Neurological Case Reports

Case Report
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Effective Treatment with High-Dose Methotrexate for Erdheim-Chester Disease with Tumor-Like Presentation

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Abstract

Erdheim-Chester Disease (ECD) is a non-Langerhans cell histiocytosis affecting multiple organs, particularly the central nervous system causing various manifestations such as dementia, cerebellar ataxia, headaches and seizures. Diagnosis is confirmed by a tissue biopsy. Standard treatments include interferon-alpha and several targeted therapies. We report the case of a 65-year-old woman initially presenting with an intra-axial brain lesion. Pathological examination was consistent with ECD. The patient was successfully treated with high-dose methotrexate regimen.

Keywords: Erdheim-Chester disease; Methotrexate; Neuroimaging; Seizures

Introduction

Erdheim-Chester Disease (ECD) is a rare non-Langerhans cell histiocytosis, characterized by foamy macrophages infiltration in various tissues including bones, heart, lungs, Central Nervous System (CNS), skin, kidneys and retroperitoneum [1]. Common neurologic manifestations include cognitive impairment, cerebellar ataxia, pyramidal tract dysfunction, headaches, seizures, peripheral and cranial neuropathy [2,3]. Diagnosis is confirmed by biopsy of an affected tissue, which typically identifies CD68+, CD163+, S100-, CD1a- foamy histiocytes [1]. The BRAFV600E mutation is found in more than 50% of cases [1]. First-line therapies are usually Interferon-alpha and BRAF-inhibitor Vemurafenib [1,2].

We report a case of CNS ECD, with tumor-like presentation, that responded well to high-dose methotrexate. The clinical picture and the treatment adopted in our patient are rarely reported in literature. Written informed consent was obtained from the patient to report this case and adjunctive image.

Case Presentation

A 65-year-old right-handed female, heavy smoker, with an unremarkable medical history, presented in January 2023 with an acute fluctuating expressive aphasia. There were no other neurological or extra-neurological symptoms. Initial brain MRI revealed a 2 cm, left frontal lesion, showing diffusion restriction, hyperintense on T2/FLAIR, hypointense on T1 with faint peripheral contrast enhancement, with nonspecific white matter changes (Figure 1). Given the high suspicion of a brain tumor or a pseudo-tumoral inflammatory lesion, a stereotactic brain biopsy was performed. Pathological examination showed reactive gliosis with non-Langerhans CD163+, S100- and CD1a- xanthomatous cells, without glial tumoral proliferation. Testing for BRAFV600E mutation was negative. Cardiac workup (US and MR) revealed a dilated cardiomyopathy with global hypokinesia. There was no abnormal contrast uptake nor an abnormal tissue infiltrating cardiac or pericardiac structures. EEG showed left frontal slowing and intermittent epileptiform discharges. An antiseizure medication was initiated. After a multidisciplinary discussion, the patient was treated with high-dose methotrexate (4.5 g IV every 2 weeks) and leucovorin, with clinical and serial brain MRI follow-up. After a year, a significant reduction in the left frontal lesion size was observed (Figure 2).

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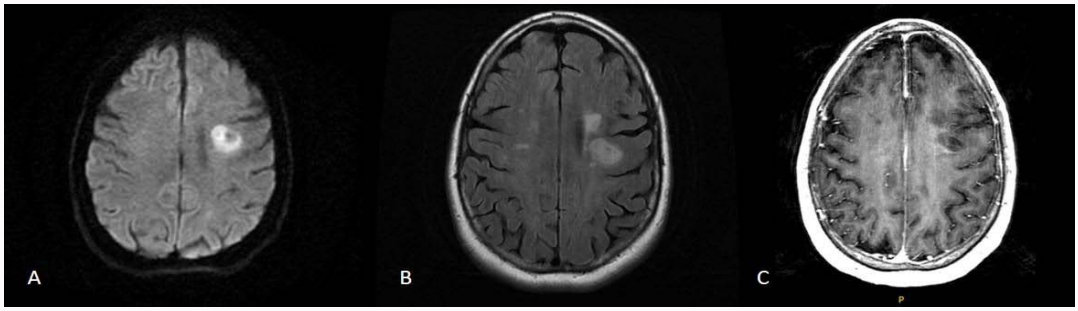

Figure 1: Brain MRI acquired in January 2023 showing lesion characteristics on (A) axial diffusion-weighted image, (B) axial FLAIR sequence image and (C) axial T1-weighted post-contrast image.

