

Letters to the Editor

Elevated lipid peaks during the recovery phase of Baló's concentric sclerosis: A case report



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Dear Editor,

Baló's concentric sclerosis (BCS) is a very rare inflammatory demyelinating disease and is considered a variant of multiple sclerosis (MS) [1]. Brain MRI examinations of BCS reveal large, concentric, ring-like lesions in white matter with alternating hyper- and hypointense bands on T2-weighted images (T2WI). Serial MRI has shown that BCS lesions radially spread from the central core and gradually diminish.

Proton magnetic resonance spectroscopy ($^1\text{H-MRS}$) during the acute phase of BCS lesions has been reported to show increased choline (Cho), decreased *N*-acetylaspartate (NAA), and the appearance of lactate (Lac) or lipid (Lip) peaks [2–4]. Elevated Lac peaks indicate disturbances in energy metabolism due to ischemia, hypoxia, and respiratory chain disturbance. Elevated Cho and Lip peaks indicate myelin destruction, and decreased NAA peaks indicate axonal loss similar to that seen with acute MS lesions [5].

Although BCS pathology changes dynamically during the disease course—from hypoxia-like tissue injury to inflammation, demyelination, and remyelination—serial changes in metabolite concentrations in BCS lesions measured with $^1\text{H-MRS}$ have been reported rarely. Here we report a case of BCS that was analyzed by using serial $^1\text{H-MRS}$ and MRI from the early through the late phase.

1. Case report

A 36-year-old woman with no medical history presented with subacute clumsiness of the right limbs and 7 hospital days after she was admitted to the hospital. Neurological examination revealed right hemiparesis that affected the leg (MRC manual muscle test (MMT) grade 1) and the arm (MMT 4). Brain MRI showed a solitary lesion with a diameter of 3.0 cm in the juxtacortical white matter of the left parietal lobe. The lesion comprised a core of high intensity on T2WI and a marginal layer of mildly high intensity on T2WI. Fluoro-2-deoxy- D -glucose (FDG) positron emission tomography (PET) uptake was decreased in the lesion. Cerebrospinal fluid (CSF) examination revealed normal protein levels without pleocytosis and an elevated IgG index of 1.02; the CSF was negative for oligoclonal bands. Serum aquaporin-4 IgG was also negative. Diagnostic workup was for suspected inflammatory demyelinating disease. She was treated for 3 days with

1000 mg intravenous methylprednisolone but developed total paralysis of the right limbs. A second brain MRI on day 9 of hospitalization showed an increase in the size of the lesion with partial rim Gd enhancement and revealed concentric layering typical of BCS (Fig. 1A, B). She was diagnosed with BCS and received 6 days of 12 mg IV bethamethasone beginning on day 10 of hospitalization, without clinical improvement. $^1\text{H-MRS}$ on hospital day 14 revealed increased Cho, decreased NAA, increased Lac (doublet peaks at 1.3 ppm) and increased Lip (two broad peaks at 0.9 and 1.3 ppm), which were consistent with previous reported findings of BCS lesions (Fig. 1C).

She underwent a second course of intravenous methylprednisolone, without clinical improvement, and then was treated with 6 sessions of plasma exchange and high-dose intravenous immunoglobulin therapy (400 mg/kg/day, 5 days). Mild improvement of weakness was observed. During intravenous immunoglobulin therapy, a second $^1\text{H-MRS}$ showed that the Lip peaks were higher and the Lac peak was considerably lower than previously (Fig. 1D). Finally, she underwent 380 mg/m² IV cyclophosphamide therapy on hospital day 78. She continued to improve and became able to move her right limbs; the size of concentric lesion was reduced on MRI. A third $^1\text{H-MRS}$ showed that the Lip and Lac peaks disappeared in parallel with her clinical improvement (Fig. 1E). At 6 months after initial presentation, her right limb weakness had improved (MMT 4), and there was no further relapse.

2. Discussion

The diagnosis of BCS was supported by the subacute onset, rapid progression, and response to immunotherapy. In addition, the pathognomonic radiologic appearance of a lesion with alternating layers of hyper- and hypointensity on T2WI and an outer layer of Gd enhancement verified the diagnosis. In the early phase, $^1\text{H-MRS}$ showed increased Cho and Lac peaks and decreased NAA peaks, consistent with previous reports [2–4].

