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# Paraneoplastic Polyneuritis Cranialis Associated With Breast Carcinoma: A Case Report

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## Abstract

Paraneoplastic neurological syndromes (PNSs) are rare immune-mediated disorders that occur as remote manifestations of malignancy and may precede the diagnosis of the underlying cancer. Polyneuritis cranialis is an uncommon neurological condition characterized by the involvement of multiple cranial nerves and rarely occurs as a paraneoplastic manifestation of breast carcinoma. Recognition of this association is important as neurological symptoms may represent the first clue to an occult malignancy.

A 107-year-old female patient was referred from the eye clinic with progressive left eye pain, partial ptosis, ophthalmoplegia, and facial weakness. Neurological examination demonstrated involvement of the left third, sixth, and seventh cranial nerves. Initial neuroimaging and routine investigations were unremarkable. Further evaluation revealed an elevated carcinoembryonic antigen level, prompting comprehensive malignancy screening. Computed tomography of the chest identified a left breast lesion, and subsequent ultrasound-guided biopsy confirmed poorly differentiated invasive breast carcinoma (NST, Grade III). A diagnosis of paraneoplastic polyneuritis cranialis associated with breast carcinoma was possible. However, extensive workup had to be done to exclude other vascular, neoplastic, and immune causes of polyneuritis cranialis. While the patient was undergoing specific imaging and laboratory testing, she was treated with intravenous immunoglobulin, with subsequent partial neurological improvement.

Although breast cancer is a recognized cause of PNSs, cranial nerve predominance is uncommon. Previously reported cases revealed brainstem and cerebellar syndromes as known paraneoplastic presentations associated with breast cancer. Autoantibody production seems to be the suspected cause of such manifestations, such as anti-Yo and anti-Ri antibodies. The current available management includes treating the underlying malignancy, in combination with immunotherapy. Unexplained presentations with cranial polyneuropathy should be considered alarming for the presence of an occult malignancy and should therefore be investigated thoroughly.

Paraneoplastic polyneuritis cranialis may represent a very early manifestation of occult malignancy and precede the eventual diagnosis of cancer. Clinicians should maintain a high index of suspicion for an underlying malignancy in patients presenting with unexplained progressive cranial neuropathies. Early recognition, comprehensive cancer screening, and timely immunomodulatory treatment may improve neurological outcomes and facilitate earlier oncological management.

**Categories:** Neurology, Oncology
**Keywords:** breast carcinoma, cranial neuropathy, onconeural antibodies, paraneoplastic neurological syndrome, polyneuritis cranialis

## Introduction

Paraneoplastic neurological syndromes (PNSs) are a heterogeneous group of immune-mediated disorders that occur as remote effects of malignancy and are not attributable to direct tumor invasion, metastasis, infection, or treatment-related complications. These syndromes are believed to arise from an autoimmune response directed against shared antigens expressed by both tumor cells and components of the nervous system. They are typically rare, with an incidence of around 1.6 to 8.9 per million person-years [1]. Polyneuritis cranialis is an uncommon neurological disorder characterized by the simultaneous or sequential involvement of multiple cranial nerves, resulting in clinical manifestations such as ophthalmoplegia, ptosis, facial weakness, diplopia, and sensory disturbances. Among the rare causes of polyneuritis cranialis are PNSs [1,2].

Owing to their heterogeneous presentation, the condition may mimic a wide range of neurological, infectious, inflammatory, and vascular disorders, making diagnosis particularly challenging. PNSs are rare, and cranial nerve-predominant presentations represent an especially uncommon subset. Although breast carcinoma is a recognized cause of PNS, presentation as paraneoplastic polyneuritis cranialis remains exceptionally rare. In PNSs, neurological manifestations may precede the diagnosis of the underlying malignancy and may therefore serve as an important clue to occult cancer. However, breast cancer is one of

the recognized cancers that metastasize to the brain, skull base, and meninges, also leading to neurological manifestations, so excluding metastasis first would be crucial before considering a paraneoplastic association. Early recognition is essential, as prompt identification of the underlying malignancy and initiation of immunomodulatory and oncological therapy may improve neurological outcomes and overall prognosis [3-5].

