Radiology Case Reports 19 (2024) 5332–5335

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/radcr

Case Report

Utility of MR spectroscopy and MR perfusion in characterizing intracranial pathology in Erdheim-Chester disease: A case report ☆

Momin Muzaffar, MD[a,*], *Mohamad F. Bazerbashi, MD*[b]

[a] *The University of Chicago, Department of Radiology, 5841 S. Maryland Avenue, MC 2026, Chicago, IL 60637, USA*
[b] *Duly Health and Care, Department of Radiology, 430 Pennsylvania Ave, Glen Ellyn, IL 60137, USA*

ARTICLE INFO

Article history:
Received 6 June 2024
Accepted 3 August 2024

Keywords:
Erdheim-Chester disease
Histiocytosis
MR spectroscopy
MR perfusion
Brain
Neuroradiology

ABSTRACT

This case report describes the potential utility of MR spectroscopy and MR perfusion imaging in a patient with central nervous system involvement of Erdheim-Chester disease (ECD). A 57-year-old male presented with a variety of neurological symptoms, and conventional MRI of the brain showed multiple supratentorial and infratentorial findings that generated a wide differential diagnosis. Advanced MRI sequences along with subsequent CT imaging of the abdomen and ultimately a renal biopsy helped narrow the differential and confirm the diagnosis of ECD. Case reports of ECD are sporadic, and the role of advanced neuroimaging in diagnosing this disease has not been fully elucidated.

Introduction

Erdheim-Chester disease (ECD) is a rare non-Langerhans cell, non-familial multisystemic histiocytosis characterized by accumulation of inflammatory foamy macrophages [1]. Up to half of ECD patients may present with neurological symptoms, and imaging manifestations in the brain are protean with both intra-axial and extra-axial lesions which enhance to variable degrees and can mimic primary brain tumors, granulomatous disease, and other inflammatory disorders [2,3]. Because of the complex array of imaging findings, diagnosis is difficult and frequently delayed. Imaging case reports of ECD are sporadic, and the use of advanced imaging techniques such as MR spectroscopy (MRS) and MR perfusion (MRP) have rarely been reported as adjunct tools in narrowing the differential in ECD and histiocytic disorders in general [4]. Herein we present a patient with ECD who presented with a multitude of supratentorial and infratentorial findings on initial brain MRI and in whom the subsequent acquisition of MR spectroscopy and MR perfusion assisted in narrowing the differential diagnosis.

☆ Competing Interests: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

* Corresponding author.
E-mail addresses: mominmuzaffar@uchicago.edu (M. Muzaffar), mbazer2@gmail.com (M.F. Bazerbashi).

https://doi.org/10.1016/j.radcr.2024.08.008

Case report

A 57-year-old male presented to neurology with intermittent bilateral hand tingling and positional dizziness over 10 months characterized by transient disequilibrium provoked by standing. On neurological examination, a left beating non-extinguishing horizontal jerk nystagmus was elicited on leftward gaze but not evident on primary gaze. The remainder of the neurological exam was normal including a negative Dix Hallpike test.

A contrast-enhanced brain MRI demonstrated a large intra-axial mildly expansile, infiltrative FLAIR hyperintense mass-like lesion with patchy enhancement centered in the pons and extending into the midbrain, medulla, cerebellar peduncles, and right dentate nucleus (Fig. 1). There was associated regional mass effect including mild compression of the fourth ventricle and mild downward cerebellar tonsillar herniation. In addition, there was a subcentimeter intra-axial enhancing lesion in the left medial temporal lobe and additional punctate enhancing lesions in the supratentorial parenchyma. There was also a small extra-axial plaque-like dural based homogenously enhancing lesion along the left frontotemporal convexity reminiscent of a meningioma as well as a small extra-axial enhancing lesion in the left prepontine cistern.

A broad differential diagnosis was provided based on the conventional brain MRI findings including high-grade brainstem glioma, metastatic disease, lymphoma, and sarcoidosis. The patient returned two weeks later for advanced MR imaging including MRS and MRP on a 3 Tesla magnet. Findings were unchanged on the conventional MR sequences compared to the prior study. MRP including pulsed continuous arterial spin labeling (ASL) perfusion with cerebral blood flow (CBF) color map and dynamic-susceptibility contrast-enhanced (DSC) perfusion with cerebral blood volume (CBV) color map demonstrated hypoperfusion throughout the brainstem lesion (Fig. 2).

