

CASE REPORT

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Bilateral facial nerve palsy associated with amphiphysin antibody in metastatic breast cancer: a case report

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Abstract

Background: Paraneoplastic neurological syndrome is an immune-mediated phenomenon where antibodies from tumor cells are produced against neuronal proteins. Amphiphysin antibody is an onconeural antibody linked to the diagnosis of breast cancer and small-cell lung cancer. It is uncommon and typically associated with stiff-person syndrome, of which 90% of patients are eventually diagnosed with breast cancer.

Case presentation: We present a case of a 47-year-old Caucasian woman with metastatic hormone receptor-positive breast cancer who developed bilateral facial nerve palsy while on treatment with nab-paclitaxel. The patient was found to have anti-amphiphysin antibody in the serum and cerebrospinal fluid. She was treated with methylprednisolone and intravenous immunoglobulin, which resulted in partial improvement in her facial nerve palsy.

Conclusions: This case highlights a rare presentation of bilateral facial nerve palsy that likely related to paraneoplastic syndrome associated with the presence of anti-amphiphysin antibody.

Keywords: Facial nerve palsy, Bell's palsy, Amphiphysin antibody, Breast cancer, Nab-paclitaxel, Paraneoplastic syndrome

Background

Paraneoplastic neurological syndrome (PNS) is an immune-mediated phenomenon in which antibodies respond against neuronal proteins produced by tumor cells (onconeural antibodies) [1]. The presence of onconeural antibodies is a useful diagnostic marker of PNS [2]. They are specific to a group of malignant diseases rather than identified as a neurological syndrome [3]. An amphiphysin antibody is an onconeural antibody that has been identified and linked to the diagnosis of breast cancer and small-cell lung cancer (SCLC) [4–6].

We describe the first case in the literature of bilateral facial nerve palsy with the presence of anti-amphiphysin antibodies in a patient diagnosed with metastatic

hormone receptor-positive, estrogen receptor (ER)/progesterone receptor (PR) positive, human epidermal growth factor receptor 2 (HER2)-negative breast cancer.

Case presentation

A 47-year-old Caucasian woman with Eastern Cooperative Oncology Group (ECOG) grade 0 presented with a palpable mass in the left breast associated with an enlarging scalp lesion over 4 months. Biopsy confirmed a diagnosis of metastatic ER/PR positive, HER2-negative breast carcinoma (Fig. 1). Computerized tomography staging demonstrated a multifocal primary lesion fixed to the chest wall, axillary lymphadenopathy, and lung and liver lesions, as well as omental, scalp, and bony involvement. She had no other significant comorbidity. She was started on chemotherapy with nab-paclitaxel, a commonly used agent in the first-line treatment of metastatic breast cancer.