We report a rare case of paraneoplastic polyneuritis cranialis associated with occult breast carcinoma, highlighting the diagnostic challenges and emphasizing the importance of considering a paraneoplastic etiology in patients presenting with unexplained multifocal cranial neuropathies.

## Case Presentation

A 107-year-old female patient, with multiple comorbidities, presented to the Ophthalmology Clinic with complaints of aching left eye pain and left ear pain for one day. The pain was acute and was not preceded by any precipitating illness, was not relieved by painkillers, and worsened with movement of the affected eye. She also reported a gritty sensation and occasional visual blurring in the left eye. On further inquiry, there was no diplopia, headache, trauma, fever, or rash. The ear pain was not associated with rashes, vertigo, or hearing loss. The patient is a known hypertensive, diabetic, dyslipidemic, on polypharmacy, and follows up with multiple physicians regarding her chronic conditions. Surgical history includes cataract surgery for both eyes, bilateral pseudophakia, and multiple coronary artery stents. Examinations done by the ophthalmologist yielded normal age-related changes; lubricating and sterilizing eye drops were prescribed, and she was sent home. Three weeks after her initial presentation, she presented again, however this time to the Neurology Clinic, with worsening symptoms; her left eye pain did not resolve; although she no longer had left ear pain, she noticed downward deviation of the left side of the face.

Upon cranial nerve examination, the left eye had an enlarged pupil not reactive to light or accommodation, with partial ptosis present, accompanied by inability to abduct or adduct the eye; moreover, there was weakness in the muscles of the left side of the face with downward deviation, inability to raise the left eyebrow, an asymmetrical smile with the mouth pointing downwards on the left side, all consistent with left sixth and seventh cranial nerve palsy, and partial left third cranial nerve palsy. The right eye and right side of the face were not affected. The rest of the neurological exam yielded no remarkable findings, and higher functions were normal.

The patient was admitted under Neurology for investigations. Her diagnostic workup consisted of intraocular pressure measurement, which was normal, and CT brain without contrast and MRI with and without contrast, which were also reassuring; no masses, no ischemic or hemorrhagic regions, and no abnormal contrast-enhancing areas were seen. Routine blood and urine tests were performed (seen in Table *1* and Table *2*), which were unremarkable or showed derangement consistent with normal aging and her chronic diseases. Tumor biomarkers, protein electrophoresis, and panels for autoantibodies and autoimmune disorders were requested, in addition to ultrasound examinations of the pelvis, abdomen, and thyroid. A lumbar puncture was planned to test for neuronal antibodies and perform a thorough CSF analysis with cytology, but unfortunately, the patient and her family members, who were her current caregivers, refused despite negotiation. Carcinoembryonic antigen and Cytokeratin 19 Fragment (Cyfra 21.1) levels were elevated, as seen in Table *3*; therefore, we decided to get a CT scan of the abdomen, pelvis, and thorax. An isodense lump was incidentally found in the left breast on the CT study of the chest, as seen in Figure *1*, which prompted further investigation. An ultrasound revealed a malignant-looking hypoechoic spiculated mass lesion measuring about 2.3 x 1.4 cm in size with internal vascularity and foci of microcalcifications, inseparable from the chest wall, and few bilateral reactionary axillary lymph nodes, which were classified as Breast Imaging Reporting and Data System (BI-RADS) 5 [6], as seen in Figure *2*.

**Complete Blood Count**

| Test | Results | Reference range | Unit |
|---|---|---|---|
| WBC | 11.13 | 4.00-11.00 | x10^3/mcL |
| RBC | 5.4 | 3.80-4.80 | x10^6/mcL |
| Hgb | 13.5 | 12.00-15.00 | mg/dL |
| Hct | 41.1 | 36.00-46.00 | % |
| MCV | 76.0 | 80.00-100.00 | fL |
| MCH | 24.9 | 27.00-32.00 | pg |
| MCHC | 32.8 | 31.50-34.50 | mg/dL |
| RDW | 14.0 | 11.50-14.50 | % |

