Journal of the Neurological Sciences 334 (2013) 172–175

Contents lists available at ScienceDirect

Journal of the Neurological Sciences

journal homepage: www.elsevier.com/locate/jns

Short communication

Isolated mammillary body involvement on MRI in Wernicke's encephalopathy

Shin C. Beh [a,*], Teresa C. Frohman [a], Elliot M. Frohman [a,b]

[a] Department of Neurology, University of Texas Southwestern Medical Center at Dallas, United States
[b] Department of Ophthalmology, University of Texas Southwestern Medical Center at Dallas, United States

ARTICLE INFO

Article history:
Received 26 May 2013
Received in revised form 24 July 2013
Accepted 26 July 2013
Available online 2 August 2013

Keywords:
Wernicke's encephalopathy
Thiamine deficiency
Mammillary bodies
Papez circuit
Bariatric surgery
MRI

ABSTRACT

A 48-year-old woman, with a remote history of gastric-banding as well as recent-onset post-prandial vomiting and excessive wine-drinking, was admitted with progressively-worsening gait incoordination. She showed gaze-evoked nystagmus and gait ataxia. Brain MRI revealed conspicuous, isolated, symmetrical T2/FLAIR-hyperintensities and gadolinium-enhancement of the mammillary bodies. Serum thiamine and folate were low. Following thiamine and folate replacement therapy, her ataxia resolved. Given the rising number of bariatric procedures, we discuss the importance of recognizing thiamine-deficiency in these patients. Additionally, while isolated involvement of the mammillary bodies is a rare finding in this disorder, we highlight radiologic changes that neurologists should recognize.

1. Introduction

1.1. Case report

A 48-year-old woman was admitted to the hospital complaining of progressive gait instability and paresthesias and weakness in the legs. She was well until about two weeks prior to coming to our hospital emergency room. Her initial symptom was perceived as leg weakness and she began falling almost every day.

She had had a gastric-banding bariatric procedure about six years prior to the recent onset of symptoms. She suffered from post-prandial vomiting occurring nearly daily and could vomit many times on a single day. She admitted to drinking about six glasses of wine each day.

On neurological examination, the patient was alert, attentive, and oriented to person, place, and date. She was not abulic or withdrawn. Her mini-mental status examination (MMSE) score was 28/30; she was able to immediately recall all three items read to her but five minutes later, could only remember one item without any clues. Examination revealed gaze-evoked horizontal nystagmus but otherwise normal ocular movements, smooth pursuit, saccades, vestibular-ocular reflexes (VOR) and VOR suppression. In her legs she had normal strength, diminished reflexes (+ at the knees and 0 at the ankles), a stocking-pattern loss of pinprick and temperature sensation, mild vibratory loss, and normal proprioception at the great toes. There was no incoordination or dysmetria in her arms or legs but her gait was wide-based and ataxic. The remainder of the neurologic examination was unremarkable.

An MRI of the brain revealed conspicuous, symmetrical T2/FLAIR-hyperintensities and gadolinium-enhancement of the mammillary bodies (Fig. 1). Additionally, sagittal views revealed superior cerebellar vermal atrophy. Serum thiamine and folate were low at 34 nmol/L (70–180 nmol/L) and 3.5 ng/mL (>7.3 ng/mL), respectively. MRI of the spine, nerve conduction studies, electromyography, cerebrospinal fluid analysis, and other laboratory studies were unremarkable.

Wernicke's encephalopathy (WE) was diagnosed and intravenous replacement of thiamine and folate was begun immediately. Her symptoms gradually resolved and examination four months later in the outpatient clinic was normal. Neuropsychological testing was performed during the same time period and revealed intact cognitive capabilities.

2. Discussion

WE was originally characterized by localized hemorrhagic changes in the gray matter of the mammillary bodies of three chronic alcoholics [1].

A consequence of thiamine-deficiency, WE has classically been associated with malnutrition from chronic alcoholism, but has also been reported in pyloric stenosis, gastrointestinal surgery, bariatric procedures, protracted vomiting (e.g. hyperemesis gravidarum, and bulimia nervosa), chronic diarrhea, magnesium deficiency, malignancies and chemotherapy, systemic diseases, a staple diet of polished rice, and dietary imbalances [2–6].

