Teaching NeuroImage: Spontaneously Resolving Ring-Enhancing Lesions Due to Immunodeficiency-Associated CNS Lymphoma

A Case of "Vanishing Lymphoma"

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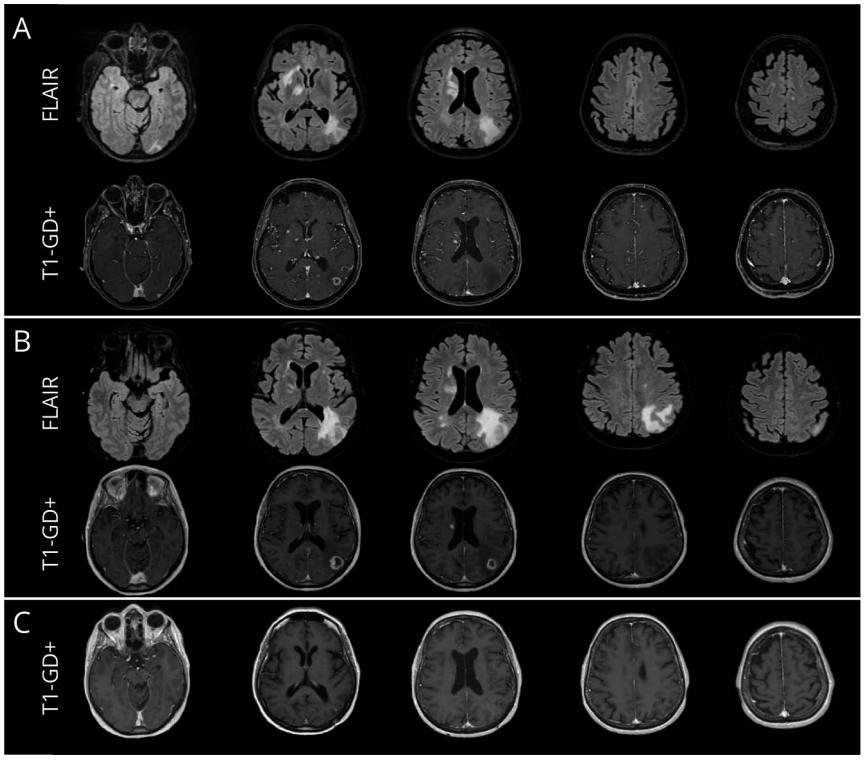
Figure 1 Baseline and Follow-Up MRI Scans



(A) Baseline brain MRI showing 7 Gd-enhancing lesions in the left occipital and parieto-temporal lobe, right basal ganglia, and right and left superior frontal gyrus; (B) Substantial resolution of most of the lesions at 1-month follow-up, with increase in size of the largest one; (C) Further improvement at 5-month follow-up.

A 57-year-old woman with systemic lupus erythematosus on mycophenolate mofetil (MMF) presented after a tonic-clonic seizure. Brain MRI revealed 7 gadolinium-enhancing lesions (Figure 1A). CSF protein, glucose, and cell count were normal, and microbiological tests for opportunist agents were negative, raising our suspicion for lymphoma. Prebiopsy MRI showed spontaneous improvement of most lesions, with increased size of the largest lesion (Figure 1B).

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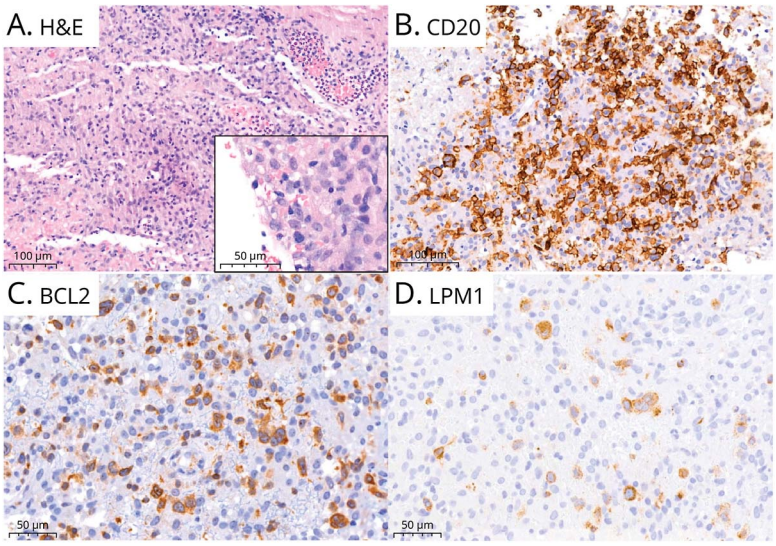
Figure 2 Histologic Sections From Brain Biopsy of the Largest Lesion



Hematoxylin-eosin (H&E) sections at 20× magnification (A) show dense inflammatory background with evidence of larger lymphoid cellular elements with nuclear atypia (inset) and immunohistochemistry positivity for CD20 (B), BCL-2 (C), BCL-6, and MUM1 (markers of B-cell lymphoma) and for Epstein-Barr virus marker LPM1 (D), consistent with EBV-associated large B-cell lymphoma.

Brain biopsy (Figure 2) was consistent with immunodeficiency-associated CNS lymphoma. MMF treatment cessation led to substantial improvement after 5 months (Figure 1C).

Immunodeficiency-associated CNS lymphoma is a distinct diagnosis within primary CNS lymphoma (PCNSL) with unique image features.[1] It is associated with immunocompromise arising from autoimmune diseases or iatrogenesis and can be associated with lesions that resolve without treatment, a rare pattern known as "vanishing lymphoma."[2] These findings are unexpected in infectious diseases or glial neoplasms and can guide differential diagnosis.

Author Contributions

M. Azzimonti: drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data; study concept or design; analysis or interpretation of data. F. Esposito: drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data; analysis or interpretation of data. P.L. Poliani: drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data; analysis or interpretation of data. F. Gagliardi: drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data; analysis or interpretation of data. N. Anzalone: drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data; analysis or interpretation of data. P. Panni: drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data; analysis or interpretation of data. A. Giordano: drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data; analysis or interpretation of data. V. Martinelli: drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data; analysis or interpretation of data. M.A. Rocca: drafting/revision of the manuscript for content, including medical writing for content; study concept or design; analysis or interpretation of data. M. Filippi: drafting/revision of the manuscript for content, including medical writing for content; study concept or design; analysis or interpretation of data.

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References

1. Pons-Escoda A, Naval-Baudin P, Velasco R, Vidal N, Majós C. Imaging of lymphomas involving the CNS: an update-review of the full spectrum of disease with an emphasis on the World Health Organization Classifications of CNS Tumors 2021 and Hematolymphoid Tumors 2022. *AJNR Am J Neuroradiol*. 2023;44(4):358-366. doi: 10.3174/ajnr.A7795
2. Takekawa H, Hozumi A, Hirata K, Yamazaki K. A spontaneously vanishing primary cerebral lymphoma "ghost tumour". *J Neurol Neurosurg Psychiatry*. 2008;79(10):1159. doi:10.1136/jnnp.2007.132282

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