| | | | |
|---|---|---|---|
| Platelet | 284 | 150.00-450.00 | x10^3/mcL |
| MPV | 11.7 | 8.00-9.00 | fL |
| Neutrophils % | 66.9 | 40.00-80.00 | % |
| Lymphocytes % | 25.5 | 18.00-42.00 | % |
| Monocytes % | 5.3 | 2.00-10.00 | % |
| Eosinophils % | 2.4 | 1.00-6.00 | % |
| Basophils % | 0.2 | 0.00-2.00 | % |
| **Coagulation Studies** | | | |
| **Test** | **Results** | **Reference range** | **Unit** |
| PT | 11.10 | 9.00-14.00 | seconds |
| PTT | 23.60 | 25.00-35.00 | seconds |
| INR | 0.96 | 0.80-1.29 | NA |
| **Renal Profile and Electrolytes** | | | |
| **Test** | **Results** | **Reference range** | **Unit** |
| Sodium | 141 | 136-145 | mmol/L |
| Potassium | 3.60 | 3.50-5.10 | mmol/L |
| Chloride | 107.0 | 98.0-107.0 | mmol/L |
| CO2 | 22.0 | 21.00-32.00 | mmol/L |
| AGAP | 12.00 | 5.00-15.00 | mmol/L |
| BUN | 4.14 | 2.50-6.40 | mmol/L |
| Creatinine | 77.00 | 49.00-90.00 | umol/L |
| Uric acid | 196.00 | 115-357 | umol/L |
| Glucose | 15.7 | 3.9-11.1 | mmol/L |
| Hgb A1c | 10.80 | 4.80-6.00 | % |
| eGFR | 57 | N/A | N/A |
| **Liver Profile** | | | |
| **Test** | **Results** | **Reference range** | **Unit** |
| Total protein | 71.50 | 64.00-82.00 | mg/L |
| Albumin | 36.87 | 34.00-50.00 | mg/L |
| Bilirubin total | 6.90 | 3.00-17.00 | umol/L |
| ALT | 25.00 | 14.00-59.00 | IU/L |
| AST | 18 | 15-17 | U/L |
| ALP | 101.00 | 46.00-116.00 | IU/L |
| **Minerals** | | | |
| **Test** | **Results** | **Reference range** | **Unit** |
| Calcium | 2.39 | 2.12-2.52 | mmol/L |
| Phosphorus | 1.35 | 0.81-1.58 | mmol/L |
| Magnesium | 0.89 | 0.74-0.99 | mmol/L |
| **Anemia Profile** | | | |
| **Test** | **Results** | **Reference range** | **Unit** |

| | | | |
|---|---|---|---|
| Ferritin | 76.10 | 10.00-291.00 | ng/mL |
| Transferrin | 246 | 202-364 | mg/dL |
| Vitamin B12 | 585.00 | 151.00-497.00 | pmol/L |
| Folate | 7.33 | N/A | nmol/L |
| Iron level | 28.70 | 9.00-30.40 | umol/L |
| **Lipid Profile** | | | |
| **Test** | **Results** | **Reference range** | **Unit** |
| Cholesterol | 5.21 | 3.6-5.2 | mmol/L |
| Triglycerides | 1.77 | 1.0-2.0 | mmol/L |
| HDL | 1.68 | 1.3-3.4 | mmol/L |
| LDL | 2.72 | 0.7-1.7 | mmol/L |
| **Infectious Disease** | | | |
| **Test** | **Results** | **Reference range** | **Unit** |
| CRP | 0.90 | <1.0 | mg/dL |
| ESR | 15.00 | 0.00-30.00 | mm/hr |

**TABLE 1: Laboratory investigations done on blood samples.**

The table shows the blood tests done for this patient, with the results stated alongside the normal values and units. WBC: white blood cell count; RBC: red blood cell count; Hgb: hemoglobin; Hct: hematocrit; MCV: mean corpuscular volume; MCH: mean corpuscular hemoglobin; MCHC: mean corpuscular hemoglobin concentration; RDW: red cell distribution width; MPV: mean platelet volume; PT: prothrombin time; PTT: partial thromboplastin time; INR: international normalized ratio; $CO_2$: carbon dioxide; AGAP: anion gap; BUN: blood urea nitrogen; eGFR: estimated glomerular filtration rate; HbA1c: glycated hemoglobin; ALT: alanine aminotransferase; AST: aspartate aminotransferase; ALP: alkaline phosphatase; HDL: high-density lipoprotein; LDL: low-density lipoprotein; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate.

