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Original Research Paper

Neurology

PARANEOPLASTIC LIMBIC ENCEPHALITIS IN BREAST CARCINOMA PRESENTING WITH ACUTE APHASIA AND BEHAVIORAL CHANGE

Dr. Sachin Bangar	Associate Professor, Dept. of Medicine, Dr. V.M.G.M.C, Solapur
Dr. Harshal Meshram*	Junior Resident, Dept. of Medicine, Dr. V.M.G.M.C, Solapur*Corresponding Author
Dr. Revati Sontakke	Junior Resident, Dept. of Medicine, Dr. V.M.G.M.C, Solapur
Dr. Fahad Kolharkar	Junior Resident, Dept. of Medicine, Dr. V.M.G.M.C, Solapur
Dr. Junaid Shaikh	Junior Resident, Dept. of Medicine, Dr. V.M.G.M.C, Solapur

ABSTRACT Paraneoplastic limbic encephalitis is an immune-mediated neurological syndrome occurring as a remote effect of malignancy. It is characterized by subacute neuropsychiatric dysfunction, commonly involving memory impairment, behavioral change, seizures, and altered cognition. We report the case of a 50-year-old female with known carcinoma breast on chemotherapy who presented with one week of progressive behavioral abnormality and language impairment in the absence of fever or focal motor deficits. Neurological examination revealed disorientation, impaired attention, expressive aphasia with impaired comprehension, irritability, and disinhibition. Magnetic resonance imaging of the brain showed unilateral left medial temporal lobe T2/FLAIR hyperintensity involving the hippocampal–amygdala region, suggestive of limbic encephalitis. Cerebrospinal fluid analysis showed mild lymphocytic pleocytosis, while herpes simplex virus PCR was negative. Serum paraneoplastic antibody testing was positive for anti-Hu antibody, supporting the diagnosis of paraneoplastic limbic encephalitis. The patient was treated with intravenous methylprednisolone 1 g daily for five days followed by oral steroid taper, resulting in significant improvement in behavior and language function. This case highlights the importance of considering paraneoplastic limbic encephalitis in oncology patients presenting with acute or subacute cognitive, behavioral, or language disturbances, even in the absence of fever. Although anti-Hu-associated limbic encephalitis is classically linked to small cell lung carcinoma, it can rarely occur in association with breast carcinoma. Early recognition, exclusion of infective mimics, prompt immunotherapy, and coordinated oncological management are crucial for improving neurological outcomes.

KEYWORDS : Paraneoplastic Limbic Encephalitis; Anti-hu; Breast Carcinoma; Autoimmune Encephalitis; Temporal Lobe

INTRODUCTION

Paraneoplastic limbic encephalitis is an immune-mediated neurological syndrome occurring as a remote effect of malignancy. It is characterized by subacute neuropsychiatric dysfunction, commonly involving memory impairment, behavioral change, seizures, and altered cognition. We report the case of a 50-year-old female with known carcinoma breast on chemotherapy who presented with one week of progressive behavioral abnormality and language impairment in the absence of fever or focal motor deficits. Neurological examination revealed disorientation, impaired attention, expressive aphasia with impaired comprehension,irritability, and disinhibition. Magnetic resonance imaging of the brain showed unilateral left medial temporal lobe T2/FLAIR hyperintensity involving the hippocampal–amygdala region, suggestive of limbic encephalitis. Cerebrospinal fluid analysis showed mild lymphocytic pleocytosis, while herpes simplex virus PCR was negative. Serum paraneoplastic antibody testing was positive for anti-Hu antibody, supporting the diagnosis of paraneoplastic limbic encephalitis. The patient was treated with intravenous methylprednisolone 1 g daily for five days followed by oral steroid taper, resulting in significant improvement in behavior and language function.

This case highlights the importance of considering paraneoplastic limbic encephalitis in oncology patients presenting with acute or subacute cognitive, behavioral, or language disturbances, even in the absence of fever. Although anti-Hu-associated limbic encephalitis is classically linked to small cell lung carcinoma, it can rarely occur in association with breast carcinoma. Early recognition, exclusion of infective mimics, prompt immunotherapy, and coordinated oncological management are crucial for improving neurological outcomes.

Case Report

A 50-year-old female presented with a one-week history of progressive behavioral changes and language disturbance. According to family members, she had become increasingly irritable and socially inappropriate, with episodes of disinhibition. She also developed reduced verbal output, word-finding difficulty, occasional irrelevant speech, and difficulty understanding spoken commands.

