Anti-RI–Associated Paraneoplastic Syndrome in Breast Cancer and Multiple Sclerosis: An Unusual Comorbidity

L. Bonanni[1,2], D. Travaglini[1], P. Ajdinaj[1,3], S. Varanese[1], M. Buongarzone[1], R. Speranza[1], S. Viola[1], L. Fiorelli[1]

1. Neurology Clinic, San Pio da Pietrelcina Hospital, Vasto, Italy
2. Department of Medicine and aging sciences, University G. D'Annunzio of Chieti-Pescara, Chieti, Italy
3. Department of Neuroscience, Imaging and Clinical Sciences, University G. D'Annunzio of Chieti-Pescara, Chieti, Italy

Introduction

Paraneoplastic neurological syndromes (PNS) are rare, immune-mediated disorders triggered by an underlying malignancy and often associated with onconeural antibodies. Anti-RI antibodies (ANNA-2) are typically linked to breast and small-cell lung cancers and are associated with opsoclonus-myoclonus or brainstem encephalitis.

Multiple sclerosis (MS) is a chronic, immune-mediated demyelinating disease of the central nervous system. While the coexistence of MS and cancer is not uncommon, the simultaneous occurrence of MS and PNS is extremely rare and poorly understood.

Diagnosing PNS in patients with MS is particularly challenging due to overlapping clinical features, which may delay appropriate treatment and worsen outcomes. The interaction between tumor-driven immune responses and pre-existing neuroinflammation adds further complexity.

Case report

We report a rare and complex case of a 48-year-old woman with relapsing multiple sclerosis (MS), newly diagnosed breast cancer, and a paraneoplastic neurological syndrome (PNS) associated with anti-RI antibodies. The coexistence of these conditions posed significant diagnostic challenges, particularly in distinguishing between MS relapse and paraneoplastic manifestations. The patient experienced clinical worsening in mid-2024, with MRI showing a new cerebellar lesion. After stabilization with corticosteroids, an incidental breast cancer diagnosis (HER2-overexpressing, luminal B-like subtype) was made during routine screening. A mastectomy was performed in October 2024.

Soon after surgery, the patient developed new neurological symptoms unresponsive to corticosteroids. MRI showed no MS activity, and anti-RI antibodies were detected, confirming a diagnosis of PNS. Treatment included intravenous immunoglobulins, corticosteroids, symptomatic therapies (benzodiazepines and botulinum toxin), and a combined regimen of oral cyclophosphamide and subcutaneous trastuzumab. This approach led to partial neurological improvement and clinical stabilization.

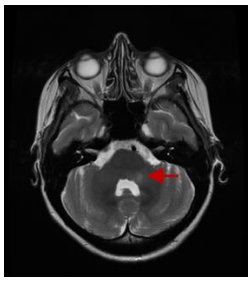

Fig.1 Axial T2 image of MRI obtained in June 2024 (the red arrow indicates the lesion)

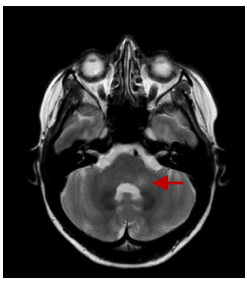

Fig.2 Axial T2 image of MRI obtained in July 2024 (the red arrow indicates the lesion)

Conclusion

This case illustrates the importance of early recognition of PNS in patients with pre-existing neuroinflammatory diseases. The detection of anti-RI antibodies was critical for diagnosis and therapeutic guidance. To our knowledge, this is the first reported case involving MS, breast cancer, and anti-RI–associated PNS concurrently.

A multidisciplinary approach was essential for managing overlapping neurological and oncological conditions. This case highlights the need for vigilance in evaluating new neurological symptoms in cancer patients and the role of integrated care in optimizing outcomes.

Bibliography

1. Fanous I. et al., Paraneoplastic neurological complications of breast cancer. Exp Hematol Oncol. 2016 Oct 24:5:29.
2. Dubey A. et al., Breast Cancer and the Brain: A Comprehensive Review of Neurological Complications. Cureus. 2023 Nov 17;15(11):e48941.
3. Kouliavtseva T. et al., Neuroinflammation, neurodegeneration and regeneration in multiple sclerosis: intersecreted manifestations of the immune response. Neural Regen Res. 2016 Nov;11(11):1727–1730.
4. Qiangzhao L. et al., Association between multiple sclerosis and cancer risk: An extensive review/meta and Mendelian randomization analyses. Mult Scler Relat Disord. 2023 Aug;76:104798.
5. Rim T. et al., Anti-RI-Associated Paraneoplastic Neurological Syndrome Revealing Breast Cancer: A Case Report. Cureus. 2022 Jan 11.
6. Norrito R.L. et al., Paraneoplastic Cerebellar Degeneration Associated with Breast Cancer: A Case Report and a Narrative Review. Brain Sci. 2024 Feb 14.