Neurologic complications of bariatric surgery have an estimated annual incidence of 16% and are most commonly a consequence of

* Corresponding author at: Department of Neurology, University of Texas Southwestern Medical Center at Dallas, 5323 Harry Hines Blvd., Dallas, TX 75390, United States. Tel.: +1 214 645 0555; fax: +1 214 645 0556.
E-mail address: scjbeh@gmail.com (S.C. Beh).

0022-510X/$ – see front matter © 2013 Elsevier B.V. All rights reserved.
http://dx.doi.org/10.1016/j.jns.2013.07.2516

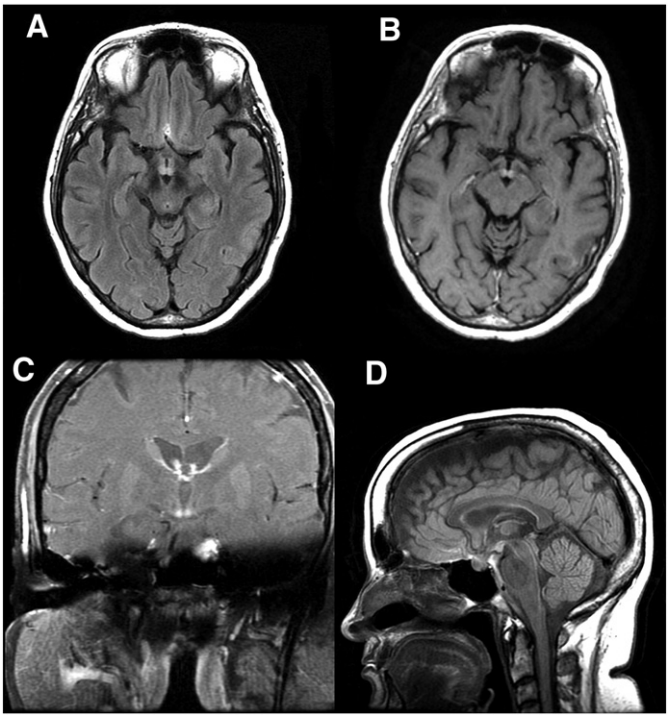

Fig. 1. Brain MRI in our patient demonstrating isolated T2/FLAIR (A) hyperintense signal changes and Gadolinium-enhancement (B,C and D) of both mammillary bodies. Also note the anterior vermal atrophy, a common finding in patients with chronic excessive alcohol consumption.

nutritional deficiencies [7]. Given the increasing epidemic of obesity and rising numbers of bariatric procedures [3], it is imperative for clinicians to recognize the potential nutritional deficiencies that may ensue, particularly WE, since it is easily-treatable and potentially-catastrophic if left unrecognized. Following bariatric surgery, more than 90% of patients will experience recurrent vomiting, culminating in eating avoidance in many, and predisposing to alterations in gastrointestinal tract absorption of thiamine [3]. While most cases of WE occur four and twelve weeks postoperatively (reflecting the depletion of thiamine stores) [8], a substantial number of other patients develop a more insidious and imperceptible deficiency over a substantially longer time period, even many years following the bariatric procedure (which may camouflage the etiology of the evolving constellation of neurologic manifestations) [3]. There are a few reports of WE occurring many years after the procedure [9,10]; these late cases may be associated with alcohol abuse, or dietary non-compliance that worsen chronic subclinical thiamine-deficiency [10,11].

WE is characterized by an acute, potentially-reversible encephalopathy (confusion, confabulation, amnesia, and psychosis), ocular motor abnormalities (nystagmus, gaze palsies, ophthalmoparesis, vestibular hypofunction), and gait ataxia [12,13]. However, only 16–38% of patients with WE demonstrate this classic triad; they more commonly show two or only one of these cardinal features [3,4,13].