There was no history of fever, headache, seizures, vomiting, loss of consciousness, limb weakness, sensory symptoms, abnormal involuntary movements, or recent head trauma. There was no history suggestive of recent systemic infection or toxin exposure.

She was a known case of carcinoma breast and was receiving chemotherapy for the same.

Clinical Examination

Patient was conscious but disoriented to time and place. Attention and concentration were impaired. Higher mental function testing revealed language dysfunction in the form of expressive aphasia with impaired comprehension. Her speech output was reduced, with word-finding difficulty and occasional inappropriate responses.

Behavioral assessment revealed irritability and disinhibition. There were no hallucinations or clear psychotic features documented.

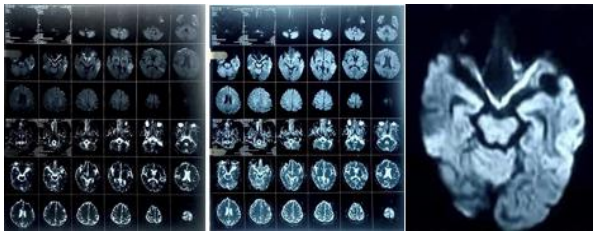
Cranial nerve examination was normal. Motor examination showed normal tone, power, and deep tendon reflexes in all four limbs. There were no signs of pyramidal tract involvement. Sensory and cerebellar examinations were unremarkable. There were no meningeal signs.

The clinical syndrome was therefore characterized by acute-

to-subacute behavioral disturbance, altered cognition, and dominant temporal language dysfunction without focal motor deficit or systemic febrile illness.

Investigations

Hematology/biochemistry: within normal limits Magnetic resonance imaging of the brain showed unilateral left medial temporal lobe T2/FLAIR hyperintensity involving the hippocampal and amygdala region, without significant mass effect. The imaging appearance was suggestive of limbic encephalitis. On the provided MRI images, page 2 shows T2-weighted and diffusion-weighted images with left temporal involvement, supporting the localization to the dominant medial temporal region.



A. **B.** **C.**

Figure A,B,C: Figure A: T2w MRI Brain. B. DWI MRI Brain. C. DWI MRI Brain section showing Left sided Temporal sclerosis.

Herpes simplex virus PCR was negative, making HSV encephalitis less likely in the given clinical context. Autoimmune/paraneoplastic antibody panel was positive for anti-Hu antibody.

Based on the clinical presentation, MRI findings, exclusion of common infectious mimics, known underlying malignancy, and anti-Hu antibody positivity, a diagnosis of anti-Hu-associated paraneoplastic limbic encephalitis in a patient with carcinoma breast was made.

Differential Diagnosis

The main differential diagnoses considered were:

1. Herpes simplex virus encephalitis

HSV encephalitis is an important mimic because it commonly involves the temporal lobes and can present with altered sensorium, seizures, fever, and behavioral abnormalities. However, the absence of fever, negative HSV PCR, clinical background of malignancy, and anti-Hu positivity favored paraneoplastic limbic encephalitis.

2.Autoimmune encephalitis due to neuronal surface antibodies

Autoimmune encephalitis due to antibodies such as anti-NMDAR, LGI1, CASPR2, AMPAR, or GABA-B receptor antibodies may present with behavioral change, seizures, cognitive decline, and limbic MRI abnormalities. These disorders often show better response to immunotherapy compared with anti-Hu-associated disease. In the present case, anti-Hu positivity and underlying carcinoma supported a paraneoplastic etiology.

3. Brain metastasis

Given the background of carcinoma breast, brain metastasis was an important consideration. However, MRI showed medial temporal T2/FLAIR hyperintensity without a mass lesion or significant mass effect, favoring an inflammatory limbic process rather than metastatic disease.

4. Primary brain tumor or glioma

Low-grade glioma involving the temporal lobe can produce seizures, behavioral change, or language dysfunction. However, the subacute onset, CSF inflammatory findings, and anti-Hu antibody positivity supported encephalitis rather than a neoplastic brain lesion.

5. Vascular event

Dominant temporal lobe infarction can cause aphasia and behavioral change. However, the progressive course over one week, limbic MRI pattern, absence of focal motor deficits, and paraneoplastic antibody positivity made a vascular etiology less likely.

6.Chemotherapy-related neurotoxicity or metabolic encephalopathy

Chemotherapy-related neurotoxicity and metabolic disturbances can cause altered mentation. However, the focal medial temporal MRI changes and positive anti-Hu antibody favored paraneoplastic limbic encephalitis.