Single voxel MRS acquired at a long echo time (TE = 144 ms) with a voxel placed over the enhancing lesion in the pons showed a mildly elevated choline (Cho) to creatine (Cr) ratio of approximately 2.5 indicative of increased cell turnover. The N-acetylaspartate (NAA) peak was diminished indicative of neuronal loss. Single voxel MRS acquired at a short echo time (TE = 35 ms) confirmed an elevated Cho:Cr ratio and decreased NAA peak and also revealed an elevated lactate peak at 1.3 ppm which inverted on the long echo spectrum. In addition, the short TE spectrum demonstrated a mildly elevated glutamate-glutamine (Glx) peak at 2.4 ppm suggestive of an inflammatory process (Fig. 3).

A subsequent contrast-enhanced chest, abdomen, and pelvis CT acquired to search for an occult primary malignancy demonstrated bilateral symmetric irregular perinephric soft tissue infiltration with mild dilation of the renal pelves (Fig. 4). The possibility of ECD was suggested based on this finding of "hairy kidneys" with the differential diagnosis including lymphoma and IgG4-related disease [5].

A percutaneous CT-guided core biopsy of the perinephric soft tissue infiltration demonstrated histiocytic proliferation with a positive CD68 stain compatible with the radiologic impression of ECD. Histiocyte stains for S100, CD1a, and pankeratin were negative. Immunohistochemistry was reportedly positive for BRAF V600E mutation. A follow up 18-fluorodeoxgyglucose (FDG)- PET demonstrated hypermetabolism in the intra-axial enhancing pontine and medial temporal lobe lesions without evidence for hypermetabolism elsewhere in the body.

Discussion

ECD is a multisystem histiocytic disorder classified as an inflammatory neoplasm of myeloid progenitor cells, similar to Langerhans cell histiocytosis (LCH). However, unlike LCH which presents in children, ECD affects the adult population, predominantly in the fifth to seventh decades with a male to female predilection of 3:1 [1]. While skeletal manifestations predominate, occurring in 80-95% of patients, cardiovascular, renal, pulmonary, endocrine, orbital and

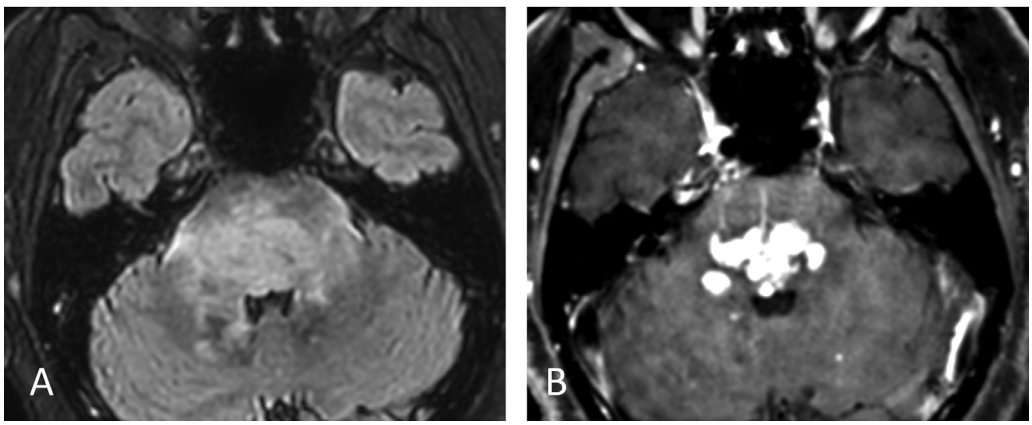

Fig. 1 – (A) Axial FLAIR image demonstrates a mildly expansile, infiltrative FLAIR hyperintense mass-like intra-axial lesion centered in the pons and extending into the middle cerebellar peduncles and dentate nuclei. (B) Axial 3D SE T1 fat-suppressed post contrast image demonstrates corresponding patchy avid enhancement in the pontine lesion as well as smaller enhancing foci in the right middle cerebellar peduncle and left dentate nucleus.