In present case, serial $^1\text{H-MRS}$ revealed that elevated Lip and Lac peaks occurred during the early phase and elevated Lip peaks were prominent even after the disappearance of the Lac peak during the recovery phase. In a previous case report, elevated Lip peaks were detected during the acute phase when the NAA peak was normal;

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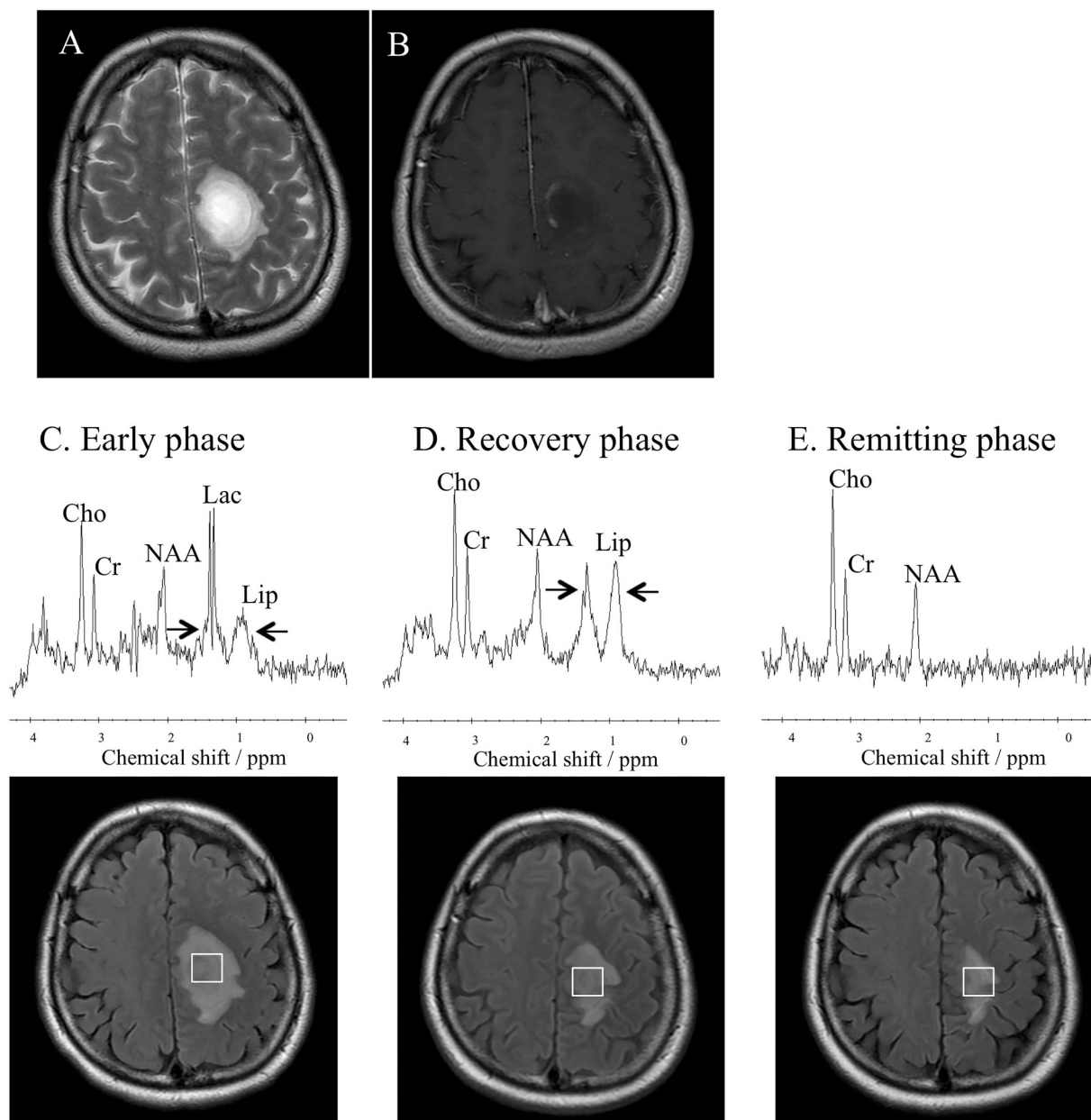


Fig. 1. Brain MRI and MRS of the patient.

