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Hippocampal Microbleed on a Post-Mortem T_2*-Weighted Gradient-Echo 7.0-Tesla Magnetic Resonance Imaging?

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Key Words
Microbleed · Hippocampus · Alzheimer dementia · T_2*-weighted 7.0-T MRI sequence · Neuropathology · Iron deposits

Abstract
The present post-mortem study of a brain from an Alzheimer patient showed on a T_2*-weighted gradient-echo 7.0-T MRI of a coronal brain section a hyposignal in the hippocampus, suggesting a microbleed. On the corresponding histological examination, only iron deposits around the granular cellular layer and in blood vessel walls of the hippocampus were observed without evidence of a bleeding. This case report illustrates that the detection of microbleeds on MRI has to be interpreted with caution.

Introduction

Cerebral microbleeds are frequently detected on magnetic resonance imaging (MRI) in patients with small-vessel diseases such as cerebral amyloid angiopathy and lipohyalinosis [1]. They are frequently observed in brains of patients suffering from Alzheimer dementia (AD) and are mainly related to cerebral amyloid angiopathy [2].

The clinical significance of microbleeds in AD is poorly understood [3]. Post-mortem verifications of MRI-detected microbleeds become more and more mandatory [4].

We present the clinical history and the post-mortem T_2*-weighted gradient-echo (GRE) 7.0-T MRI findings with the neuropathological correlates of a suspected hippocampal microbleed in a patient with AD.

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Case Report

This female patient died at the age of 88 years from a neurodegenerative disease of unknown etiology. The prior clinical history included thrombophlebitis, complicated by lung embolism, gout, knee arthrosis, cholecystectomy and dyslipidemia.

Memory disturbances started at the age of 82 years. She had a cognitive evaluation at the age of 86 years. On the Mattis Dementia scale she had a score of 102/144. An MRI of the brain showed bilateral hippocampal atrophy and symmetrical hypersignals in the brainstem on a T_2 sequence. No T_2* sequence was performed at that time. The patient's cognitive status rapidly deteriorated with periodic hallucinations. Rivastigmine dermal patches did not improve the mental status. The patient had frequent falls and became more and more dependent. She had many episodes of urinary retention. Walking became impossible due to the development of a parkinsonian syndrome with extreme axial rigidity. The patient had to enter a nursing home at the age of 87 years, due to rapid physical deterioration. She became bedridden, developed skin scars and died a few months later.

Post-mortem brain examination was obtained by written informed consent from the nearest family. The brain tissue samples were first used for diagnosis and afterward integrated in the Lille Neuro-Bank, dependant from the Lille University and co-federated by the 'Centre des Resources Biologiques', acting as institutional review board.

On histological examination the diagnosis of AD, stage VI, was made according to the Braak and Braak criteria [5]. Mild deposits of amyloid were found in a few cortical and leptomeningeal vessels. The bleeding load in the brain was quantified according to a method previously described [6]: only a few widespread small bleeds were observed. No other cerebrovascular lesions were found.

Three coronal sections of a cerebral hemisphere were submitted to a T_2*-weighted GRE 7.0-T MRI, and afterwards compared to the corresponding histological sections for the detection of microbleeds, according to a previously described method [7]. A moderate number of hyposignals were observed, predominantly in the deep cortical layers of the central and occipital sections on the T_2* sequence. All of them were confirmed to be small bleeds on the corresponding histological slides. In addition, a strong hyposignal was observed in the hippocampus (**fig. 1**). However, the corresponding histological slide showed only amorphous iron deposits around the granular cellular layer and inside the layer of pyramidal neurons (**fig. 2**a, b). Moreover, iron deposits were present in the walls of small vessels (**fig. 3**).

Discussion

The present study shows a false-positive microbleed signal in the hippocampus on a T_2* weighted GRE 7.0-T MRI sequence, due to iron deposition. Overall, cerebral microbleeds are rarely observed in the hippocampus, compared to other brain regions, in patients with suspected cerebrovascular disease [8]. Brain iron deposits are mainly observed in the basal ganglia and were recently found to be associated with general cognitive ability and cognitive ageing [9]. Increased iron accumulation has been demonstrated in the hippocampus of AD brains [10, 11].

This case report shows that one has to be careful in the interpretation of hyposignals as microbleeds on T_2* sequence MRI.

