Wernicke encephalopathy (WE) is an uncommon neurologic disorder classically characterized by changes in consciousness, ocular dysfunction, and ataxia.1,2 Neuroradiologic findings usually show symmetric signal intensity alterations in the mammillary bodies, medial thalami, tectal plate, and periaqueductal area.3 WE results from a deficiency of vitamin B1 (thiamine).4,5 Thiamine represents an essential coenzyme in intermediate carbohydrate metabolism but is also an osmotic gradient regulator.5 Its deficiency may cause swelling of the intracellular space and local disruption of the blood-brain barrier.6 WE represents a medical emergency, and treatment consists of intravenous administration of thiamine.1,2 The classic clinical triad of WE is not always present at clinical onset.2 Thus, diagnostic imaging modalities are useful to achieve a prompt diagnosis and treatment. In this retrospective, multicenter study, we describe the imaging findings and clinical presentations of 26 patients affected by WE because of various causes of malnutrition and malabsorption.

**Results**

**Clinical Histories**

Thirteen (50%) patients affected by WE had a history of chronic alcohol abuse. Thirteen (50%) patients affected by
Axial FLAIR (11000/140/2 [TR/TE/NEX]) image shows marked hyperintensity of the tectal region, after prolonged voluntary food starvation.

We did not have a history of alcohol abuse. In the nonalcoholic group, the most frequent cause of thiamine deficiency was malabsorption as a result of malignant tumors of the gastrointestinal tract (6/13 patients, 46%). Among these, 4 patients underwent surgery for gastric cancer. For 31% of patients had severe malnutrition caused by prolonged voluntary starvation (1), anorexia nervosa (1), and socioeconomic poverty (in 1 pediatric patient).

Neurologic Findings at Clinical Presentation

The most frequent neurologic findings were changes in consciousness in 21/26 patients (81%), 10 in the alcohol abuse group [AL] versus 11 in the group with no alcohol abuse [NA]). These changes showed a wide spectrum of presentations ranging from mild disorientation to coma. Twenty patients (77%, 12 AL and 8 NA) showed ocular symptoms. Fourteen patients (54%, 10 AL and 4 NA) showed ataxia. With reference to changes in consciousness and ocular symptoms, no statistical associations were found between the alcohol abuse and the nonalcoholic groups. The alcohol abuse group showed a statistically positive correlation with ataxia ($P = .047, \Phi = 0.463$). Only 10/26 patients (38%, 7 AL and 3 NA) showed the classic triad of the disease at clinical presentation.

Imaging Features

All 26 patients underwent MR. The MR sensibility was $0.92 \pm 0.10$, confidence interval = 0.95. Twenty-three (88%) patients showed high signal intensity alterations on long TR spin-echo sequences; 8 (31%) showed low signal intensity alterations on short TR spin-echo images. Twenty-two (85%) patients showed symmetric lesions of the medial thalami and the periventricular region of the third ventricle (9 AL and 13 NA). Seventeen (65%) patients showed alterations of the periaqueductal area (7 AL and 10 NA) (Fig 1). Fifteen (58%) patients showed alterations of the mamillary bodies (10 AL and 5 NA) (Fig 2). Eight (31%) patients showed alterations of the tectal plate (2 AL and 6 NA). Only 2 (8%) patients showed lesions of the dorsal medulla with selective involvement of the prepositus hypoglossal nuclei (Fig 3). Only 1 (4%) patient showed symmetric alterations of the cerebellum. Regarding the presence of signal intensity alterations in unenhanced sequences involving anatomic regions typical and atypical for the disease, no significant statistical associations were observed between the 2 groups.

Contrast media was administered in 17/26 (65%) patients (8 AL and 9 NA). Among these patients, 8/17 (47%, 7 AL and 1 NA) showed contrast enhancement. The anatomic structures that most frequently showed contrast enhancement were the mamillary bodies (6 patients), followed by the tectal plate (3 patients), thalamus (3 patients), and periaqueductal area (2 patients). In Patient 1 in the alcohol abuse group, the alteration seemed to be only in contrast enhancement that symmetrically involved the mamillary bodies (white arrow). After administration of contrast media, central enhancement (white arrows) of both mamillary bodies is seen on coronal T1-weighted image (532/15/2 [TR/TE/NEX]) (C).

Fig 1. A 33-year-old man presented with sudden and progressive changes in consciousness after prolonged voluntary food starvation.

