

Mystery Case: Eccentric target sign in CNS toxoplasmosis

A rare presentation of Good syndrome

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A 61-year-old man with myasthenia gravis who previously underwent post-thymectomy radiotherapy for a metastatic thymoma presented with altered mental status. Examination revealed papilledema and frontoexecutive dysfunction.

Brain MRI disclosed rim-enhancing lesions with the eccentric target sign pathognomonic for neurotoxoplasmosis,¹ supported by magnetic resonance spectroscopy (figure 1). Brain biopsy confirmed the presence of *Toxoplasma gondii* tachyzoites (figure 2). Absent B cells, low CD4⁺ and CD8⁺ counts, hypogammaglobulinemia, and a HIV-negative status led to the diagnosis of Good syndrome. Treatment with pyrimethamine–clindamycin resulted in mild improvement.

Neurotoxoplasmosis is a rare opportunistic infection in HIV-negative patients with thymoma.² Early recognition and prompt immunologic workup are warranted.

Mystery Case Responses: A 61-year-old man with altered mental status

The Mystery Case series was initiated by the *Neurology*® Resident & Fellow Section to develop the clinical reasoning skills of trainees. Residency programs, medical student preceptors, and individuals were invited to use this Mystery Case as an educational tool. Responses to multiple choice questions formulated using this case were solicited through a group email sent to the American Academy of Neurology Consortium of Neurology Residents and Fellows and through social media. We received 299 responses. The majority of respondents (68%) had been in practice for 1–4 years; 64% were residents or fellows while 27% were faculty/board-certified physicians; the remainder were medical students or advanced practice providers. A total of 69% resided outside the United States. A wide range of practice settings was represented.

When shown a brief vignette about the patient's clinical presentation followed by representative MRI brain sections (figure 1, A–F), 85% of respondents correctly identified the left frontal lobe ring-enhancing lesions, but only 7% also correctly identified the smaller right parietal lobe ring-enhancing lesion. A total of 60% recognized the associated vasogenic edema and 30% also recognized the peripheral diffusion restriction. Upon then being asked to select their top 5 differential diagnoses, the most popular choices were as follows: cerebral metastases (75%), tubercular or bacterial abscesses (70%), primary CNS lymphoma (57%), and fungal abscesses (55%), followed by a close race for fifth place between glioblastoma multiforme (53%) and toxoplasmosis (51%). In this case, toxoplasmosis would be a preferred response over glioblastoma; whereas neurotoxoplasmosis typically manifests as

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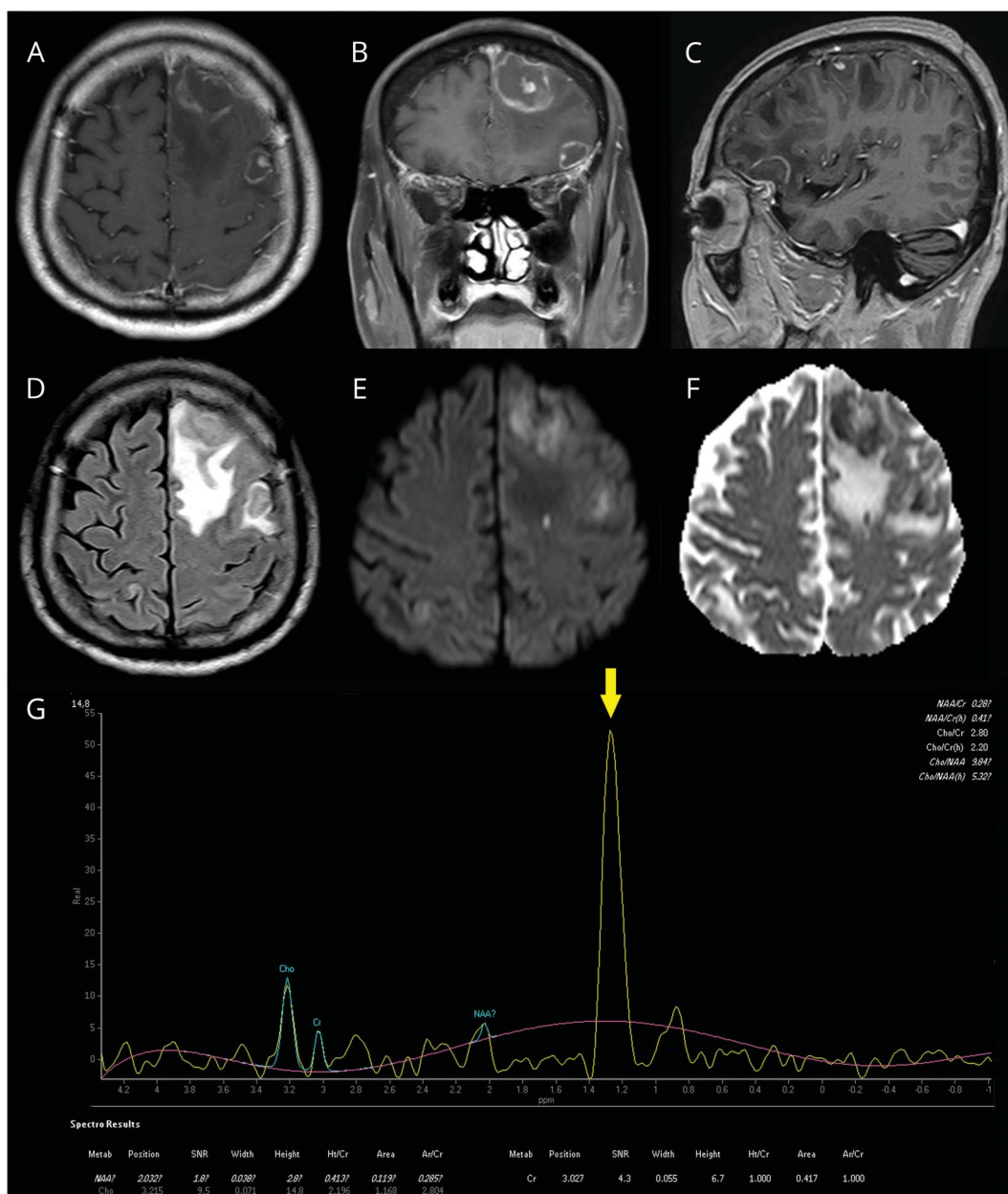
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(A) Axial, (B) coronal, and (C) sagittal contrast-enhanced MRI reveals multiple ring-enhancing lesions with the eccentric target sign pathognomonic for neurotoxoplasmosis, with (D) vasogenic edema and (E, F) corresponding peripheral diffusion restriction. (G) Magnetic resonance spectroscopy shows high lactate peak, diminished *N*-acetylaspartate, and choline metabolites.

