Comparison of Premortem Magnetic Resonance Imaging and Postmortem Autopsy Findings of a Cortical Microinfarct

Hidehiro Ishikawa, MD,* Yuichiro Ii, MD, PhD,* Atsushi Niwa, MD, PhD,* Akihiro Shindo, MD, PhD,* Ai Ito, MD,* Keita Matsuura, MD,* Ryogen Sasaki, MD, PhD,*,† Kenichiro Uno, MD,*,‡ Masayuki Maeda, MD, PhD,§ and Hidekazu Tomimoto, MD, PhD*

An 85-year-old woman diagnosed with amyotrophic lateral sclerosis died of pneumonia and was autopsied. Magnetic resonance imaging (MRI) performed 16 days before death revealed an intracortical high-intensity lesion in her right temporal cortex on three-dimensional (3D)-double inversion recovery (DIR) and 3D-fluid-attenuated inversion recovery (FLAIR) images. Histopathological examination indicated a cortical microinfarct (CMI) juxtaposed to cerebral amyloid angiopathy. Recently, in vivo detection of CMIs using 3D-DIR and 3D-FLAIR on 3-tesla MRI has been reported, and postmortem MRI study confirmed the presence of CMIs. This is the first case study to compare CMI findings detected upon premortem MRI to the CMI itself discovered upon postmortem neuropathological examination.

Key Words: Microinfarcts—small vessel disease—cerebral amyloid—angiopathy—double inversion recovery—Iba1—cerebrovascular disease—dementia—premortem MRI—histopathology.

Introduction

Cortical microinfarcts (CMIs) are frequently detected in the brains of elderly subjects upon autopsy, restricted to the cerebral cortex, with diameters varying from 50 μm to 5 mm.[1] It is likely that these infarcts are related to cognitive impairment.[1] Although CMIs are difficult to visualize upon conventional MRI, we report that the relatively large CMIs (diameter 2 mm-4 mm) can be detected using in vivo 3-tesla (3T) MRI, with the combination of 3-dimensional double inversion recovery (3D-DIR) and 3-dimensional fluid attenuated inversion recovery (3D-FLAIR).[2] Intracortical small lesions captured on these images were subsequently confirmed to represent CMIs pathologically via a postmortem MRI-histopathological correlation study.[3] Detection of CMIs via 7T MRI has also been reported,[4] and criteria and visual rating systems for durable CMIs on in vivo MRI have been proposed.[5] In clinical settings, CMIs are thought to be a novel MRI marker of cerebrovascular disease and represent an important mechanistic link between cerebrovascular disease and dementia.[6] However, definitions of specific size cutoffs and a favorable protocol for detecting durable CMIs using in vivo 3T MRI are still debatable. To date, a histopathological confirmation for CMIs detected using in vivo MRI has not been satisfactorily established.[5,7] Herein, we describe a patient with a CMI that was detected as a small cortical lesion on in vivo 3T MRI, and the CMI was confirmed by direct comparison of the MRI scan with findings of the postmortem histopathological examination.

From the *Department of Neurology, Mie University Graduate School of Medicine, Tsu, Mie, Japan; †Department of Neurology, National Mie Hospital, Tsu, Mie, Japan; ‡Department of Neurology, Matsusaka Central General Hospital, Matsusaka, Mie, Japan; and §Department of Advanced Diagnostic Imaging, Mie University Graduate School of Medicine, Tsu, Mie, Japan.

Received December 13, 2017; revision received May 15, 2018; accepted May 22, 2018.

Conflicts of Interest: The authors declare that they have no conflict of interest.

Address correspondence to Hidehiro Ishikawa, MD, Department of Neurology, Mie University Graduate School of Medicine, 2-174 Edobashi, Tsu city, Mie 514-8507, Japan. E-mailes: hidehiro-i@clin.medic.mie-u.ac.jp, dehirohidehhi@yahoo.co.jp