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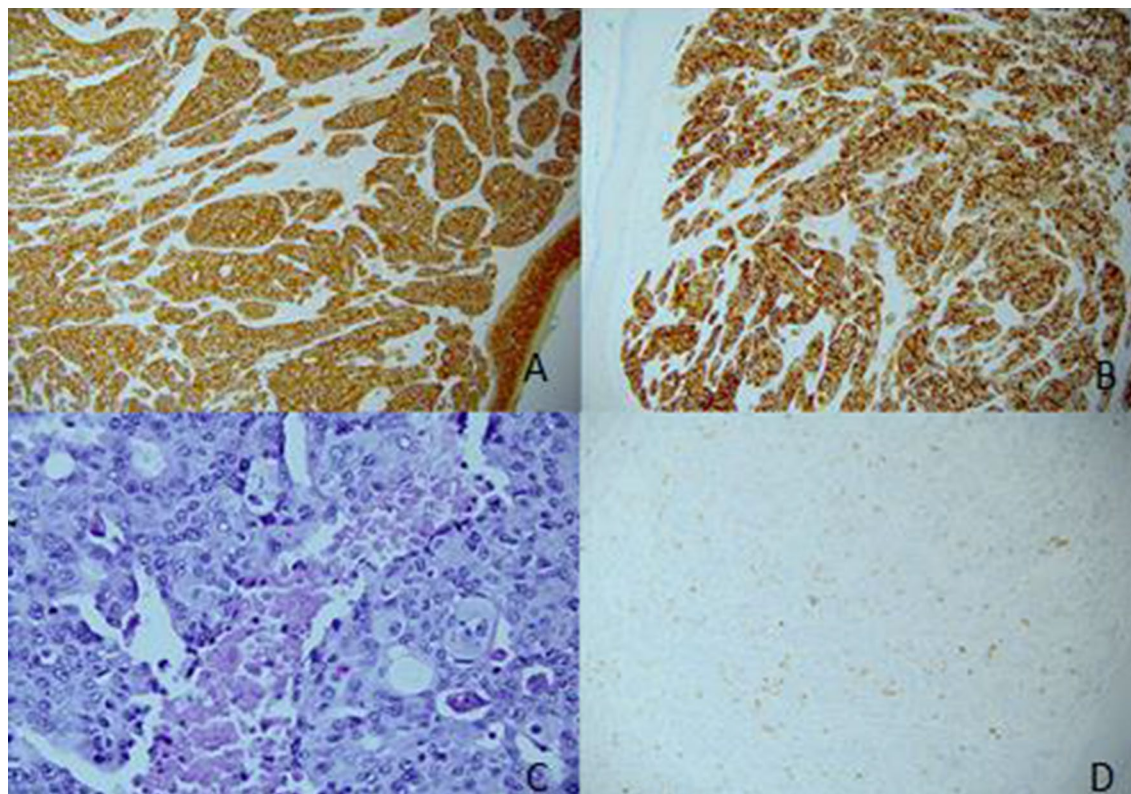


Fig. 1 Photomicrograph of breast and scalp lesions shows staining for **a** AE1/AE3, **b** CK 7, **c** focal mucin droplets, and **d** mammaglobin

Following three cycles of nab-paclitaxel (260 mg/m² every 21 days each cycle), there was a partial response with shrinkage of tumor in all areas. Her cancer antigen 15-3 declined from 179 to 25 kU/L. She continued with a further three cycles of chemotherapy. Prior to proceeding with the sixth cycle of nab-paclitaxel, she presented with a left-sided lower motor neuron weakness of the face. It was classified as severe as she was unable to close her eyes. There was no evidence of an intracranial lesion or ischemic changes on CT or MRI of the brain. At this point, she was diagnosed with bilateral facial nerve palsy and was administered a trial of oral prednisolone for 5 days without any improvement in her symptoms.

One week later, she presented with a lower motor neuron weakness of the contralateral face, giving her bilateral facial nerve palsy. The remainder of the neurological examination did not reveal additional deficits. Subsequent MRI of the brain demonstrated evidence of bilateral facial nerve neuritis involving predominantly the terminal branches. Analysis of the cerebrospinal fluid (CSF) revealed no infective or malignant etiology. Interestingly, the paraneoplastic screening showed the presence of anti-amphiphysin antibodies in both serum and CSF. All other anti-neuronal antibodies, including

anti-glutamic acid decarboxylase antibodies, were not detected. A repeat CT scan following the completion of six cycles of chemotherapy demonstrated a partial response according to Response Evaluation Criteria in Solid Tumors (RECIST) 1.1 criteria to the visceral diseases, with a further reduction in cancer antigen 15-3 (Fig. 2).