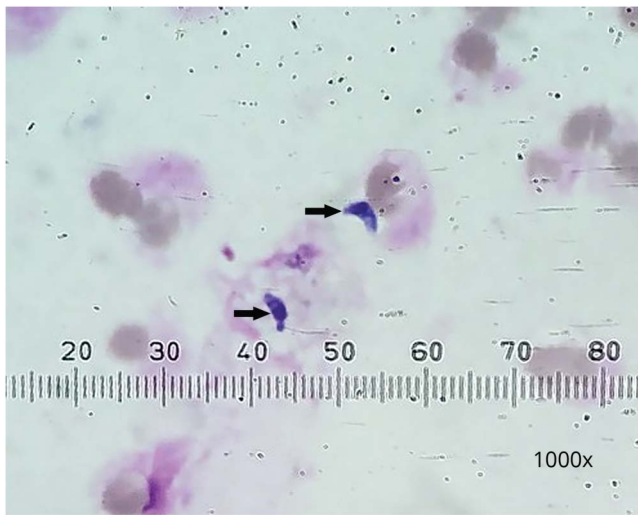
multiple lesions, with a characteristic eccentric target sign as seen in these images,¹ multicentric glioblastomas—with multiple discrete contrast-enhancing lesions not linked by T2/fluid-attenuated inversion recovery signal abnormality—are uncommon.²

Upon then being shown the brain biopsy specimen (figure 2) and asked to select their final diagnosis, 32% of respondents correctly chose toxoplasmosis. Other popular choices included tubercular or bacterial abscesses (16%), fungal abscesses (14%), and primary CNS lymphoma (12%).

However, none of these alternative diagnoses would be expected to demonstrate the pathologic finding of extracellular crescent-shaped tachyzoites with prominent centrally placed nuclei, which in this case confirms infection with *Toxoplasma gondii*.

This case complements a recent Mystery Case in addressing the differential diagnosis for ring-enhancing lesions,³ in addition to reviewing the neuroimaging and neuropathologic features of an important neuroinfectious disease.⁴

Figure 2 Histopathologic examination of the brain biopsy specimen



A smear of brain biopsy at $\times 1,000$ magnification shows 2 extracellular crescent-shaped *Toxoplasma gondii* tachyzoites with prominent, centrally placed nuclei.

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Author contributions

Y.-C. Cheng: study design, data collection, drafting the manuscript. J.-H. Yeh: study supervision, revising the manuscript. H.-L. Yeh: study design, data collection. L.-M. Lien: study design, data collection. W.-Y. Chen: study design, data collection. C.-Y. Hsiao: study design, data collection. Y.-H. Liu: study design, data collection. C.-L. Chen: study design, data collection. S.-Y. Chen: study design, data collection. C.-I. Lau: study design, data collection, drafting and revising the manuscript.

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