1052-3057/$ - see front matter

https://doi.org/10.1016/j.jstrokecerebrovasdis.2018.05.037

Case Presentation

An 85-year-old woman presented with dyspnea and progressive asymmetrical muscle atrophy in her arms. She had no medical history significant for vascular risk factors. On admission, her percent vital capacity was 32% and Mini-Mental State Examination score was 22. After neurological examination and electrophysiological and radiological study, she was diagnosed with amyotrophic lateral sclerosis (ALS). She died of pneumonia 19 days after admission. A definitive diagnosis of ALS was made based on the autopsy findings. A 3T MRI examination performed 16 days before her death revealed an intracortical high-intensity lesion (less than 4 mm across at the widest point) in her right temporal cortex, visualized on 3D-DIR (Fig 1, A,B) and 3D-FLAIR (Fig 1, C,D) images. The lesion was hypointense on 3D-T1-weighted imaging (repetition time [TR] 8 ms, echo time [TE] 5 ms; Fig 1, E,F), and isointense on diffusion-weighted imaging and susceptibility-weighted imaging (TR 23 ms, TE 34 ms). Other cerebrovascular lesions and cerebral microbleeds were not observed. Details of the 3D-DIR protocol were as follows: field of view, 250 mm; matrix, 208 × 163; and section thickness, .65 mm with over contiguous slice; TSE factor 173; TR (ms)/TE (ms), 5500/298; long inversion time (TI; ms)/short TI (ms), 2550/450; number of signals acquired, 2; and acquisition time, 5 minutes 13 seconds. 3D-FLAIR imaging was obtained in a sagittal direction, and then the axial and coronal images were reconstructed. The details of 3D-FLAIR were follows: field of view, 260 mm; matrix, 288 × 288; section thickness, 1 mm with .5 mm overlap; no parallel imaging; TR/TE, 6000/378; TI, 2000 ms; number of signals acquired, 2; and acquisition time, 5 minutes 12 seconds. Postmortem histopathological examination was performed. A premortem MRI was reconstructed (Fig 1, G) to adjust the specimen cutting plane (Fig 1, H). Hematoxylin and eosin staining revealed it as a region of pallor and tissue loss (Fig 1, I). There was a glial fibrillary acidic protein (1:1000, Millipore) positive area indicating astrogliosis (Fig 1, J), and an ionized calcium-binding adaptor molecule 1 (1:1000, Wako) weakly positive area indicating the existence of macrophages (Fig 1, K,L). These findings were compatible with a chronic CMI. An antiamyloid-beta antibody (1:200, Invitrogen) positive vessel was observed close to the CMI (Fig 1, M).[8] On the slide including CMI, there were 5 amyloid-beta positive vessels restricted to leptomeningeal and cortical arteries, not including capillaries. These findings indicate that the CMI observed upon premortem MRI of this patient was histopathologically confirmed as a microinfarction associated with cerebral amyloid angiopathy (CAA).

Discussion

In the present case, the CMI visualized upon premortem MRI was compatible with the histopathological findings that suggested chronic CMI. We previously reported in vivo detection of CMIs using 3D-DIR and 3D-FLAIR on 3T MRI, and a postmortem MRI-histopathology study confirming the presence of CMIs.[2,3] Although DIR can facilitate a faster detection of CMIs because of its high sensitivity for cortical lesions, it is also prone to many artifacts.[9] Generally, a relatively low signal/noise ratio results in the degradation of image quality. Due to the low signal/noise ratio, high signal intensity may be observed in areas where the cortex folds, such as the insula and the edge of the cortical gyri on DIR; this was observed in the present case. The use of 32-channel coils could have improved the signal/noise ratio and prevented such hyperintensities. In this case, we could assess the lesion using not only 3D-DIR but also 3D-T1-weighted imaging, 3D-FLAIR, and susceptibility-weighted imaging, in order to avoid the possibility of a false positive on DIR, the findings of which were indicative of a durable CMI.[5]

The pathogenesis of CMIs is heterogeneous, and cerebral small vessel disease (arteriolosclerosis and CAA) and microembolism are thought to be the main causes.[5] A postmortem autopsy study suggested that cerebral atherosclerosis was positively associated with both microinfarcts and large cystic infarcts and showed that microinfarcts due to embolism from atherosclerosis tended to appear as individual star-shaped lesions.[10] This study also suggested that arteriolosclerosis was positively correlated with lacunar infarcts, whereas CAA was negatively correlated.[10] On the other hand, several clinical studies using high-field MRI have also demonstrated the association between macroinfarcts and CMIs observed upon MRI in patients with cerebral atherosclerosis.[11-13] Our patient had neither macroinfarcts nor lacunar infarcts observed by either premortem MRI or autopsy specimen. Pathological examination of the patient confirmed CMI in the superficial cortical layer close to amyloid laden vessels, in accordance with previous observations that CMIs due to CAA involved the superficial cortical layers.[14] We confirmed that the CMI detected using in vivo 3T MRI was associated with CAA by directly comparing the postmortem histopathological and premortem radiological findings. The lesion size of the postmortem specimen was smaller than that detected on premortem MRI. This may have been due to shrinkage of the lesion during formalin fixation. These differences should be considered during further radiological-histopathological comparative studies on cerebral small vessel disease.

A strikingly common finding in elderly people,[15] CAA can incidentally coexist in elderly patients with ALS. An autopsy study of ALS cases found that 7 out of 28 (25%) patients exhibited CAA, and the average age of such patients was significantly higher than that of those without CAA.[16] The prevalence of CMIs seems to be similar between patients with and without ALS.[14]

To the best of our knowledge, this is the first report on the histopathological findings of CMI observed via in vivo MRI. Further studies with a large sample size are needed to investigate the correlation between the neuroradiological and neuropathological findings of CMIs.