Ro) and anti-SS-B/La antibodies; antiphospholipid antibodies (IgG and IgM); anticardiolipin antibodies (IgG and IgM); extractable nuclear antigen (ENA) panel; and anti-myeloperoxidase (MPO) antibodies. All of these rheumatological factors were within normal range, except that total IgM was lower than the normal range (36.89, normal range 45–281 mg/dL).

A nerve conduction velocity test revealed prolonged distal motor latencies in bilateral median nerves, reduced compound motor action potential and sensory actional potential amplitude in all sampled nerves, slowing of sensory conduction velocity in bilateral median and ulnar nerves and slowing of motor conduction velocities in bilateral tibial and peroneal nerves. The results of an F-response study revealed the absence of F-response and presence of A-waves in bilateral peroneal nerves and prolonged minimal F-wave latency with A-waves in bilateral tibial nerves. Based on these studies and after consultation with a neurologist, the diagnosis was pembrolizumab-related Grade 4 GBS (urgent intervention indicated) or Grade 4 according to the common terminology criteria for adverse events (CTCAE).[3] We prescribed intravenous immunoglobulins (IVIGs) 24 g per day for 5 days (total 120 g, 2 g/kg) and methylprednisolone 30 mg every 8 h (1.5 mg/kg). Within 1 week, her neurological symptoms noticeably improved at the proximal limb muscles. Four weeks after the irAE, she regained motor function and could walk without support. However, paresthesia of her extremities remained and she is currently undergoing a rehabilitation program to improve her activities of daily function [Figure 1].

In addition to pembrolizumab-related GBS, she also developed multi-organ irAEs including erythroderma (Grade 3), oral and anal mucositis (Grade 3), and transaminitis (Grade 3). The results of rheumatic serological examinations did not support any specific autoimmune disease. However, after receiving methylprednisolone therapy given as described above, her skin lesions and transaminitis gradually subsided.

Despite the severe irAEs, her tumor responded well to just two cycles of pembrolizumab along with weekly carboplatin and paclitaxel, shrinking from 3.1 cm to 2.2 cm in maximum diameter. She was able to receive left side total mastectomy with sentinel lymph node biopsy 1 month after the diagnosis of GBS, and the pathology report showed residual cancer burden (RCB) score of 2.172 (RCB II) with no lymph node involvement.

Discussion

Metaplastic breast carcinoma is a rare and aggressive subtype of breast cancer, accounting for < 1% of all breast malignancies. It is characterized by the presence of nonglandular components, most notably squamous differentiation, which may appear alone or with mesenchymal elements such as spindle or chondroid cells.[4,5] Most metaplastic breast carcinomas are TNBC, however, metaplastic features can also rarely occur in hormone receptor-positive or HER2-positive tumors. Metaplastic breast carcinoma generally carries a poorer prognosis compared to conventional breast cancers, with lower response rates to chemotherapy and a higher risk of early recurrence.[6,7]

GBS is a multifactorial autoimmune disorder presenting with features from acute-onset polyneuropathy to chronic peripheral neuritis.[8] Symptoms typically first present 1–2 weeks after infection, usually as weakness or tingling sensations which start in the legs and then spread to the arms. Cell-mediated immunity