Management and Outcome

The patient was started on high-dose intravenous methylprednisolone at a dose of 1 g/day for five days. This was followed by tapering oral corticosteroids.

Supportive care was provided, including monitoring of neurological status, behavior, sensorium, and language function. Seizure precautions were maintained, although there was no documented history of seizures.

The oncology team was involved for continuation and optimization of cancer-directed therapy. Management of the underlying malignancy is a key component in paraneoplastic neurological syndromes, as immune activation is driven by tumor-associated neuronal antigens.

Following intravenous steroid therapy, the patient showed marked clinical improvement over the subsequent days. Behavioral symptoms reduced, irritability and disinhibition improved, and language output became more coherent. On follow-up, she had significant recovery of communication, although mild residual deficits persisted.

The patient continued oncology follow-up for breast carcinoma management.

DISCUSSION

Paraneoplastic limbic encephalitis is an uncommon but important diagnosis in patients with malignancy who develop acute or subacute neuropsychiatric symptoms. The syndrome results from an immune response initially directed against tumor antigens, which cross-reacts with neuronal antigens in the central nervous system.

Anti-Hu antibodies are directed against intracellular neuronal RNA-binding proteins. Unlike neuronal surface antibody syndromes, where antibodies directly alter receptor or synaptic function, anti-Hu-associated disease is predominantly mediated by cytotoxic T-cell injury. This distinction is clinically important because intracellular antigen-associated syndromes often cause neuronal loss and are less responsive to immunotherapy than surface-antibody-mediated autoimmune encephalitis.

The classical clinical features of limbic encephalitis include short-term memory impairment, behavioral disturbance, mood or personality change, seizures, and confusion. In the present case, the prominent features were behavioral change and aphasia. Aphasia is a particularly important feature because it suggests involvement of the dominant temporal lobe and its connections with language networks. The unilateral left medial temporal MRI abnormality in this case correlates well with the patient's language impairment.

The absence of fever is also notable. Encephalitis is often

clinically associated with fever, especially in infectious causes such as HSV encephalitis. However, autoimmune and paraneoplastic encephalitis may occur without fever or systemic inflammatory features. Therefore, lack of fever should not delay evaluation for encephalitis in a patient presenting with subacute cognitive, behavioral, or language dysfunction.

MRI brain is a key diagnostic tool. Typical findings include unilateral or bilateral T2/FLAIR hyperintensity in the medial temporal lobes. Diffusion restriction may be variable. Early MRI can occasionally be normal, and FDG-PET may show limbic hypermetabolism when MRI findings are subtle.

CSF analysis frequently shows mild lymphocytic pleocytosis, raised protein, and sometimes oligoclonal bands. These findings support an inflammatory process but are not specific.

Anti-Hu positivity strongly supports a paraneoplastic etiology. Although anti-Hu-associated paraneoplastic syndromes are most classically linked with small cell lung carcinoma, they have also been reported with other malignancies, including breast carcinoma. In patients with known malignancy, the presence of anti-Hu antibody should prompt careful oncological reassessment, evaluation of tumor status, and optimization of cancer-directed therapy.

Treatment of paraneoplastic limbic encephalitis involves three parallel strategies: immunotherapy, treatment of the underlying tumor, and symptomatic neurological management. First-line immunotherapy includes high-dose corticosteroids, intravenous immunoglobulin, or plasma exchange. In refractory cases, second-line agents such as rituximab or cyclophosphamide may be considered. However, anti-Hu-associated disease often has a variable response because of irreversible neuronal injury. Early treatment may still halt progression and produce meaningful clinical improvement, as demonstrated in this case.

This case is clinically relevant because it emphasizes that acute aphasia in a patient with cancer should not always be attributed to stroke, metastasis, or metabolic encephalopathy. A limbic encephalitis pattern, particularly with temporal lobe MRI abnormalities and inflammatory CSF findings, should prompt evaluation for autoimmune and paraneoplastic causes.

CONCLUSION

Paraneoplastic limbic encephalitis should be considered in patients with known malignancy who present with acute or subacute behavioral change, cognitive dysfunction, seizures, or language disturbance. Fever may be absent, and neurological examination may lack focal motor deficits. MRI evidence of medial temporal lobe involvement, inflammatory CSF findings, exclusion of infectious causes, and anti-Hu antibody positivity support the diagnosis.

Although anti-Hu-associated limbic encephalitis is most commonly associated with small cell lung carcinoma, it can occur with breast carcinoma. Early recognition, prompt immunotherapy, and coordinated oncological management may lead to significant neurological improvement.

Declarations

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Ethical Approval: As per institutional policy

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