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CORRESPONDENCE

Petechial Hemorrhage in Wernicke Encephalopathy

Imaging and Clinical Significance

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Introduction

Wernicke encephalopathy (WE) is a severe neurological disorder due to vitamin B1 deficiency, i.e. thiamine [1]. If untreated WE may turn over to an anamnestic syndrome or Korsakoff psychosis, which represents the irreversible part of the Wernicke-Korsakoff syndrome and causes lifelong severe disability [2]. Therefore, the earliest possible diagnosis and appropriate treatment is essential for prognosis. The typical clinical presentation of WE is the classical triad of oculomotor abnormalities, cerebellar dysfunction with prominent ataxia and an altered mental state up to a global state of confusion [2]; however, retrospective analysis of neurological symptoms and autopsy studies disclosed that only 20% of patients with WE showed the classical clinical triad and 30% had only cognitive impairment [3–5]. Thus, especially in cases with incomplete or atypical neurological presentations magnetic resonance imaging (MRI) has an important role to establish the diagnosis [6–9]. MRI often shows bilateral symmetrical lesions in the medial thalami, the hypothalamus, midbrain tectum and tectal plate, the periaqueductal gray and in the mammillary bodies [6–12]. Infrequently cortical lesions are also reported [13, 14]. Although petechial hemorrhages are a prominent neuropathological feature of the disease and accordingly the first description was as "polioencephalitis hemorrhagica superior" by Wernicke in 1881 [15], a review of the literature yielded only 2 cases with detection of such petechial hemorrhages in vivo [16, 17].

Case Report

A 53-year old man presented with a 1-week history of progressive dizziness and mental impairment, gait ataxia and additionally double vision for 4 days. Medical history disclosed chronic alcohol abuse. On neurological examination, the patient was disorientated and confused. Cranial nerves revealed bilateral exhaustless horizontal nystagmus as well as abduction deficits of both eyeballs with diplopia at lateral gaze. Motor function of the limbs, deep tendon reflexes and sensory examination were normal. Because of severe ataxia, the patient was unable to stand or walk. The MRI at admission revealed signal loss in the mammillary bodies on susceptibility weighted images (SWI), suggesting petechial hemorrhages due to WE (Fig. 1). In addition, fluid attenuated inversion recovery (FLAIR) images showed hyperintense lesions of the periaqueductal gray, the medial tectal plate and the paramedian thalamic nuclei with slight contrast enhancement (CE) on postcontrast (PC) T1WI (Figs. 2 and 3). The patient received immediate high dosage vitamin B 1 substitution, i.e. daily intravenous application of 200 mg thiamine. The oculomotor disorders and gait ataxia had completely resolved 15 days later but there were still severe cognitive impairment and distinct amnestic dysfunction. Neuropsychological exploration disclosed marked performance abnormalities in learning and memory skills as well as retrieval of information from the long-term memory. He did not seem to suffer much from the impairment and hardly resonated affectively in the conversations.

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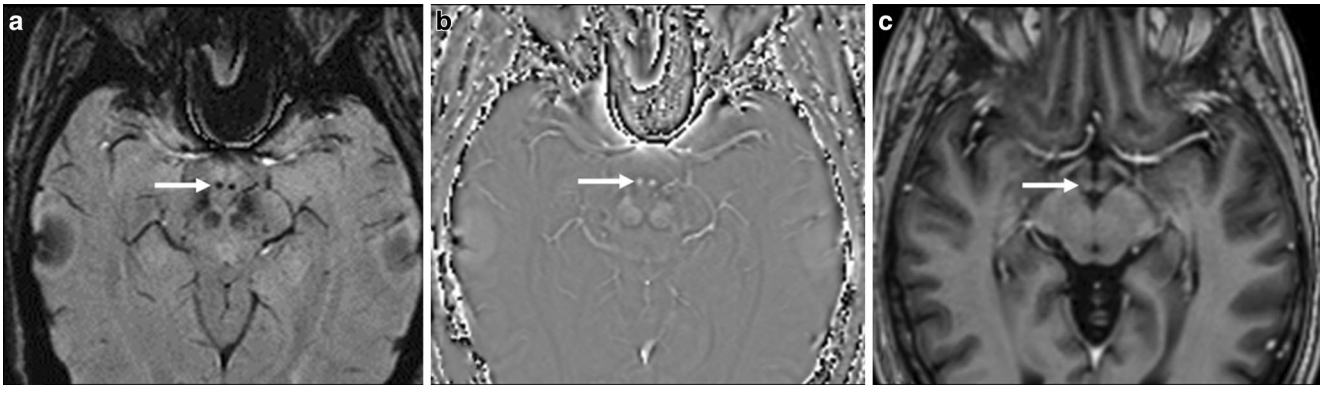

Fig. 1 Axial SWI (**a, b**) disclosing distinct nearly symmetrical signal loss in the mammillary bodies (**a**, *arrow*) with proper phase shift indicating iron/paramagnetic effects on the phase image (**b**, *arrow*; Siemens Aera; TR: 49 ms; TE: 40 ms); **c** slight contrast enhancement (CE) on axial postcontrast (pc) T1WI (*arrow*)