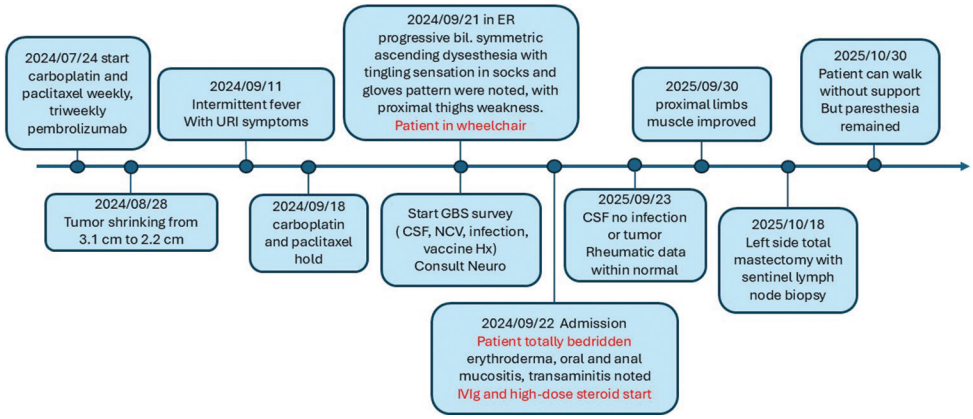

Figure 1: Clinical and treatment timeline of the reported patient

has been reported to play a crucial role in the immunopathology of all types of GBS.[9] Some evidence supports the activation of T-cells stimulated by bacteria or a virus in the acute phase of GBS, disrupting the blood nerve barrier through neutrophil activation and infiltration, causing demyelination and neuropathy.[9] In addition, PD-1 plays an important role in immune self-tolerance by inhibiting the response of T-cells in the peripheral tissues,[10] while pembrolizumab and other similar ICIs block PD-1 receptors. Due to the cross-reaction of molecular similarity, T cell-mediated autoimmunity against tumor cell antigens may also have an effect on neurons.[11] Most neurological irAEs occur within 3 months (median: 6 weeks) after initial treatment.[11] The incidence of high-grade neurological irAEs is below 1% for all types of treatment. Headaches, encephalopathies, and meningitis are the most commonly reported (21%, 19%, and 15%, respectively).[12] According to the ASCO guidelines, management varies based on the symptom severity based on CTCAE assessment. In general, severe symptoms are classified as Grade 3 toxicities that limit self-care activities of daily living and require the use of assistive devices. Grade 3 toxicities generally warrant suspension of ICP and the initiation of high-dose corticosteroids, which should be tapered over the course of at least 4–6 weeks.[13] IrAE-related GBS is an extremely rare complication, however, several cases have been reported in recent years.[11,14-16]

IVIG and plasma exchange are the standard treatments for GBS. The use of steroids in the treatment of GBS remains controversial, and the mechanism is unclear. Hughes *et al*. reported that steroid treatment is not beneficial and can be detrimental in GBS[17] and another study reported that steroids may reduce nerve regeneration, thereby delaying recovery from this disease.[18] However, Ma *et al*. suggested that high doses of corticosteroids may partly result from the duration of hospital stay and short-term outcomes.[19] Plasma exchange is mostly reserved for GBS patients who are refractory to IVIG treatment because of the need for large bore lumens and longer duration of treatment. Our patient received treatment for 2 months, and first suffered from intermittent fever with chills in week eight. She then developed rapidly progressive, symmetric, and ascending weakness of the upper and lower extremities over 4 days after the fever and was diagnosed with GBS as an irAE. She also developed multi-organ irAEs including erythroderma (Grade 3), oral and anal mucositis (Grade 3), and transaminitis (Grade 3). Therefore, we had to prescribed IVIG for irAE-GBS and steroids for other multiorgan irAEs and considered plasma exchange if IVIG failed. Our patient then recovered well within 1 week, including GBS and other irAEs. This may suggest that different approaches should be considered when treating GBS and irAE-related GBS. Finally, given the inflammatory nature of GBS, we attributed its onset in our patient to pembrolizumab treatment. While previous reports have suggested an association between platinum exposure and the development of GBS,[20] it remains unclear whether the combination of platinum and pembrolizumab – as used in the KEYNOTE-522 regimen for early-stage TNBC – confers an increased risk. Clinicians should maintain a high level of vigilance for aggressive sensorimotor neuropathy, particularly in the curative setting of early-stage breast cancer.

In Marhold *et al*.'s study, patients receiving pembrolizumab for early TNBC (clinical stage II-III) had a higher rate of developing Grade 3 or higher irAEs. Moreover, the emergence of irAEs was significantly correlated with pCR (72.2% vs. 30.8%; $P = 0.03$).[21] Our patient's tumor responded well to just two cycles of pembrolizumab along with weekly carboplatin and paclitaxel. Due to her Grade 4 pembrolizumab-induced GBS, she could not receive further ICI treatment. Fortunately, her respiratory function was not compromised and she was deemed suitable for general anesthesia after consulting the anesthesiologist. One month after GBS, she received left total mastectomy with axillary lymph node dissection. The pathology report showed a 29% decrease in the maximum diameter of the tumor and an RCB II response. Regarding adjuvant treatment after surgery, she decided not to receive anthracyclines and chose capecitabine as the adjuvant treatment.

Conclusion

GBS is a potentially life-threatening irAE during the first 3 months after pembrolizumab therapy; therefore, high awareness of the patient's neurological condition is very

important. Early diagnosis and appropriate treatment are crucial for improving patient outcomes.

Declaration of patient consent

This study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki and its amendments. The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that name and initial will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Author contributions

All authors contributed to the conception of the study, data collection, drafting of the manuscript, and approved the final version of the manuscript.

Data availability statement

Data sharing not applicable to this article as no datasets were generated or analyzed during the current study.

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Conflicts of interest

Prof. Tom Wei-Wu Chen, an editor at *Journal of Cancer Research and Practice*, had no role in the peer review process of or decision to publish this article. The other authors declared no conflicts of interest in writing this paper.

