Multiple Hemosiderin Depositions of T2*-weighted Magnetic Resonance Imaging in a Patient with Pathology-approved Systemic Diffuse Large B-cell Lymphoma

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Abstract

Background

Multiple hemosiderin depositions caused by chronic hemorrhages[1] in T2*-weighted magnetic resonance imaging (MRI) have never been identified in patients with central nervous system (CNS) involvement of systemic lymphoma.

Case presentation

This is the first report of pathologically confirmed case of secondary CNS lymphoma with multiple hemosiderin depositions on T2*-weighted MRI. A 56-year-old woman presented with lower extremities weakness and progressive cognitive decline. Brain magnetic resonance imaging demonstrated multiple bilateral lesions with hyperintensity on T2-weighted MRI. She was then transferred to our hospital. Neurological examination showed impaired cognitive functions. Contrast-enhanced MRI revealed irregular spotty enhancing within the lesions. T2*-weighted MRI demonstrated multiple diffuse hypointensity in both hemispheres and infratentorial regions, mainly adjacent to brain surface. Whole body positron emission tomography/computed tomography (PET/CT) scanning showed multiple hypermetabolic foci in pelvis and spleen. The pathologic diagnosis of biopsy specimen was consistent with diffuse large B-cell lymphoma (DLBCL).

Conclusion

Clinical awareness of these imaging features would render an early diagnosis of lymphoma. This findings also suggests the utility of T2*-weighted MRI in differentiating lymphoma from other brain lesions.

Keywords: central nervous system; lymphoma; hemosiderin deposition
Background

Systemic non-Hodgkin lymphoma (NHL) may involve the central nervous system (CNS) in many ways, of which parenchymal infiltration and leptomeningeal metastases are most common. The protean clinical and radiographic manifestations make its diagnosis sometimes difficult. Contrast-enhanced magnetic resonance imaging (MRI) of the brain is the most sensitive imaging technique in detection of CNS involvement from NHL. Novel modalities such as diffusion-weighted imaging, perfusion-weighted imaging and magnetic resonance spectroscopy\cite{2-5} are increasingly being utilized in differentiating metastases from other intracranial lesions. Intracranial hemorrhage has been found in conventional MRI in some previous case reports. However, the diagnostic significance of T2*-weighted MRI is rarely mentioned in the differentiation of systemic lymphoma from other brain lesions. Herein, we present an unexpected radiographic feature on T2*-weighted MRI of patient with CNS involvement of pathologically confirmed systemic lymphoma.

Case presentation

A 56-year-old woman presented with a four-month history of lower extremities weakness and progressive cognitive decline. Initial laboratory studies revealed a hemoglobin level of 9 g/dL (to convert to grams per liter, multiply by 10). Erythrocyte sedimentation rate and serum C-reactive protein levels were markedly elevated. Serum lactic dehydrogenase was 867U/L (to convert to µkat per liter, multiply by 0.0167), which is close to three-fold of the upper limit of the reference range (97-270U/L). The cerebrospinal fluid (CSF) analysis revealed no pleocytosis but a slightly elevated protein concentration. Brain MRI
demonstrated multiple hyperintense signals on T2-weighted MRI and fluid attenuated inversion recovery (FLAIR) in the bilateral periventricular areas, centrum semiovale and frontal lobes. She was then transferred to our hospital for further management.

On admission, neurological examination showed impaired cognitive functions including orientation, recall, calculation and language manipulation with a Mini-Mental State Exam score of 8 points. The muscle strength was graded on a scale of 5- on lower extremities bilaterally and left Babinski sign was present.

Diagnostic assay for human immunodeficiency virus infection was negative. Treponema pallidum particle agglutination assay (TPPA) and fluorescent treponemal antibody absorption (FTA-ABS) IgG was positive in the serologic tests for syphilis. Therefore, TPPA, rapid plasma reagin and FTA-ABS in CSF were tested and appeared nonreactive. In combination with a normal CSF cytology result and no previous related symptoms, neurosyphilis was excluded.

T2-weighted MRI and FLAIR showed no change from previous images and newly patchy hemorrhage within lesion was found in left temporal lobe on T1-weighted MRI. A part of lesions showed irregular spotty enhancing after contrast administration, together with the enhancement of adjacent leptomeninges. T2*-weighted MRI demonstrated multiple hemosiderin depositions in both supratentorial and infratentorial regions (Figure 1), which were not compatible with the lesions visualized on T2-weighted images. Due to the discrepancy between the lesions on T2-weighted and T2*-weighted MRI, silent hemorrhage caused by malignancy was suspected and whole body positron emission tomography/computed tomography (PET/CT) scanning was performed for determining
the presence of malignant tumor. Hypometabolizing areas were revealed in multiple hypointense lesions in the white matter of brain, not excluding foci with surrounding edema. Multiple hypermetabolic foci are present in pelvis and spleen, indicative of malignant lymphoma. Therefore, computed tomography-guided aspiration biopsy of the retroperitoneal mass was performed. Microscopic findings showed a diffuse growth pattern of atypical lymphoid cells with CD20 positive on immunohistochemistry, consistent with diffuse large B-cell lymphoma. The patient declined chemoradiotherapy, and died from tumor progression four months later.