(A, B) Brain MRI on hospital day 7. (A) This axial T2W image shows the concentric pattern in left parietal lobe and (B) Gd-enhanced T1 W1 showing partial rim enhancement. (C-E) Serial brain MRI and ^1H -MRS. Short TE (35 ms) ^1H -MRS of the left parietal lesion shown in Fig. 1A, B at 2 weeks (C; early phase), 8 weeks (D; recovery phase), and 9.5 weeks (E; remitting phase) after hospitalization. The arrows indicate Lip peaks. The arrows indicate Lip peaks (each corresponding to the upper ^1H -MRS figure) and depicting the region of interest selected for ^1H -MRS.

however, 14 days after symptom onset, the size of these peaks decreased during the phase when the NAA peak decreased [6]. In this sense, there might be two types of etiology of Lip peaks in BCS.

Lip peaks appear as two broad peaks between 0.9 and 1.5 ppm in white matter diseases such as brain tumor and acute MS [5,7]. Elevated Lip peaks with an elevated Cho peak indicate membrane lipid release due to myelin destruction or demyelination [5]. Our findings may therefore suggest that elevated Lip peaks indicate demyelination during the acute phase of BCS.

In our case, elevated Lip peaks were prominent during the recovery phase, and concurrent MRI showed that the size of the BCS lesion was reduced.

In patients with MS, elevated Lip peaks are detectable during the phase when foamy macrophages, which can contain high lipid levels,

accumulate in demyelinated lesions [5]. Foamy macrophages likely contribute to resolution of inflammation in MS patients and may be responsible for inhibiting further lesion development and promoting lesion repair [8]. In BCS patients, foamy macrophages are seen throughout the early-to-late phase [9] and may be responsible for the elevated Lip peaks in the recovery phase.

Serial ^1H -MRS and MRI may thus provide information about the phase and myelination status of BCS lesions and could aid in monitoring the progression of BCS lesions and the response to immunotherapy.

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Conflicts of interest/disclosures

The authors declare that they have no financial or other conflicts of interest in relation to this research.

References

- [1] O. Kastrup, P. Stude, V. Limmroth, Balo's concentric sclerosis. Evolution of active demyelination demonstrated by serial contrast-enhanced MRI, *J. Neurol.* 249 (7) (2002) 811–814.
- [2] E. Karaarslan, A. Altintas, U. Senol, N. Yeni, A. Dincer, C. Bayindir, N. Karaagac, A. Siva, Balo's concentric sclerosis: clinical and radiologic features of five cases, *AJNR Am. J. Neuroradiol.* 22 (7) (2001) 1362–1367.
- [3] A. Khiat, J. Lesage, Y. Boulanger, Quantitative MRS study of Balo's concentric sclerosis lesions, *Magn. Reson. Imaging* 25 (7) (2007) 1112–1115.
- [4] M.O. Kim, S.A. Lee, C.G. Choi, J.R. Huh, M.C. Lee, Balo's concentric sclerosis: a clinical case study of brain MRI, biopsy, and proton magnetic resonance spectroscopic findings, *J. Neurol. Neurosurg. Psychiatry* 62 (6) (1997) 655–658.
- [5] C.A. Davie, C.P. Hawkins, G.J. Barker, A. Brennan, P.S. Tofts, D.H. Miller, W.I. McDonald, Serial proton magnetic resonance spectroscopy in acute multiple sclerosis lesions, *Brain J. Neurol.* 117 (Pt 1) (1994) 49–58.
- [6] C.J. Chen, Serial proton magnetic resonance spectroscopy in lesions of Balo concentric sclerosis, *J. Comput. Assist. Tomogr.* 25 (5) (2001) 713–718.
- [7] P.S. Murphy, L.J. Rowland, L. Viviers, M. Brada, M.O. Leach, A.S. Dzik-Jurasz, Could assessment of glioma methylene lipid resonance by in vivo ¹H-MRS be of clinical value? *Br. J. Radiol.* 76 (907) (2003) 459–463.
- [8] L.A. Boven, M. Van Meurs, M. Van Zwam, A. Wierenga-Wolf, R.Q. Hintzen, R.G. Boot, J.M. Aerts, S. Amor, E.E. Nieuwenhuis, J.D. Laman, Myelin-laden macrophages are anti-inflammatory, consistent with foam cells in multiple sclerosis, *Brain J. Neurol.* 129 (Pt 2) (2006) 517–526.
- [9] C. Stadelmann, S. Ludwin, T. Tabira, A. Guseo, C.F. Lucchinetti, L. Leel-Ossy, A.T. Ordinario, W. Bruck, H. Lassmann, Tissue preconditioning may explain concentric lesions in Balo's type of multiple sclerosis, *Brain J. Neurol.* 128 (Pt 5) (2005) 979–987.

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