| Urine Chemistry | | | |
|---|---|---|---|
| **Test** | **Results** | **Reference range** | **Unit** |
| Urine creatinine | 1918.0 | 5300-15900 | µmol/24hrs |
| Urine Bence Jones | not detected | NA | NA |
| Urine microalbumin | 121.00 | 0.00-20.00 | mg/L |
| **Urinalysis** | | | |
| **Test** | **Results** | **Reference range** | **Interpretation** |
| Appearance | clear | NA | normal |
| Color | yellow | NA | normal |
| pH | 6.0 | 5.5-7.0 | normal |
| Protein | trace | NA | abnormal |
| Glucose | 2+ | NA | abnormal |
| WBC | 6-8 | 0-5 cells | abnormal |
| RBC | 0-2 | 0-5 cells | normal |
| Squamous epithelium | not seen | NA | normal |
| Ketones | negative | NA | normal |
| Yeast | not seen | NA | normal |
| Bilirubin | negative | NA | normal |
| Specific gravity | 1.013 | 1.005-1.025 | normal |
| Leukocyte esterase | trace | NA | normal |
| Bacteria | negative | <10/HPF | normal |
| Sperm | 0 | NA | normal |
| Hyaline cast | 0.1 | NA | normal |
| Nitrates | negative | NA | normal |
| Urobilinogen | 1.0 | 0.2-1.0 EU/dL | normal |
| Hemoglobin | negative | NA | normal |

**TABLE 2: Laboratory investigations done on urine samples.**

The table shows the urine tests done for this patient, with the results stated alongside the normal values and units where applicable. Bence Jones: urinary Bence Jones proteins; WBC: white blood cells; RBC: red blood cells; HPF: high-power field; EU: Ehrlich units; NA: not applicable.

| Tumor Markers | | | |
|---|---|---|---|
| **Test** | **Results** | **Reference range** | **Unit** |
| AFP | 2.80 | 0.00-6.72 | U/mL |
| CEA | 10.8 | 0.0-2.5 | ug/L |
| CA 19.9 | 13.9 | 0.0-35.9 | U/mL |
| CA 125 | 6.3 | 0.0-30.2 | U/mL |
| Cyfra 21.1 | 2.87 | <=2.37 | ng/ml |
| **Autoimmune Panel** | | | |
| **Test** | **Results** | **Reference range** | **Interpretation** |
| ANA | 0.20 | positive/negative | negative |
| Cardiolipin IgG | 0.90 | positive/negative | negative |
| Cardiolipin IgM | 3.30 | positive/negative | negative |
| DNA-ds antibody | 10.0 | positive/negative | negative |
| anti-SSA antibody | 0.60 | positive/negative | negative |
| anti-SSB antibody | 1.50 | positive/negative | negative |
| anti-RNP antibody | 1.10 | positive/negative | negative |
| anti-Sm antibody | 0.80 | positive/negative | negative |
| anti-Scl70 antibody | 3.80 | positive/negative | negative |
| anti-JO1 antibody | 1.70 | positive/negative | negative |
| anti-centromere antibody | 0.90 | positive/negative | negative |
| APL-IgG | 1.80 | positive/negative | negative |
| APL-IgM | 1.20 | positive/negative | negative |
| **Serum Protein Electrophoresis** | | | |
| **Test** | **Results** | **Reference range** | **Unit** |
| Albumin | 37.8 | 40.0-48.0 | g/L |
| Alpha-1-globulin | 2.6 | 2.1-3.5 | g/L |
| Alpha-2-globulin | 7.7 | 5.1-8.5 | g/L |
| Beta-1-globulin | 4.2 | 3.4-5.2 | g/L |
| Beta-2-globulin | 8.8 | 2.3-4.7 | g/L |
| Gamma-globulin | 22.0 | 8.0-13.5 | g/L |
| Total proteins | 83 | 62-82 | g/L |