2.1. Pathobiochemical underpinnings of Wernicke's encephalopathy

Thiamine pyrophosphate is an essential coenzyme for transketolase, pyruvate dehydrogenase, and alpha ketoglutarate dehydrogenase; three enzyme systems that are important for disposition of intracellular glucose. Thiamine-deficiency results in a time-dependent chronic impairment of oxidative phosphorylation (from mitochondrial dysfunction) leading to lactate accumulation, and eventually neuronal death, which is accompanied by microglia-mediated inflammatory cascades producing free radicals, superoxides, and nitric oxide. Glutamate-mediated excitotoxicity, arising from both increased glutamate production (a result of oxidative stress) and decreased reuptake (due to astrocytic energy failure and downregulation of glutamate transporters), also plays an important role in the etiopathobiological changes in WE [14,15]. The pivotal role of thiamine in human energy metabolism likely accounts for the regionally-selective damage within the central nervous system (CNS); those neuroanatomic foci most vulnerable to injury are those with higher thiamine turnover and oxidative metabolic rates.

Neuropathologically, WE is typically characterized by petechial hemorrhage, capillary proliferation, endothelial hyperplasia, edematous foci, neuronal loss and gliosis in the mammillary bodies, medial thalami, periventricular regions (third and fourth ventricles), and periaqueductal gray. Occasionally, the pontine tegmentum, mesencephalic reticular formation, posterior corpora quadrigemina, and cerebral cortex are affected [12,13,16]. Disruption of the blood–brain barrier (BBB), believed to be from perturbed endothelial cell oxidative metabolism, and edema of the end feet of astrocytes, has been shown to precede these changes, and as such, gadolinium-enhancement represents a consequence of a metabolic derangement, rather than being secondary to inflammation [14,15].

2.2. Pathophysiology of clinical features

Encephalopathy is present in most WE patients ranging from mild confusion to coma. The cognitive changes likely reflect damage to specific thalamic nuclei (particularly the anterior, dorsomedial, intralaminar and posterior nuclei), the basal forebrain, and the mammillothalamic tract [17,18]. Additionally, neurotransmitter networks, particularly the cholinergic and norepinephrine systems, including those in the locus ceruleus may be damaged, and may account for disturbances in arousal, sleep–wake cycle transitions, attention and memory, and neuroplasticity (processes commonly affected by WE) [17]. The pivotal role of the mammillary bodies in the Papez circuit is shown in Fig. 2.

Gait ataxia is common in WE, and may reflect Purkinje cell degeneration in the cerebellum, damage to the vestibular nuclei, and alterations in the medullary inferior olives [2,17]. Pathologic studies have confirmed frequent cerebellar involvement in WE [17,19] though cerebellar signal changes on MRI in patients with confirmed WE are unusual [20], However, it is important to look for anterior superior cerebellar vermal atrophy on the MRI in patients with WE, a well-known consequence of alcoholism [19].

Ocular motor abnormalities are also common in WE. They include nystagmus (gaze-evoked, horizontal, and vertical), internuclear ophthalmoparesis, complete ophthalmoplegia, abducens palsy, oculomotor palsy, conjugate gaze paresis, impaired smooth pursuit, diminished optokinetic nystagmus, and hypoactive VOR responses. They, represent thiamine deficiency-induced damage to the various brainstem and cerebellar structures that participate in the control of eye movements [21–23].

2.3. Radiologic findings in Wernicke's encephalopathy

The reversible cytotoxic edema that characterizes the pathological changes in WE is poorly-visualized on CT but readily-demonstrated on MRI [20]. MRI changes are typically present in the mammillary bodies, periaqueductal gray, and many thalamic nuclei (the dorsomedial, anterior, pulvinar, and midline nuclei). The predilection for these locations may be explained by how critical thiamine is for maintenance of cellular osmotic gradients [20].

On MRI, the most commonly affected locations are the medial thalami and region surrounding the third ventricle, followed by the periaqueductal gray [4]. While mammillary body involvement on MRI in WE is common and they are the most common neuroanatomic structure to demonstrate gadolinium-enhancement, isolated signal changes limited to the mammillary bodies are unusual [2,4]. Interestingly, alcoholism and contrast-enhancement of the mammillary body are correlated, though the mechanism is unclear [4]. Another