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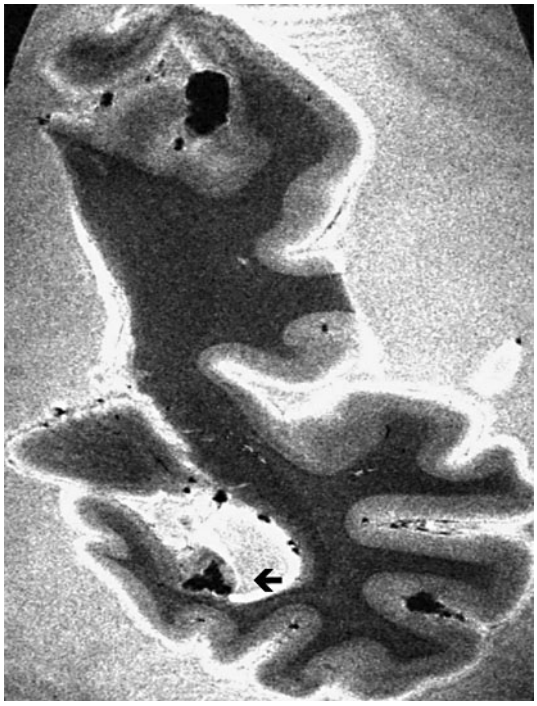

Fig. 1. T_2*-weighted GRE MRI of a coronal section of a cerebral hemisphere, showing a strong hyposignal in the hippocampus, mimicking a microbleed (arrow). Post-mortem thrombi are responsible for the hyposignals in the leptomeningeal vessels.

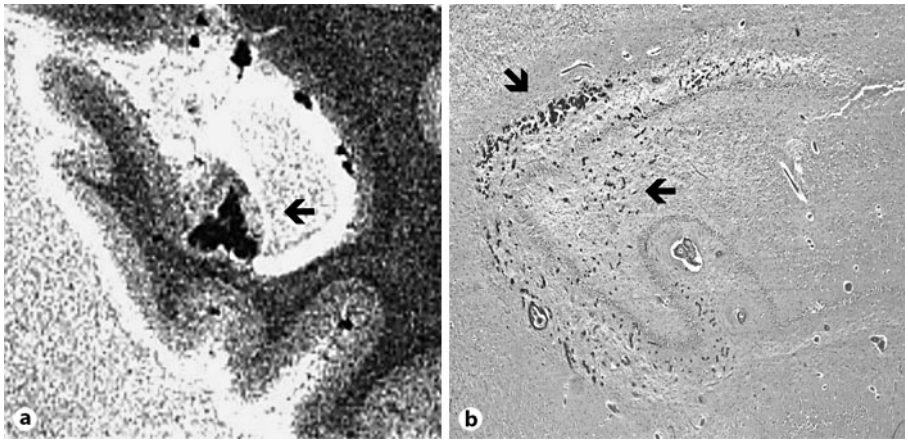

Fig. 2. **a** High magnification of the hyposignal in the hippocampus on a T_2*-weighted GRE MRI sequence. **b** Iron deposits (arrows) in the hippocampus on the corresponding histological section of the hippocampus, stained with hematoxylin-eosin.

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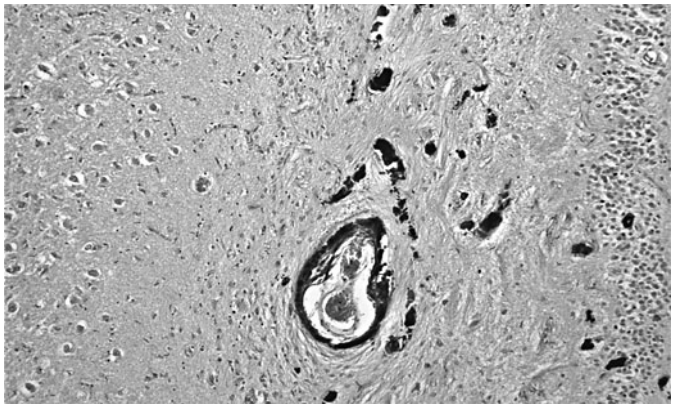

Fig. 3. Iron deposits in the walls of small hippocampal vessels on the histological slide, stained with Perl's Prussian blue.

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