**TABLE 3: Additional serum sample tests.**

The table shows additional tests done for this patient, with the results stated alongside the normal values and units where applicable. AFP: alpha-fetoprotein; CEA: carcinoembryonic antigen; CA 19-9: carbohydrate antigen 19-9; CA 125: cancer antigen 125; CYFRA 21-1: cytokeratin 19 fragment; ANA: antinuclear antibody; IgG: immunoglobulin G; IgM: immunoglobulin M; dsDNA: double-stranded DNA; SSA: Sjögren syndrome-related antigen A; SSB: Sjögren syndrome-related antigen B; RNP: ribonucleoprotein; Sm: Smith antigen; Scl-70: topoisomerase I; Jo-1: histidyl-tRNA synthetase; APL-IgG: antiphospholipid IgG; APL-IgM: antiphospholipid IgM.




**FIGURE 1: Incidental left breast lesion on chest non-contrast CT.**

Figure demonstrating an incidental isodense lesion in the left breast (yellow arrow), measuring approximately 2.45 cm. The finding prompted further clinical evaluation and investigations.

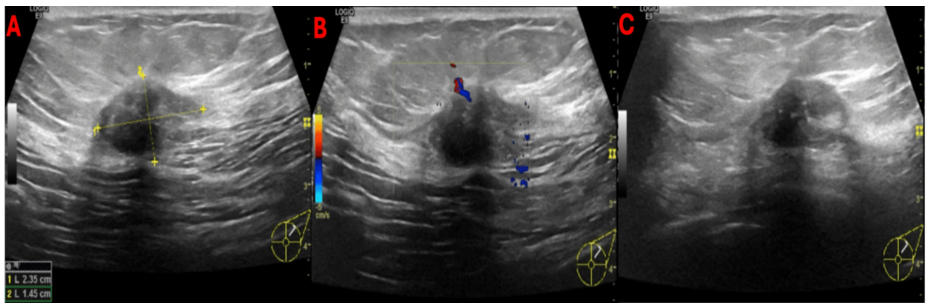



**FIGURE 2: Ultrasound findings of the suspicious left breast lesion.**

(A) A left breast upper outer quadrant hypoechoic lesion at the 2 o'clock position measuring 2.3 x 1.4 cm on axial views. (B) Some internal vascularity is shown in Doppler mode. (C) Scattered foci of microcalcifications are noted with BI-RADS 5 [6].

BI-RADS: Breast Imaging Reporting and Data System

The biopsy revealed invasive malignant cells in sheets, cords, and nests infiltrating desmoplastic fibrotic stroma with sparse chronic inflammatory cell infiltrate, necrosis, and focal ductal carcinoma in situ solid type). Tumor cells showed pleomorphic nuclear features, with some having prominent nucleoli and abundant clear to eosinophilic cytoplasm; mitotic figures were present, and a diagnosis of invasive carcinoma NST (no special type), poorly differentiated, Grade III was made.

There was a wide range of differential diagnoses for this patient's neurological manifestations, including diabetic cranial neuropathy, Ramsay-Hunt Syndrome, direct malignant (either primary or metastatic) invasion of the cranial nerves, vascular insults (either aneurysmal, occlusive, arterial, or venous) causing cranial neuropathies, and lastly PNS. Diabetic cranial neuropathies are usually mononeuropathies of the third, fourth, or sixth cranial nerves, while our patient did have poorly controlled diabetes, given her high HbA1c, as seen in Table *1*. She had multiple cranial nerves involved at once, and the fourth cranial nerve was not one of them. Moreover, diabetic third cranial neuropathy would typically spare the pupils due to its microvascular involvement mainly affecting the inner core of the nerve, sparing the outer parasympathetic fibers of the nerve, while our patient had pupil involvement. Ramsay-Hunt syndrome is a

viral reactivation within the seventh cranial nerve, which is again a mononeuropathy. Although our patient did present with some ear pain initially, the ear pain resolved spontaneously; she never developed any rashes inside the ear or on her face, and cranial nerves other than the seventh cranial nerve were also affected at the same time. MRI with contrast excluded brain masses and metastasis, as well as vascular insults. Aneurysms also usually present as mononeuropathies, if they were symptomatic. A lumbar puncture was refused, and a CSF sample was unfortunately not taken for analysis, including cell count and differentials, cytology, and neuronal antibody detection. Although paraneoplastic polyneuritis cranialis associated with breast carcinoma was our provisional diagnosis, paraneoplastic screening with serum samples was not done, considering that it would not affect the management approach to this patient whether the PNS was seronegative or seropositive. It was to be considered, along with nerve conduction studies, if the patient did not show response to the treatment proposed.