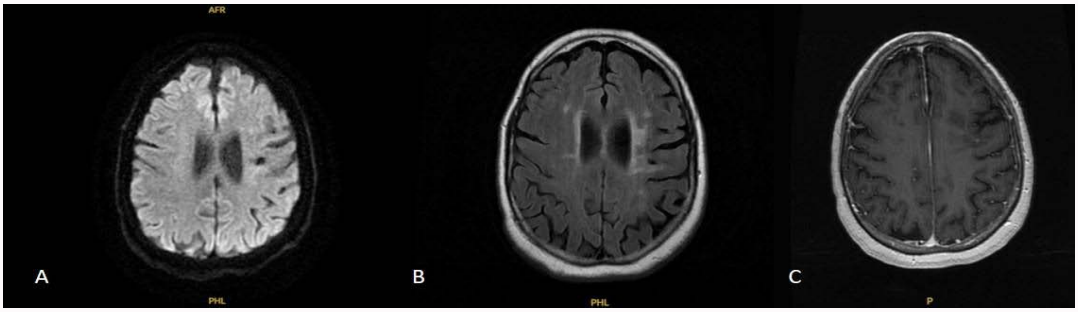

Figure 2: Brain MRI acquired in January 2024 showing lesion characteristics on (A) axial diffusion-weighted image, (B) axial FLAIR sequence image and (C) axial T1-weighted post-contrast image.

Discussion

First, this case reports a rare tumor-like presentation of ECD with CNS involvement. CNS involvement occur in almost one half of patients with ECD, and is often associated with poor prognosis [2,3]. The most common CNS manifestations of ECD, include neuroendocrine disturbances (e.g. diabetes insipidus, variable degree of hypopituitarism) [4], cognitive impairment, cerebellar ataxia, brainstem syndrome, seizures, myelopathy and peripheral neuropathies [2,3]. MRI findings are nonspecific and may include single or multiple, supratentorial or infratentorial meningioma-like enhancing dural masses, T2-hyperintense white matter changes, T2-hyperintense lesions affecting the cerebellum and the brainstem namely the pons with variable gadolinium enhancement, mesial temporal lobe T2-hyperintensity, thickening of the infundibular stalk, cortical laminar necrosis, orbital and spinal cord lesions [5]. Cases of ECD mimicking a solitary parenchymal brain tumor are rarely reported in literature.

Furthermore, conventional treatments in ECD often involve interferon-α-2a and pegylated interferon-α-2a [6]. Novel targeted therapies mainly include BRAF-inhibitors (e.g. Vemurafenib), in BRAFV600E mutant ECD, and MEK-inhibitors (e.g. cobimetinib, trametinib) in ECD cases without BRAFV600E mutation [6]. Cytokine-directed therapies such as IL-1 receptor antagonists, IL-6 receptor antagonist tocilizumab, and TNF-α inhibitors have been tried with variable success, but their efficacy is limited in ECD with CNS involvement [6]. Response to some chemotherapeutic agents, particularly cladribine, have been reported [6,7]. To the best of our knowledge, the use of high-dose methotrexate for the treatment of ECD with CNS involvement is rarely reported in literature. Ho et al., reported one case of rapidly progressive CNS ECD, with significant and sustained improvement to high-dose methotrexate [8]. The documented effectiveness, may be due to rapid onset of action and good CNS penetrance of high-dose methotrexate [8].

This report contributes to expanding the understanding of ECD and introduces a novel and effective treatment approach for CNS involvement.

References

1. Haroche J, Arnaud L, Cohen-Aubart F, Hervier B, Charlotte F, Emile JF, et al. Erdheim-Chester disease. Rheum Dis Clin North Am. 2013;39(2):299-311.
2. Boyd LC, O'Brien KJ, Ozkaya N, Lehky T, Meoded A, Gochuico BR, et al. Neurological manifestations of Erdheim-Chester Disease. Ann Clin Transl Neurol. 2020;7(4):497-506.
3. Benson JC, Vaubel R, Ebne BA, Mark IT, Peris Celda M, Hook CC, et al. Erdheim-Chester Disease. Am J Neuroradiol. 2023;44(5):505-10.
4. Manaka K, Sato J, Makita N. Neuroendocrine manifestations of Erdheim-Chester disease. Handb Clin Neurol. 2021;181:137-47.
5. Parks NE, Goyal G, Go RS, Mandrekar J, Tobin WO. Neuroradiologic manifestations of Erdheim-Chester disease. Neurol Clin Pract. 2018;8(1):15-20.
6. Goyal G, Heaney ML, Collin M, Cohen-Aubart F, Vaglio A, Durham BH, et al. Erdheim-Chester disease: Consensus recommendations for evaluation, diagnosis, and treatment in the molecular era. Blood. 2020;135(22):1929-45.
7. Azadeh N, Tazelaar HD, Gotway MB, Mookadam F, Fonseca R. Erdheim Chester disease treated successfully with cladribine. Respir Med Case Rep. 2016;18:37-40.
8. Ho P, Smith C. High-dose methotrexate for the treatment of relapsed central nervous system Erdheim-Chester disease. Case Rep Hematol. 2014;2014:269359.