Discussion

This is the first report of hemosiderin depositions revealed on T2*-weighted MRI of brain in pathologically confirmed systemic lymphoma. Even though uncommon, our report offers an insight that lymphoma might be considered as a possible diagnosis for patients with such rare imaging characteristics. It also suggests the potential significance and utility of T2*-weighted MRI in facilitating the differential diagnosis of lymphoma from other brain lesions.

Multiple hemosiderin depositions caused by chronic hemorrhages[1] have never been identified in patients with CNS involvement of systemic lymphoma. Even in primary CNS lymphoma, hemorrhagic lesions are extremely rare in immunocompetent patient [6]. The rarity of hemorrhagic lesion might be one of the major factors. Since 1990 to 2013, only three cases of intracranial hemorrhage were reported in primary CNS lymphoma. Rubenstein et al[7] firstly reported a case of intracranial hemorrhage at presentation in primary CNS lymphoma. The intratumoral hemorrhage appeared hypointense on
multiplanar gradient-refocused image, due to magnetic susceptibility effect caused by the blood-breakdown products. Kimura et al.[8] described a patient of primary CNS lymphoma with cortical laminar hemorrhage in the frontal cortex, showing hypointensity in the cortex on T2*-weighted image. The biopsy specimen revealed diffuse large B-cell lymphoma with hemosiderin deposits. Different from these two studies, our case showed multiple bilateral lesions mainly in the periventricular areas, centrum semiovale and frontal lobe on MRI. These lesions demonstrated hyperintensity on T2-weighted images and FLAIR, and irregular enhancement after contrast administration. Of note, T2*-weighted MRI revealed diffuse hemosiderin depositions with hypointense signals mostly adjacent to the brain surface, which are not compatible with the lesions visualized on T2-weighted images. It was this unusual radiographic presentation which raised the clinical suspicion of malignant tumor and lead to the final pathological diagnosis of systemic lymphoma.

Conventional MRI is commonly used for the detection of CNS lymphoma, on which lymphoma appears as non-hemorrhagic lesion. However, gradient-recalled echo or T2*-weighted imaging, sensitive to cerebral hemorrhage, is not routinely employed. This may result in undetection of silent hemorrhage or microhemorrhage in some patients. In our case, T2*-weighted MRI happened to provide the valuable clue in the diagnosis of CNS lymphoma, which supplemented the limited information on conventional MRI. This suggests that the conventional MRI including non-enhanced and contrast-enhanced MRI are insufficient for detecting lesions of CNS lymphoma with diverse properties. T2*-weighted MRI could be taken into account when confronted with patients suspected of having CNS lymphoma, aiding in the discrimination of brain lesions. Further
radiographic studies may provide more evidence for the diagnostic importance of T2*-weighted MRI in lymphoma.

Cerebral amyloid angiopathy (CAA) is ranked highly in the differentiation of multiple hemosiderin deposition among elderly patients[9]. The most common clinical manifestation of spontaneous lobar hemorrhage and radiographic feature of restricted location in lobar, cortical, or corticosubcortical regions were not shown in this case. Thus, the possible diagnosis of CAA was ruled out.

**Conclusion**

This is the first report of secondary CNS lymphoma with multiple hemosiderin depositions on T2*-weighted MRI. Clinical awareness of this rare imaging feature would render an early diagnosis of lymphoma. This findings also suggests the utility of T2*-weighted MRI in differentiating lymphoma from other brain lesions. Further radiographic studies may provide more evidence for the diagnostic importance of T2*-weighted MRI in lymphoma.

**Consent**

Written informed consent was obtained from the patient for publication of this Case report and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

**Abbreviations**
MRI: Magnetic resonance imaging; CNS: central nervous system; PET/CT: positron emission tomography/computed tomography; NHL: non-Hodgkin lymphoma; CSF: Cerebrospinal fluid; FLAIR: fluid attenuated inversion recovery; TPPA: Treponema pallidum particle agglutination assay; FTA-ABS: fluorescent treponemal antibody absorption; CAA: Cerebral amyloid angiopathy.

**Competing interests**

The authors declare that they have no competing of interests.

**Authors’ contributions**

XZY collected the patient’s data and drafted manuscript. JN interpretated the data and revised the manuscript. LYC participated in the interpretation of the study and revised the manuscript. All authors read and approved the final manuscript.

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**References:**


**Figure legend**

Figure 1. Axial brain magnetic resonance imaging (MRI) findings. T1-weighted MRI shows patchy hemorrhage within the lesion in left temporal lobe. FLAIR shows bilateral multiple hyperintense lesions. T2*-weighted MRI demonstrates multiple hemosiderin depositions in both supratentorial and infratentorial regions which are incompatible with the lesions visualized on FLAIR.