While investigations were ongoing, she was treated with intravenous immunoglobulin (IVIG) 5% at a dose of 400 mg/kg daily for five days, and she reported improvement in her symptoms on the fifth day. High-dose intravenous corticosteroids were avoided as her diabetes was poorly controlled. Lateral eye movement of the left eye and right eye blinking were better than before, and there was improvement in visual symptoms, less itching, pain, and tearing in the left eye. She still had drooping of the left eyelid and drooping in the left mouth angle, due to left lower motor neuron-facial nerve palsy. While admitted, she received treatment for her chronic conditions as well as prophylactic aspirin. The patient was fit for discharge five days after admission. A whole-body CT was done again and was reassuring. Furthermore, she was advised to follow up in the Ophthalmology Clinic, the Neurology Clinic, and the General Surgery Clinic. She decided to continue her breast mass monitoring in another facility. After contacting one of her family members, it was revealed that the patient did not want any intervention done regarding her breast cancer and would prefer palliative care. The patient also followed up in Ophthalmology, however a bit late, almost six months after discharge, and the ophthalmologist reported partial improvement in the left third and seventh cranial nerves; some asymmetry was still present, and only partial abduction of the eye was present, but a totally resolved left sixth cranial nerve palsy.

## Discussion

Polyneuritis cranialis is a rare paraneoplastic disease that is recognized as a variant of Guillain-Barré syndrome, characterized by the presence of multiple cranial neuropathies in the absence of limb weakness. The median age of presentation was 40 years, based on a historical review of 15 case reports. The initial presentation was predominantly ocular signs seen in 73% of the cases, while 33% of the cases initially presented with bulbar signs, including slurred speech and difficulty swallowing [7].

Cranial nerve predominant paraneoplastic presentations associated with breast cancer are rare but have previously been documented. One study reported anti-Ri-associated ophthalmoplegia ataxia preceding the diagnosis of breast carcinoma, whereas another described breast cancer presenting with a cerebellar syndrome, cervical dystonia, and multiple cranial nerve palsies. These cases demonstrate that breast cancer-associated PNS may involve multiple cranial nerves; however, they represented broader anti-Ri-associated brainstem or cerebellar syndromes rather than polyneuritis cranialis as a distinct Guillain-Barré syndrome phenotype characterized by multiple cranial neuropathies without limb weakness [8,9]. Paraneoplastic cerebellar degeneration is among the best characterized manifestations and is classically associated with anti-Yo antibodies, whereas anti-Ri-associated syndromes more frequently involve the brainstem, cerebellum, and ocular motor pathways [1-3,10].

Breast cancer has a recognized association with paraneoplastic neurological manifestations such as cerebellar degeneration, sensorimotor neuropathy, and stiff person syndrome [10]. A systematic review consisting of 172 reported cases of breast cancer-associated movement disorders revealed cerebellar syndromes as the most frequent manifestation, accounting for 47.7% of cases [11]. To the best of our knowledge, although breast cancer-associated paraneoplastic syndromes involving ophthalmoplegia have previously been reported, very few published cases that explicitly classified polyneuritis cranialis associated with breast carcinoma were identified. Our study therefore represents a typically rare association with this specifically defined neurological phenotype.

The proposed pathophysiology of breast cancer-associated PNSs involves an antitumor immune response directed against neuronal antigens aberrantly expressed by tumor cells. Recognition of shared tumor-neural antigens activates humoral and cell-mediated immune responses. Through antigenic cross-reactivity, antibodies and immune cells generated against the tumor may recognize homologous antigens within the nervous system, causing inflammation, neuronal dysfunction, and potentially irreversible neuronal injury despite the absence of direct tumor invasion or metastasis [2,3,7].