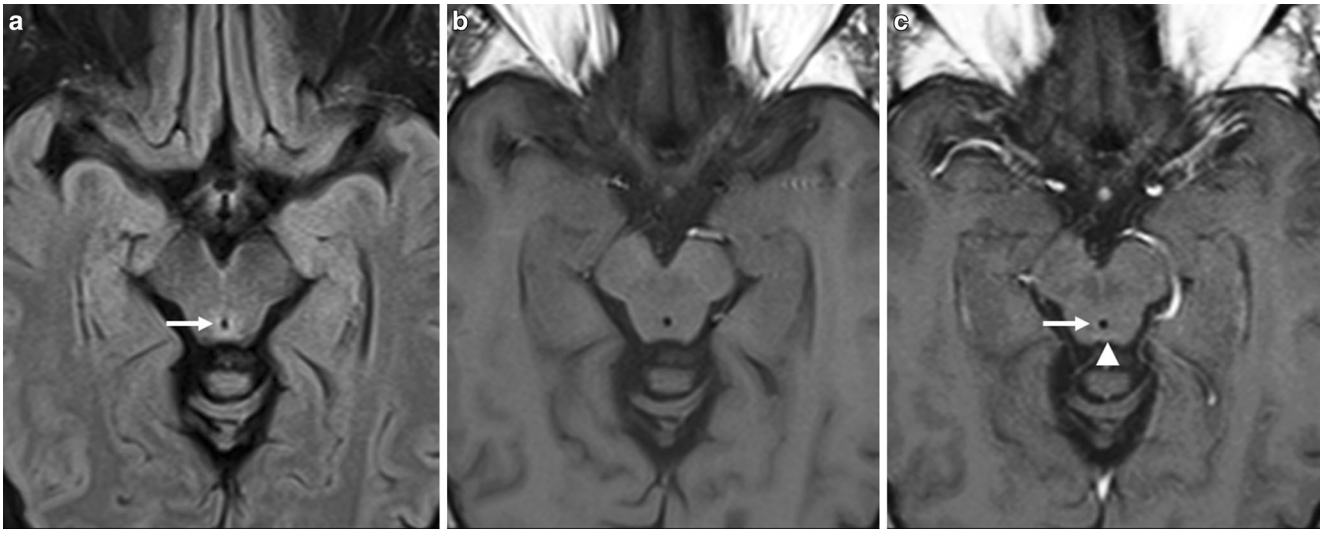

Fig. 2 Axial fluid attenuated inversion recovery (FLAIR) image (**a**) showing a periaqueductal hyperintense lesion with blurred margins and involvement of the medial and paramedical quadrigeminal plate (*arrow*); **b, c** axial postcontrast (pc) T1WI (**c**) disclosing slight periaqueductal (**c**, *arrow*) and tectal (*arrowhead*) contrast enhancement (CE)

Discussion

Although thiamine deficiency most often occurs in association with chronic alcoholism [3, 4], further causes may be hyperemesis (gravidarum), cancer, bariatric surgery, anorexia nervosa, prolonged infectious febrile conditions and HIV infection [1, 5–8]. Thiamine deficiency causes impaired cerebral energy metabolism resulting in decreased osmotic gradients across cell membranes with swelling of intracellular spaces and blood-brain barrier breakdown. Preferential brain regions are the medial thalamus with anterior principal and dorsomedial nuclei, the hypothalamus, the periaqueductal gray, the midbrain tectum and tectal plate, and the mammillary bodies. All these locations have a pronounced thiamine-related glucose and oxidation metabolism [1, 2].

Macroscopic and microscopic findings depend upon the stage and the severity of the disease. Neuropathological specimens show petechial hemorrhages and symmetrical necrosis with neuronal loss in the acute stage, capillary proliferation in the subacute phase and increased capillaries in a rarefied atrophic parenchyma in the chronic stage [1, 2, 5].

On T2WI, the lesions show typically hyperintense signal changes due to focal edema with potentially diffusion restriction in the early acute stage 18 In addition, postcontrast T1WI may detect CE due to blood-brain barrier disruption [6–8, 11, 19]. In the subacute phase, hyperintense signal conversion on T2WI corresponds to spongy disintegration of the neuropil. In correlation to neuropathological studies, volumetric MR investigations show volume deficits in the affected regions [1, 3, 20]. While oculomotor and cerebellar ataxic symptoms usually resolve completely with adequate