The patient was started on 1 g IV pulse methylprednisolone for 3 days. This was followed up with intravenous immunoglobulins (IVIG) at a dose of 2 g/kg divided over 5 days. She completed four cycles of IVIG at the 2 g/kg dose, which resulted in a subtle improvement of the frontalis muscle; however, the loss of nasolabial folds and inability to close her eyes persisted. A repeat MRI revealed resolution of facial nerve neuritis. A repeat analysis of CSF showed a high level of anti-amphiphysin antibodies titer of 1:640. Nerve conduction study and electromyography suggested evidence of peripheral nerve reinnervation. She continued with monthly IVIG for the next 6 months. Her chemotherapy was stopped and switched to maintenance hormonal therapy with letrozole 2.5 mg daily to help control her malignant disease. A repeat CT scan 3 months later showed overall stable malignant disease.

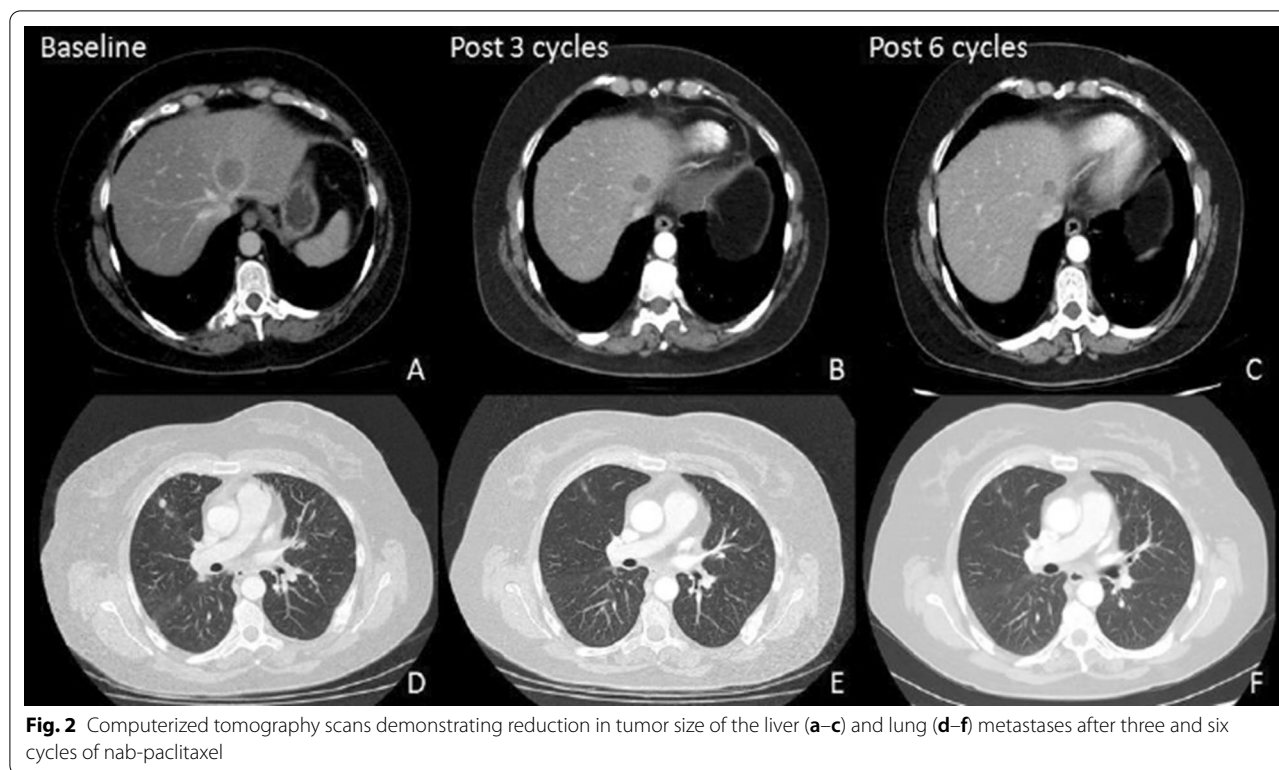


Fig. 2 Computerized tomography scans demonstrating reduction in tumor size of the liver (a–c) and lung (d–f) metastases after three and six cycles of nab-paclitaxel