A. Axial FLAIR (11000/140/2 [TR/TE/NEX]) image shows marked hyperintensity of the tectal region (white arrow), periaqueductal area (black arrowheads), and mamillary bodies (white arrowheads). The lesions are compatible with reversible cytotoxic edema.

B. On sagittal T1-weighted (530/13/2 [TR/TE/NEX]) image, low signal intensity areas with respect to the pons of both periaqueductal areas (black arrowheads) and tectal plate (white arrowheads) are seen. Note that the local swelling determines mild stenosis of the cerebral aqueduct.

C. Ten days after thiamine replacement, a partial regression of the lesions involving the aqueductal region (black arrowheads) and mamillary bodies (white arrowheads) is easily seen on axial FLAIR image.

D. This finding is confirmed by a sagittal T1-weighted image showing reopening of the cerebral aqueduct (white arrows).

Fig 2. A 53-year-old woman with an history of chronic alcohol abuse presented with the classic neurologic triad of Wernicke encephalopathy. Coronal T2-weighted (2500/90/2 [TR/TE/NEX]) (A) and coronal FLAIR images (9000/105/2 [TR/TE/NEX]) (B) show high signal intensity circumscribed to the mamillary bodies (white arrow). After administration of contrast media, central enhancement (white arrow) of both mamillary bodies is seen on coronal T1-weighted image (532/15/2 [TR/TE/NEX]) (C).
abuse, Patient 11 showed symmetric involvement of the cerebellum. Hydrocephalus due to occlusion of the cerebral aqueduct was not found in any of the patients. Data on histories, symptoms, imaging modalities, and findings in both groups are summarized in on-line Tables 1 and 2. On-line Table 3 shows the topographic distribution of lesions in both groups. On-line Figure 1 compares the groups by anatomic abnormalities. On-line Table 4 shows the neurologic symptoms typical for the disease in both groups. On-line Figure 2 compares the groups by neurologic symptoms.

Discussion

WE is a life-threatening condition, and its prognosis depends on prompt diagnosis followed by intravenous administration of thiamine.²,⁵ If left untreated, severe amnesic deficits, Korsakoff psychosis, and even death may follow the acute phase of the disease.¹,²,⁴,⁵,⁷ WE is frequently associated with chronic alcohol abuse, but many other pathologic conditions can cause the disease. Some of them include tumors of the gastrointestinal tract, gastroplasty for obesity, psychogenic refusal of food, hydremesis gravidarum, anorexia nervosa, prolonged infectious-febrile disease, voluntary food starvation, chronic uremia, and parenteral therapy.²,⁷-¹³ Although the hallmark of the disease is represented by a clinical triad of altered consciousness, ocular dysfunction, and ataxia, many studies show incomplete neurologic presentation.¹,² This finding has been confirmed by our results, with only 38% of patients showing the classic triad of WE. It is noteworthy that most of them (7 AL vs 3 NA) had a history of alcohol abuse. In our study, altered consciousness, the most frequent neurologic symptom at clinical onset, was almost equally balanced between the 2 groups (AL and NA). On the other hand, ocular symptoms and ataxia were more frequently seen in the alcohol abuse group, with a positive correlation.

In our casuistry, the anatomic regions most frequently involved by symmetric lesions were the medial thalami and the periventricular area of the third ventricle. To explain these findings, we speculated that these areas represent regions where maintenance of cellular osmotic gradients is strictly related to physiologic levels of thiamine concentration and that any reduction in thiamine may determine early symmetric metabolic breakdown, as easily evidenced by MR as cytotoxic edema.⁵ The lesions of the thalamus and periventricular region of the third ventricle were always associated with other alterations typical of the disease (except in Patient 3 in the nonalcoholic group), which confirms a previous report.¹⁴

When sudden onset of symptoms such as somnolence and altered consciousness are present, the differential diagnosis of lesions of the symmetric medial thalami should include ischemia as a result of occlusion of the artery of Percheron and
deep cerebral vein thrombosis. It is easy to understand why the ischemic diagnosis should be reasonably excluded in patients who show the association of lesions in the thalamus, periaqueductal area, tectal plate, and mamillary bodies, especially in the presence of neurologic symptoms typical of WE. Influenza A virus infection, primary acute disseminated encephalomyelitis, cytomegalovirus encephalitis, primary cerebral lymphoma, variant Creutzfeldt-Jakob disease, and West Nile virus meningoencephalitis represent other possible differential diagnoses of symmetric medial thalamic lesions.