Several well-characterized onconeural antibodies have been associated with breast cancer-related PNSs. Anti-Yo antibodies are most strongly associated with paraneoplastic cerebellar degeneration, whereas anti-Ri antibodies are linked to ophthalmoplegia, ataxia, opsoclonus-myoclonus, dystonia, and other brainstem manifestations. Anti-amphiphysin antibodies are primarily associated with stiff-person spectrum disorder but may also occur with encephalomyelitis and peripheral neuropathy. Because anti-Yo, anti-Ri, and anti-amphiphysin target intracellular neuronal antigens, they are generally considered biomarkers of the

underlying antitumor immune response rather than the sole direct mediators of neurological injury; cytotoxic T-cell responses are believed to contribute substantially to neuronal damage [3,7-9].

Importantly, the absence of detectable neuronal antibodies does not exclude a PNS. Contemporary assessment integrates the neurological phenotype, neuronal antibody status when available, the biological and temporal relationship with the underlying malignancy, and exclusion of alternative etiologies. In our patient, involvement of the third, sixth, and seventh cranial nerves, unrevealing neuroimaging, absence of an identifiable structural or metastatic neurological lesion, and subsequent detection of occult invasive breast carcinoma support a possible immune-mediated paraneoplastic association. However, because confirmatory neuronal antibody testing was unavailable and no direct immunopathological evidence was obtained, the precise mechanism remains presumptive rather than antibody-confirmed [2,4,7].

Multiple studies have shown that the approach to managing neurological paraneoplastic syndromes mainly consists of two parts: treatment of the tumor itself, followed by an aggressive course of immunotherapy. Managing the tumor would stop the production of autoantibodies, consequently minimizing their effects and limiting further damage, and, as for the previous damages, immunotherapy is the treatment of choice. Although immunotherapy sounds ideal for targeting autoantibodies, not all neurological paraneoplastic syndromes manifest as a result of autoantibodies in the first place. Moreover, even those tumors that do produce the antibodies, their paraneoplastic syndromes tend to show limited response to first-line treatment, which consists of high-dose IV corticosteroids, plasma exchange, and/or IV immunoglobulin therapy, and often require trials of second- and third-line treatment options like immunosuppressants [2,5].

Because the treatment options are limited, the available reported outcomes of the aforementioned management are also very concise. The outcomes differed from one case to another. Some cases reported that better outcomes were more evident with tumor resection/radio-chemotherapy in comparison to immunotherapy. In contrast to other studies, which showed that autoantibody-targeted therapy was the key factor to resolving the neurological symptoms and was preferred over cancer management [2,5]. The gaps in the literature regarding the outcomes of the management stem from the few treatment options available for such cases, the versatility of the neurological paraneoplastic manifestations themselves, and the many malignancies that those paraneoplastic syndromes could be associated with.

This case highlights the importance of considering paraneoplastic syndromes, secondary to malignancy, in the context of cranial neuropathies. Early recognition of this neurological association can prompt early investigation and management of possible underlying malignancies, improving oncological prognosis.

## Conclusions

Paraneoplastic polyneuritis cranialis is a rare neurological manifestation of breast carcinoma and may precede the diagnosis of the underlying malignancy. This case highlights the importance of considering a paraneoplastic etiology in patients presenting with unexplained progressive multifocal cranial neuropathies, particularly when neuroimaging fails to demonstrate a structural or metastatic cause. The identification of occult breast cancer following comprehensive malignancy screening underscores the value of maintaining a high index of suspicion in such presentations. Clinical improvement following IVIG therapy was consistent with an immune-mediated mechanism and suggests a potential benefit of early immunomodulatory treatment alongside oncological management. This case adds to the limited literature demonstrating that unexplained multifocal cranial neuropathies may represent an early manifestation of occult malignancy.

## Additional Information

### Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

**Concept and design:** Mohammed Naji AlAbsi, Esraa Ismail, Sami Alsalem, Muaz Elsayed, Hala A. Mesmar

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**Supervision:** Muaz Elsayed

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