Discussion

PNS is a rare event that affects < 1% of patient with an underlying malignancy [3]. An international panel of neurologists categorize the diagnosis of PNS into two subgroups—“definite” and “possible.” A definite diagnosis can be made when there is a classical or nonclassical neurological syndrome with the presence of onconeural antibodies (that is, amphiphysin antibody), with or without evidence of malignancy. The classical neurological syndromes include encephalomyelitis, limbic encephalitis, subacute cerebellar degeneration, and opsoclonus-myoclonus [7]. A small number of case reports have described the link between amphiphysin antibodies with these classical neurological syndromes in patients with breast cancer and SCLC [8, 9].

Amphiphysin is a nerve-terminal protein that is found in high concentration in the nervous system and is presumed to have a role in synaptic vesicle endocytosis [10, 11]. The anti-amphiphysin autoantibody reacts with 128-kD protein in synaptic vesicles [8]. They are usually seen in both serum and CSF in a subset of patients with stiff-person syndrome (SPS), breast cancer, and SCLC [9]. Around 90% of SPS patients with amphiphysin antibody have been found to have breast cancer during their illness [12].

There has been no published report on the association between the presence of amphiphysin antibodies in

breast cancer and bilateral facial nerve palsy. The diagnosis of bilateral facial nerve palsy is itself a rare entity. It is unlikely to be idiopathic in nature and usually reflects an underlying pathology. The potential causes include bilateral acoustic neuroma, Lyme disease, Guillain–Barre syndrome, syphilis, HIV, sarcoidosis, or a tumor, among others [13–15].

Our case highlights an unusual presentation of bilateral facial nerve palsy and a diagnostic dilemma. The potential causes may be either PNS or drug-induced nerve palsy with nab-paclitaxel. The presence of amphiphysin antibody in her blood and CSF despite four cycles of IVIG and a modest response to treatment led us to believe the underlying process to be due to paraneoplastic syndrome. However, the indolent nature and stable state of her breast cancer does not support PNS, as it usually behaves aggressively.

Alternatively, nab-paclitaxel can commonly cause sensory peripheral neuropathy and motor neuropathy [16]. One important risk factor for this is high dosing and frequency of treatment. A case report previously described a case of bilateral facial nerve palsy in metastatic breast cancer following one cycle of high-dose paclitaxel (825 mg/m²), which eventually resolved after 23 months [17]. Another case described a case of unilateral facial nerve palsy following nab-paclitaxel (260 mg/m²), which improved after 9 months [18]. Though drug-induced

facial nerve palsy is a possible cause for our patient's presentation, her facial nerve palsy has not significantly improved since cessation of nab-paclitaxel. Moreover, it does not explain the presence of amphiphysin antibody in our case.

Conclusions

Identifying the cause of PNS can sometimes be challenging. Our approach to the case was to stop nab-paclitaxel because of the possibility of its being a direct cause of bilateral facial nerve palsy and switch to endocrine therapy as well as treat the underlying PNS with IVIG and high-dose methyl prednisolone. Currently, there are no guidelines for the management of PNS; however, the principle of treatment suggests treating the underlying tumor with surgery, chemotherapy, or radiotherapy [3]. Other modalities of treatment include immunotherapy with high-dose methyl prednisolone or IVIG.

Abbreviations

CSF: Cerebrospinal fluid; CT: Computerized tomography; HIV: Human immunodeficiency virus; IVIG: Intravenous immunoglobulins; MRI: Magnetic resonance imaging; PNS: Paraneoplastic neurological syndrome; SCLC: Small-cell lung cancer; SPS: Stiff-person syndrome.

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Authors' contributions

VK was involved in writing the manuscript. MC and NK supervised the case and helped with revision and final proofreading. All authors read and approved the final manuscript.

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Ethics approval and consent to participate

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Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal

Competing interests

The authors declare that they have no competing interests

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