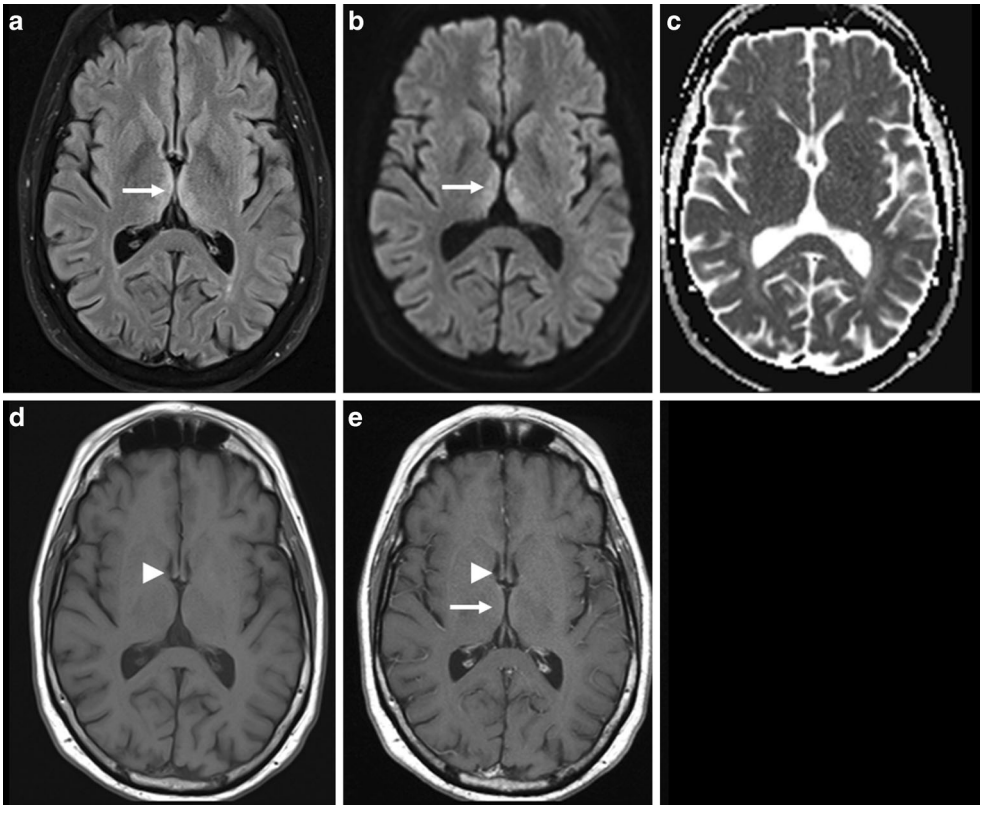

Fig. 3 Axial fluid attenuated inversion recovery (FLAIR) images (**a**) representing symmetrical hyperintense lesions of the periventricular region of the III. ventricle and the paramedian thalamic nuclei (**a**, *arrow*) with hyperintense signal conversion on DWI (diffusion weighted imaging, **b**, axial; $b = 1000\,s/mm^2$) without lowered apparent diffusion coefficient (ADC) value (**c**) and slight contrast enhancement (CE) on postcontrast (pc) T1WI (**e**, *arrow*); note hyperintense signal of the fornix (**d, e**: *arrowhead*)

vitamin B1 substitution, the course of mental dysfunction is inconsistent, with significant deficits persisting in up to 50% [5]. Hyperintense signal changes of the paramedian thalamic nuclei on T2WI and CE of the mammillary bodies might suggest poor prognosis of initial global state of confusion, especially regarding amnestic syndromes [6–8]. In line with the literature, in the presented patient oculomotor symptoms, i.e. nystagmus, abduction deficits of both eyeballs with consecutive diplopia on lateral gaze and cerebellar ataxic features completely resolved within a 2-week period after intravenous thiamine substitution.

However, concerning the neuropsychological deficits, there was a slight improvement of wakefulness and orientation, whereas the amnestic and cognitive deficits did not improve. In addition to the CE of the mammillary bodies, MRI also showed a signal reduction on SWI due to petechial hemorrhages, so that with reference to histopathological descriptions the clinical course was not surprising [1, 2, 15]. Regarding an unfavorable prognosis of mental and especially memory deficits with turn over into a Korsakoff psychosis despite efficient thiamine substitution, the detection of petechial hemorrhages in the mammillary bodies might have a higher prognostic value than blood-brain barrier disturbances [16, 17].

However, it should be emphasized that the hyperintense signal changes on T2WI in the mesencephalic and paramedian thalamic regions are not specific for WE [6–12]. Differential diagnosis includes vascular diseases, e.g. inferior-medial thalamic infarcts (posterior thalamus-perforating arteries and variants, e.g. artery of Percheron) and deep cerebral venous thrombosis [9, 21], inflammatory diseases (e.g. Cytomegalovirus encephalitis, West Nile virus meningoencephalitis, acute disseminated meningoencephalitis) [9, 11], neoplastic diseases (e.g. lymphoma) [22], and also the variant Creutzfeldt-Jakob disease [6, 9]. A likely consequence might be that routine use of SWI with evidence of petechial hemorrhages in the mammillary bodies will facilitate initial differential diagnostic narrowing and prognostic value.

Conflict of interest S. Weidauer, N. Treusch and E. Hattingen declare that they have no competing interests.

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