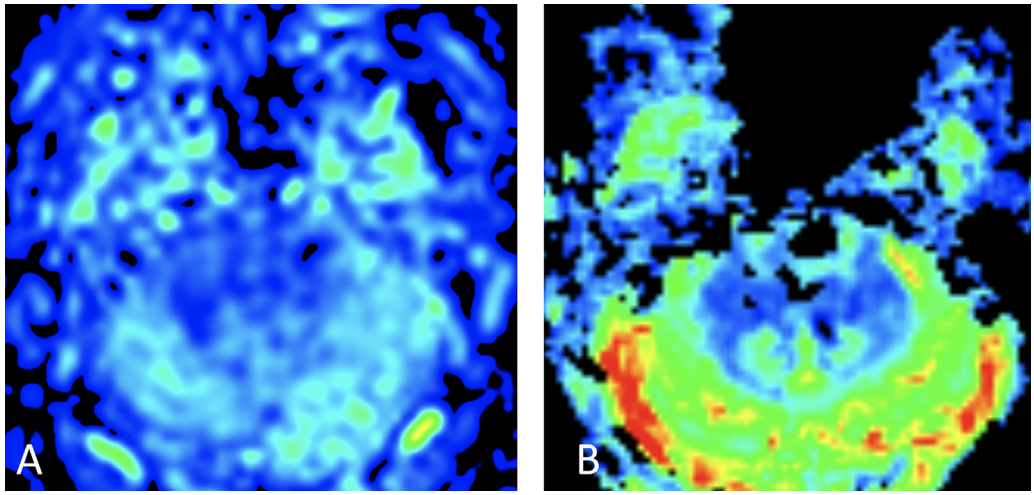

Fig. 2 – (A) Color map of cerebral blood flow (CBF) from ASL perfusion and (B) color map of cerebral blood volume (CBV) from DSC perfusion demonstrate hypoperfusion within the pontine lesion.

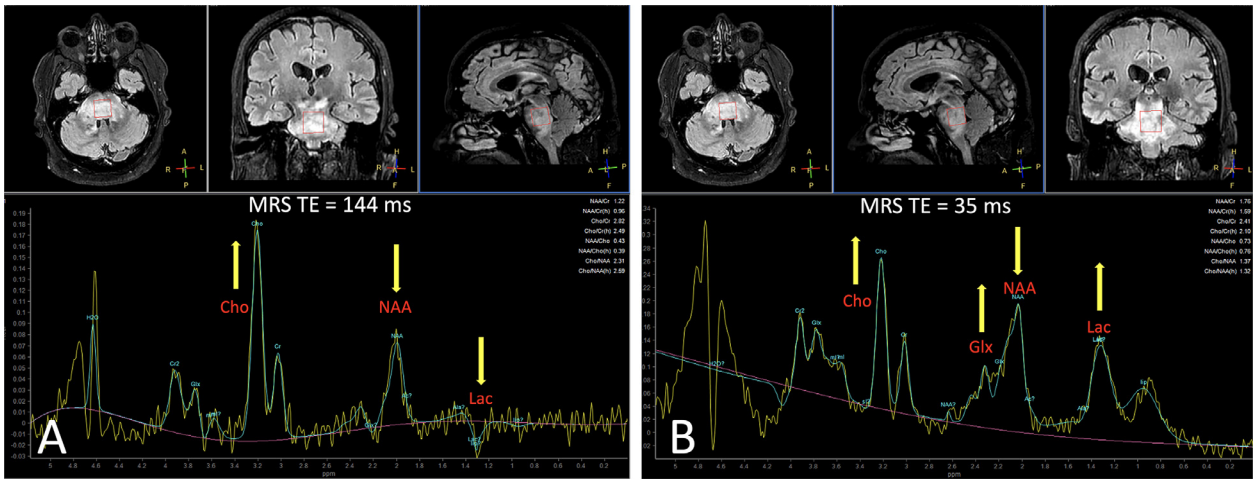

Fig. 3 – (A) Single voxel long echo time MRS (TE = 144 ms) shows a mildly elevated choline (Cho) to creatine (Cr) ratio indicative of increased cell turnover, diminished N-acetylaspartate (NAA) peak indicative of neuronal loss, and an inverted lactate peak.(B) Single voxel short echo time MRS (TE = 35 ms) confirms an elevated Cho:Cr ratio and decreased NAA peak but also reveals an elevated lactate peak at 1.3 ppm peak indicating anerobic glycolysis. In addition, the short TE spectrum demonstrates a mildly elevated glutamate-glutamine (Glx) peak at 2.4 ppm suggestive of an inflammatory process.

