Breast Cancer Presenting as AMPA-R Paraneoplastic Encephalitis

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Background

- Paraneoplastic Alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor (AMPA-R) encephalitis is a rare immune-mediated encephalitis characterized by the collection of immune-mediated nervous system symptoms that arise due to malignancy.
- AMPA-R encephalitis is a rare manifestation of breast cancer.
- We present the case of a 31-year-old female with progressive neurological decline due to paraneoplastic encephalitis with a subsequent breast cancer diagnosis. Treatment with tamoxifen led to significant improvement of encephalitis, emphasizing the importance of diagnosing AMPA-R encephalitis, and early initiation of effective anti-cancer therapy.

Clinical Course

- A 31-year-old female presented with an 11-month history of progressive neurological decline characterized by confusion, psychosis, dysarthria, severe ataxia, amnesia, aggression, violence, and insomnia. Subsequently, she experienced progressive dysphagia and dysarthria resulting in an inability to speak beyond grunts. She was admitted to the psychiatric unit 3 times within this 11-month period.
- The patient was admitted to the Rush University Medical Center's neurology floor and then transferred to Neurology intensive care unit due to hypoxic respiratory failure requiring tracheostomy and PEG placement.
- Initial diagnostic testing demonstrated +ANA, +SSA, CRP 21.5, and ESR 40.
- Lumbar puncture (LP) was unremarkable. EEG showed activity consistent with mild encephalopathy. MRI brain demonstrated hyperintense areas in bilateral frontal, parietal, and right temporal lobe suggestive of autoimmune encephalitis (Figure 1). Encephalitis antibody panel was positive for AMPA receptor Ab.
- CT chest showed right axillary adenopathy without evidence of distant disease. Breast MRI demonstrated masses in breast (Figure 3). Right axillary LN and breast biopsies confirmed a cT1cN1 invasive ductal carcinoma, ER+(81-90 %), PR+ (61-70 %), HER2 2+, FISH not amplified, Ki-67 20-30%.

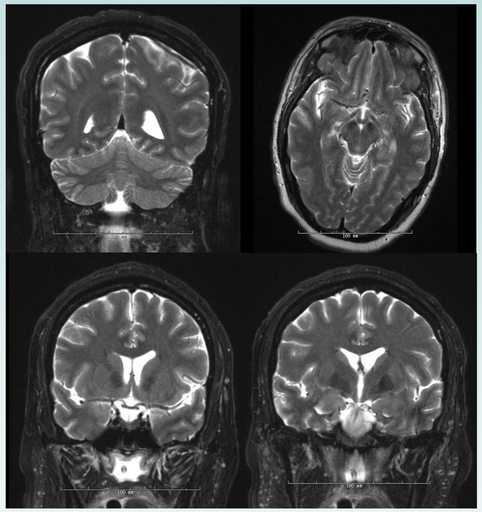


Figure 1. MRI brain coronal and coronal views showing several cortical and subcortical T2 hyperintense areas in the bilateral frontal, parietal, and R temporal lobes, evidence of autoimmune encephalitis.

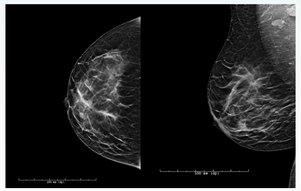


Figure 2. Bilateral mammogram shows multiple highly suspicious right breast masses (dominant masses at 5:00 and 3:00, 1 cm from nipple) and suspicious right axillary lymphadenopathy.

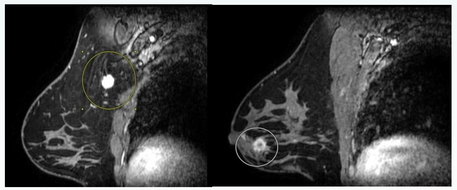


Figure 3: Right breast MRI shows two suspicious masses (5:00 and 3:00, both 1 cm from the nipple) and associated right axillary lymphadenopathy.

Management and Outcome

- She received IV methylprednisolone 1g daily and 40g of IVIG for 5 days, followed by 7 sessions of therapeutic plasmapheresis without improvement. She received 6 sessions of electroconvulsive therapy, lorazepam, and transitioned to Chlorpromazine without improvement.
- For the breast cancer, she started Tamoxifen as an inpatient with gradual improvement in her symptoms. Patient regained complete neuromechanical function after three months of Tamoxifen.
- Once her performance status improved, tamoxifen was discontinued and she received neoadjuvant dose-dense Adriamycin and Cyclophosphamide followed by Paclitaxel. Her stage after a bilateral mastectomy was ypT0N1mi. She received adjuvant post-mastectomy radiation.
- She will be starting ovarian function suppression, aromatase inhibitor, and adjuvant abemaciclib soon. Her neurological status remains normal 15 months post-breast cancer diagnosis.

Discussion and Conclusion

- Paraneoplastic encephalitis is rare, reported in less than 1% of patients with breast cancer. Alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor (AMPA-R) is a paraneoplastic syndrome caused by onconeural antibodies directed against GluA1 or GluA2 subunits of the AMPA receptor, resulting in inflammation and injury to limbic strictures in the brain.
- AMPA-R encephalitis has been associated with breast, lung, thymus, and ovarian cancers. Classical onconeural antigens are intracellular targets for antibodies that do not directly induce pathogenesis, but initiate cell-mediated cytotoxicity. This damage can cause acute or subacute symptoms such as cognitive impairment, personality changes, seizures, confusion, hallucinations, sleep disorders, short-term memory loss, and loss of consciousness.
- While abnormalities on MRI and EEG can support a diagnosis of limbic encephalitis, they lack the specificity required for confirmation. The detection of AMPA-R antibodies in the serum or CSF remains the gold standard for diagnosis.
- Treatment requires immunosuppressive therapy and identification and treatment of underlying malignancy.
- This case highlights the importance of a thorough assessment in the evaluation of unexplained neurologic and psychological decline which includes imaging, LP, antibody testing, EEG, and biopsy of any tumor. It also stresses the importance of identifying and treating the underlying malignancy which may result in resolution of symptoms.

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