Symmetric alterations in the mamillary bodies were evident in 57% of our patients. It is noteworthy that the prevalence of lesions in the mamillary bodies was observed in the alcohol abuse group. Furthermore, we found a statistically positive correlation between contrast enhancement in the mamillary bodies and chronic alcohol consumption. We could not explain these data; we could only observe that thiamine-related deficiency from chronic alcohol abuse affected the mamillary bodies more frequently by swelling of the intracellular space and local disruption of the blood-brain barrier, compared with the patients with no alcohol abuse. In 1 patient, we found a sole alteration: contrast enhancement in the mamillary bodies, which confirmed a unique case report described previously in the English-language literature. A T2-weighted normal signal intensity associated with contrast enhancement in the mamillary bodies has also been described in a pediatric patient affected by WE, which also showed lesions of the periaqueductal gray matter and medial thalamus. To explain this infrequent finding, Shogry et al. proposed the T2-weighted “fogging effect” hypothesis previously described in cerebral infarction. However, this effect has been reported only in 3 patients affected by WE to date, including one of our patients with alcohol abuse and only at the level of the mamillary bodies. This finding enforces the idea that this phenomenon may be linked to the increased detection of small cortical lesions with contrast-enhanced T1-weighted images compared with the T2-weighted ones.

We found MR findings atypical for WE in 2 nonalcoholic patients in which the dorsal medulla was involved at the level of the mamillary bodies. Simultaneously, 2 patients in which the dorsal medulla was involved at the level of the mamillary bodies were seen in 1 patient. We could not explain these data; we could only observe that thiamine-related deficiency from chronic alcohol abuse affected the mamillary bodies more frequently by swelling of the intracellular space and local disruption of the blood-brain barrier, compared with the patients with no alcohol abuse. In 1 patient, we found a sole alteration: contrast enhancement in the mamillary bodies, which confirmed a unique case report described previously in the English-language literature. A T2-weighted normal signal intensity associated with contrast enhancement in the mamillary bodies has also been described in a pediatric patient affected by WE, which also showed lesions of the periaqueductal gray matter and medial thalamus.

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We found MR findings atypical for WE in 2 nonalcoholic patients in which the dorsal medulla was involved at the level of the prepositus hypoglossal nuclei. Furthermore, symmetric hyperintense lesions of the cerebellum were seen in 1 patient. Similar atypical findings have been described by Bae et al., which confirmed that symmetric selective alterations of the cranial nerve nuclei and cerebellum may be seen in Wernicke encephalopathy.

Conclusion
Our study confirms that the classic neurologic triad of WE occurs in a minor part of affected patients. Thus, clinicians should suspect the diagnosis of WE, especially if changes in consciousness are present not only in alcohol abusers but also in patients with malnutrition or malabsorption, particularly if the malnutrition is the result of malignant tumors of the gastrointestinal tract and prolonged vomiting. Brain MR imaging should be included in the diagnostic flow chart of any malnourished patient with sudden onset of changes in consciousness, ocular abnormalities, and ataxia even if the symptoms are isolated. In patients with a history of alcohol abuse, contrast media should always be administered to identify lesions typical for the disease at the level of the mamillary bodies, even in the presence of normal unenhanced MR images.