cutaneous involvement are not uncommon, and most patients present with multisystem involvement. Central nervous system (CNS) involvement is variable but has been reported in 30-50% of ECD cases, and approximately 20% of patients initially present with neurological symptoms including cerebellar ataxia, cognitive impairment, pyramidal tract signs, and cranial nerve and peripheral neuropathies [2,6]. Significantly, the presence of CNS involvement in ECD has been reported to be an independent predictor of death and therefore may have prognostic implications [7]. Additionally, involvement of the hypothalamic-pituitary axis is commonly reported and often manifests as diabetes insipidus [8]. As a result, brain imaging may be the first imaging study that an undiagnosed patient with ECD may undergo, and the neuroradiologist should be familiar with the variegated imaging stigmata of this disease. CNS manifestations most commonly include diffuse and patchy FLAIR hyperintensity with variable enhancement in the pons, brachium pontis, and cerebellum, similar to our case, but other documented findings included extra-axial enhancing lesions mimicking meningiomas, an enlarged pituitary infundibulum, supratentorial intra-axial enhancing lesions extending to the ependymal surfaces of the ventricles, and orbital involvment [8–10].

Infiltrative involvement of the pons as in our case can mimic a brainstem glioma, CNS lymphoma, infectious rhomboencephalitis, and chronic lymphocytic inflammation with pontine perivascular enhancement responsive to steroids (CLIPPERS). The lack of restricted diffusion militated against lymphoma in our case, and the hypoperfusion on ASL and DSC

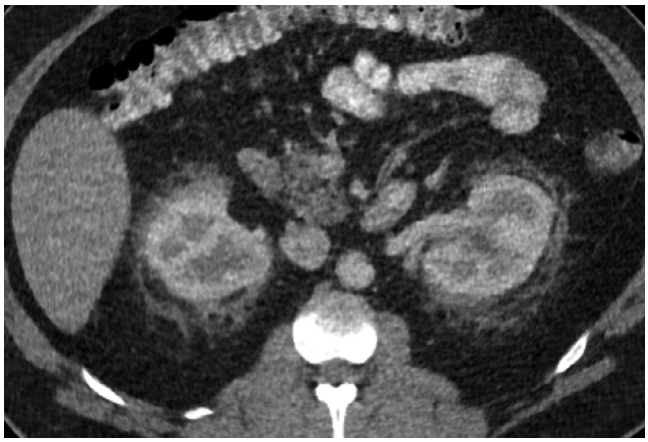

Fig. 4 – Axial contrast-enhanced abdomen CT shows bilateral, relatively symmetric perinephric soft tissue infiltration.

perfusion and the older age of our patient were atypical for a diffuse midline glioma.

On MRS, the elevated Cho:Cr ratio and decreased NAA peak indicated high cell turnover and neuronal loss respectively, and when interpreted in isolation would suggest a glioma. However, the elevation of Cho:Cr was relatively modest compared to many high grade gliomas. The elevated lactate peak indicated anaerobic glycolysis secondary to macrophage activation after cell membrane breakdown, a finding which can be seen with ischemia, necrosis, acute demyelination and CNS lymphoma [11]. However, conventional imaging showed no significant diffusion restriction to support ischemia or lymphoma, nor were any frankly necrotic foci appreciated. The sum of glutamate and glutamine peaks (commonly designated Glx) resonates at 2.4 ppm and has been reported to be a distinguishing factor between tumefactive demyelinating lesions and aggressive intra-axial neoplasms [12]. More broadly, the presence of an elevated Glx peak implies cell breakdown of both neural and glial elements and should prompt the neuroradiologist to consider inflammatory processes over a glioma. Case series describing the MRS findings in histiocytic brain masses are scant and corroborate the elevated Cho:Cr ratio and decreased NAA peak seen in our case [4]. Another limited case series illustrated an elevated lipid peak on long TE MRS in ECD involving the orbit, a finding that was not appreciated in our case [13]. To our knowledge, this is the first case showing an elevated lactate and Glx peaks as potential distinguishing factors in ECD.