References

1. Kwok G, Yau TC, Chiu JW, Tse E, Kwong YL. Pembrolizumab (keytruda). Hum Vaccin Immunother 2016;12:2777-89.
2. Schmid P, Cortes J, Dent R, McArthur H, Pusztai L, Kümmel S, *et al.* Overall survival with pembrolizumab in early-stage triple-negative breast cancer. N Engl J Med 2024;391:1981-91.
3. National Cancer Institute. Common Terminology Criteria for Adverse Events (CTCAE) v5.0, 2017.
4. Lien HC, Hsu CL, Lu YS, Chen TW, Chen IC, Li YC, *et al*. Transcriptomic alterations underlying metaplasia into specific metaplastic components in metaplastic breast carcinoma. Breast Cancer Res 2023;25:11.
5. Lien HC, Lee YH, Chen IC, Lin CH, Chen TW, Lu YT, *et al*. Tumor-infiltrating lymphocyte abundance and programmed death-ligand 1 expression in metaplastic breast carcinoma: Implications for distinct immune microenvironments in different metaplastic components. Virchows Arch 2021;478:669-78.
6. Thapa B, Arobelidze S, Clark BA, Xuefei J, Daw H, Cheng YC, *et al*. Metaplastic breast cancer: Characteristics and survival outcomes. Cureus 2022;14:e28551.
7. Rayson D, Adjei AA, Suman VJ, Wold LE, Ingle JN. Metaplastic breast cancer: Prognosis and response to systemic therapy. Ann Oncol 1999;10:413-9.
8. Dalakas MC. Pathogenesis of immune-mediated neuropathies. Biochim Biophys Acta 2015;1852:658-66.
9. Ebrahim Soltani Z, Rahmani F, Rezaei N. Autoimmunity and cytokines in Guillain-Barré syndrome revisited: Review of pathomechanisms with an eye on therapeutic options. Eur Cytokine Netw 2019;30:1-14.
10. Chen L, Flies DB. Molecular mechanisms of T cell co-stimulation and co-inhibition. Nat Rev Immunol 2013;13:227-42.
11. Li Y, Zhang X, Zhao C. Guillain-Barré syndrome-like polyneuropathy associated with immune checkpoint inhibitors: A systematic review of 33 cases. Biomed Res Int 2021;2021:9800488.
12. Cuzzubbo S, Javeri F, Tissier M, Roumi A, Barlog C, Doridam J, *et al*. Neurological adverse events associated with immune checkpoint inhibitors: Review of the literature. Eur J Cancer 2017;73:1-8.
13. Hazim A, Guiance IR, Shreve J, Ruan G, McGlothlin D, LeMahieu A, *et al.* Clinical characteristics, outcomes, and predictive modeling of patients diagnosed with immune checkpoint inhibitor therapy-related pneumonitis. Cancer Immunol Immunother 2025;74:194.
14. Oguri T, Sasada S, Shimizu S, Shigematsu R, Tsuchiya Y, Ishioka K, *et al*. A case of Guillain-Barré syndrome and Stevens-Johnson syndrome/toxic epidermal necrosis overlap after pembrolizumab treatment. J Investig Med High Impact Case Rep 2021;9:23247096211037462.
15. Han C, Ma JA, Zhang Y, Jiang Y, Hu C, Wu Y. Guillain-Barre syndrome induced by pembrolizumab and sunitinib: A case report. Mol Clin Oncol 2020;13:38-42.
16. Thompson JA, Schneider BJ, Brahmer J, Zaid MA, Achufusi A, Armand P, *et al*. NCCN Guidelines® insights: Management of immunotherapy-related toxicities, version 2.2024. J Natl Compr Canc Netw 2024;22:582-92.
17. Hughes RA, Newsom-Davis JM, Perkin GD, Pierce JM. Controlled trial prednisolone in acute polyneuropathy. Lancet 1978;2:750-3.
18. Wang YZ, Lv H, Shi QG, Fan XT, Li L, Yi Wong AH, *et al*. Action mechanism of corticosteroids to aggravate Guillain-Barré syndrome. Sci Rep 2015;5:13931.
19. Ma L, Liu S, Xiao Z, Guan J, Liu Y, Yao J, *et al*. Comparison of the effects of different doses of Glucocorticoids on distinct subtypes of Guillain-Barré syndrome in Southern China. BMC Neurol 2022;22:46.
20. Pappa E, Berzero G, Herlin B, Ricard D, Tafani C, Devic P, *et al*. Guillain-Barré syndrome during platinum-based chemotherapy: A case series and review of the literature. Oncologist 2020;25:e194-7.
21. Marhold M, Udovica S, Halstead A, Hirdler M, Ferner M, Wimmer K, *et al*. Emergence of immune-related adverse events correlates with pathological complete response in patients receiving pembrolizumab for early triple-negative breast cancer. Oncoimmunology 2023;12:2275846.