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References
1. Harper CG, Giles M, Finlay-Jones R. Clinical signs in the Wernicke-Korsakoff complex: a retrospective analysis of 131 cases diagnosed at necropsy. J Neurol Neurosurg Psychiatry 1986;49:341–45
2. Ogershok PR, Rahman A, Nester S, et al. Wernicke encephalopathy in nonalcoholic patients. Am J Med Sci 2002;323:107–11
3. Gallucci M, Bozzo A, Splendiani A, et al. Wernicke encephalopathy: MR findings in five patients. AJNR Am J Neuroradiol 1990;11:887–92
4. Victor M. The Wernicke-Korsakoff syndrome. In: Vinken PJ, Bruyn GW, eds. Handbook of Clinical Neurology, Vol 28. Amsterdam: North Holland; 1976:243–70
5. Harper CG, Butterworth R. Nutritional and metabolic disorders. In: Graham DJ, Lantos PL, eds. Greenfield’s Neuropathology, vol 1, 6th ed. London: Hodder Arnold; 1997:601–52
6. Schnorr G, Wichmann W, Valavanis A. Blood-brain-barrier disruption in acute Wernicke encephalopathy: MR findings. J Comput Assist Tomogr 1991;15:1059–61
7. Harper CG. Sudden, unexpected death and Wernicke’s encephalopathy: a complication of prolonged intravenous feeding. Aust NZ J Med 1980;10:230–35
8. Frantzen E. Wernicke’s encephalopathy. 3 cases occurring in connection with severe malnutrition. Acta Neurol Scand 1966;42:426–41
9. Parkin AJ, Blunden J, Rees JE, et al. Wernicke-Korsakoff syndrome of nonalcoholic origin. Brain Cogn 1991;15:659–82
10. Cirignotta F, Manconi M, Mondini S, et al. Wernicke-Korsakoff encephalopathy and polyneuropathy after gastroplasty for morbid obesity: report of a case. Arch Neurol 2000;57:1536–59
11. Dostouzany PM, Massey EW, Enright K, et al. Wernicke-Korsakoff syndrome caused by psychogenic food refusal: MR findings. AJNR Am J Neuroradiol 1994;15:594–96
12. Gárdian G, Voroș E, Jardanhazy T, et al. Wernicke’s encephalopathy induced by hyperemesis gravidarum. Acta Neurol Scand 1999;99:154–98
13. Ohkoshi N, Ishii A, Shoji S. Wernicke’s encephalopathy induced by hyperemesis gravidarum, associated with bilateral candidate lesions on computed tomography and magnetic resonance imaging. Eur Neurol 1994;34:177–80
14. Donnal JF, Heinz ER, Burger PC. MR of reversible thalamic lesions in Wernicke syndrome. AJNR Am J Neuroradiol 1990;11:893–94; discussion 895–96
15. Percheron G. The anatomy of the arterial supply of the human thalamus and its use for the interpretation of the thalamic vascular pathology. J Neurol 1972;205:1–13
16. Mathieu MG, Castillo M. Imaging of acute bilateral paramedian thalamic and mesencephalic infarcts. AJNR Am J Neuroradiol 2003;24:2005–08
17. Forsting M, Krieger D, Seiferth U, et al. Reversible bilateral thalamic lesions caused by primary internal cerebral vein thrombosis: a case report. J Neurol 1989;236:484–86
18. Nagai T, Yagishita A, Tsuchiya Y, et al. Symmetrical thalamic lesions on CT in influenza A virus infection presenting with or without Reye syndrome. Brain Dev 1993;15:87–73
19. Neumann C, Colombani JM. Primary acute disseminated encephalomyelitis in the adult. Study of 6 year follow-up of two patients. Presse Med 2002;31:1739–45
20. Brechtelsbauer DL, Urbach H, Sommer T, et al. Cytomegalovirus encephalitis and primary cerebral lymphoma mimicking Wernicke’s encephalopathy. Neuroradiology 1997;39:19–22
21. Zeidler M, Sellar RJ, Collie DA, et al. The pulvinar sign on magnetic resonance imaging in variant Creutzfeldt-Jakob disease [published erratum appears in Lancet 2000;356:170. Colchester AF is corrected to Colchester AC], Lancet 2000; 355:1412–18
22. Rosas H, Wippold FJ 2nd. West Nile virus: case report with MR imaging findings. AJNR Am J Neuroradiol 2003;24:1376–78
23. Petropoulou KA, Gordon SM, Prayson RA, et al. West Nile virus meningoencephalitis: MR imaging findings. AJNR Am J Neuroradiol 2005;26:885–95
24. Ali M, Safriy S, Sobi J, et al. West Nile virus infection: MR imaging findings in the nervous system. AJNR Am J Neuroradiol 2005;26:2889–97
25. Shogry ME, Curnes JT. Mamillary body enhancement on MR as the only sign of acute Wernicke encephalopathy. AJNR Am J Neuroradiol 1994;15:172–74
26. Harter SB, Noker SR. Gadolinium-enhanced MR findings in a pediatric case of Wernicke encephalopathy AJNR Am J Neuroradiol 1995;16:700–02
27. Asato R, Okomura R, Konishi J. “Fogging effect” in MR of cerebral infarct. J Comput Assist Tomogr 1991;15:160–62
28. Sze G, Milanelo E, Johnson C, et al. Detection of brain metastases: comparison of contrast-enhanced MR with unenhanced MR and enhanced CT. AJNR Am J Neuroradiol 1990;11:1785–91
29. Bae SJ, Lee HK, Lee JH, et al. Wernicke’s encephalopathy: atypical manifestation at MR imaging. AJNR Am J Neuroradiol 2001;22:1480–82

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