Conclusion

ECD presents with a wide range of imaging manifestations in the brain, and prospective diagnosis can be extremely difficult. MRP showing hypoperfusion can help exclude high grade glioma or intracranial metastases, while MRS demonstrating a modestly elevated Cho:Cr ratio, decreased NAA, increased lactate, and the presence of an elevated Glx peak favor an inflammatory process and may help suggest the diagnosis of ECD. MRS and MRP are useful adjuncts to conventional MR sequences and should be incorporated into the imaging algorithm if a histiocytic disorder is in consideration.

Patient consent

A written and informed consent was obtained for publication of this case report.

REFERENCES

[1] Haroche J, Cohen-Aubart F, Amoura Z. Erdheim-Chester disease. Blood 2020;135(16):1311–18. doi:10.1182/blood.2019002766.

[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. doi:10.1002/acn3.51014.

[3] Benson JC, Vaubel R, Ebne BA, Mark IT, Peris Celda M, Hook CC, et al. Erdheim-Chester Disease. AJNR Am J Neuroradiol 2023;44(5):505–10. doi:10.3174/ajnr.A7832.

[4] Luna LP, Drier A, Aygun N, Mokhtari K, Hoang-Xuan K, Galanaud D, et al. MRI features of intra-axial histiocytic brain mass lesions. Clin Radiol 2021;76(2):159.e19–159.e28. doi:10.1016/j.crad.2020.09.015.

[5] Chazal T, Pegoraro F, Manari G, Bettiol A, Maniscalco V, Gelain E, et al. Clinical phenotypes and long-term outcome of kidney involvement in Erdheim-Chester histiocytosis. Kidney Int 2023;103(1):177–86. doi:10.1016/j.kint.2022.09.027.

[6] Aktan Suzgun M, Everest E, Kucukyurt S, Tutuncu M, Uygunoglu U, Eskazan AE, et al. Erdheim-Chester disease of brain parenchyma without any systemic involvement: a case report and review of literature. Neuropathology 2024;44(1):59–67. doi:10.1111/neup.12930.

[7] Arnaud L, Hervier B, Néel A, Hamidou MA, Kahn JE, Wechsler B, et al. CNS involvement and treatment with interferon-alpha are independent prognostic factors in Erdheim-Chester disease: a multicenter survival analysis of 53 patients. Blood 2011;117:2778–82. doi:10.1182/blood-2010.

[8] Sedrak P, Ketonen L, Hou P, Guha-Thakurta N, Willams MD, Kuzrock R, et al. Erdheim-Chester disease of the central nervous system: new manifestations of a rare disease. AJNR Am J Neuroradiol 2011;32(11):2126–31. doi:10.3174/ajnr.A2707.

[9] De Abreu MR, Chung CB, Biswal S, Haghighi P, Hesselink J, Resnick D. Erdheim-Chester disease: MR imaging, anatomic, and histopathologic correlation of orbital involvement. AJNR Am J Neuroradiol 2004;25(4):627–30.

[10] Johnson MD, Aulino JP, Jagasia M, Mawn LA. Erdheim-chester disease mimicking multiple meningiomas syndrome. AJNR Am J Neuroradiol 2004;25(1):134–7.

[11] Mader I, Rauer S, Gall P, Klose U. 1H MR spectroscopy of inflammation, infection and ischemia of the brain. Eur J Radiol 2008;67(2):250–7. doi:10.1016/j.ejrad.2008.02.033.

[12] Cianfoni A, Niku S, Imbesi SG. Metabolite findings in tumefactive demyelinating lesions utilizing short echo time proton magnetic resonance spectroscopy. AJNR Am J Neuroradiol 2007;28(2):272–7.

[13] Mohan S, Verma A, Lim CCT, Hui F, Kumar S. Lipid resonance on in vivo proton MR spectroscopy: value of other metabolites in differential diagnosis. Neuroradiol J 2010;23(3):269–78. doi:10.1177/197140091002300302.