PICTORIAL REVIEW

Non-alcoholic Wernicke's encephalopathy: broadening the clinicoradiological spectrum

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ABSTRACT. Wernicke's encephalopathy (WE) is a serious neurological disorder secondary to thiamine deficiency. Improved recognition by radiologists and allied health providers of the different clinical settings and imaging findings associated with this emergency can optimise the management of this condition and help prevent its severe consequences. The aim of this study is to illustrate the broad clinicoradiological spectrum of non-alcoholic WE, while emphasising atypical MRI findings.

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Wernicke's encephalopathy (WE) is a medical emergency clinically characterised by sudden onset of ataxia, changes in consciousness and abnormal eye movements. However, the classic clinical triad is present in only a minority of patients [1–4], making early clinical diagnosis challenging. A high level of suspicion and awareness of the various typical and atypical MRI findings are essential for early accurate diagnosis and prompt treatment.

The purpose of this article is to highlight the variety of clinical settings in which non-alcoholic WE may ensue and to illustrate the broad spectrum of MR findings, focusing on atypical findings.

Pathogenesis and clinical issues

WE is caused by a deficiency in thiamine (vitamin B1), a water-soluble compound essential for carbohydrate metabolism. However, the disease may not manifest in all patients with thiamine deficiency because genetic susceptibility may be involved in some patients who develop the disorder [5]. Moreover, blood serum levels of thiamine may not be reduced at the time of clinical onset [3], and replacement of the vitamin does not always fully reverse the clinical picture, limiting the value of a therapeutic test under certain circumstances.

The classic clinical triad is present in only a subset of patients [1–4]. Clinical presentation is usually subtle especially in non-alcoholic patients and in those with

deep coma whose neurological evaluation is often limited. Non-alcoholic WE manifests in many different clinical settings, such as gastrointestinal tumours, hyperemesis gravidarum, chemotherapy, acquired immunodeficiency syndrome, prolonged therapeutic fasting, prolonged parenteral nutrition and bariatric surgery, anorexia nervosa and can even be secondary to socioeconomic factors [1–9].

Atypical MRI findings appear to be more prevalent in non-alcoholic WE [4].

Imaging features

MR abnormalities in WE patients are classically reported in the literature as bilateral and symmetrical lesions around the third ventricle, in the dorsomedial portions of the thalami and the periaqueductal region of the mid-brain, characterised by high signal intensity on T_2 weighted sequences (Figure 1).

Mamillary bodies are frequently involved in WE, but this finding is sometimes not clearly evident in all sequences, with mamillary bodies often unremarkable on T_1 and T_2 weighted images. Contrast-enhanced images, on the other hand, may disclose breakdown of the blood–brain barrier only in the mamillary bodies and sometimes their involvement is more conspicuous on such enhanced images (Figure 2). Coexistence of typical abnormalities involving other structures can also be helpful in these settings. In a few cases reported in the literature, contrast enhancement of the mamillary bodies was the sole MR finding of the disease [2, 4].

Follow-up examinations may show reversal of mamillary body enhancement, although in one of our cases these structures evolved with a clear T_2^* hypointense

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Figure 1. Male patient, 63 years old, with persistent vomiting, presented ocular disturbances and vertigo after surgery for gastric adenocarcinoma. Coronal fluid-attenuated inversion recovery images show bilateral and symmetrical hyperintense lesions bordering the third ventricle in the dorsomedial thalami and the periaqueductal region (arrows).

Figure 2. 37-year-old female patient with total colectomy due to ulcerative rectocolitis presented severe pancreatitis and vomiting and manifested vertical and horizontal nystagmus 1 week after surgery. T_1 and T_2 fast spin-echo (FSE) images disclose no abnormalities in the mammillary bodies (not shown), while sagittal enhanced T_1 weighted image shows conspicuous enhancement of the mammillary bodies (arrow).

signal assigned to haemosiderin deposition (Figure 3). Considering that imaging findings of WE reflect the underlying disease pathology, T_2^* hypointensity in the mammillary bodies is a congruent finding. We assumed this finding to be the result of haemosiderin deposition, since petechial haemorrhages in pathological samples, associated with variable degrees of necrosis, vascular proliferation, astroglial and microglial proliferation, have been described [6, 9]. To our knowledge it is the first time that this finding is unequivocally demonstrated in the radiological literature.

Besides the more frequently reported structures involved in WE, there are many other less typically affected locations that can show abnormal signal intensity on MRI and help towards confirming this diagnosis. Such structures include the caudate nucleus (Figures 4 and 5), perirolandic cortex (Figures 5 and 6) and posterior putamina (Figure 6). Cranial nerve nuclei may also be involved, such as hypoglossal, medial vestibular, facial and abducens nuclei (Figure 7) [1, 2, 4].

This broad spectrum of presentation is very illustrative of WE, but infrequent and only recently described in the literature. Fei et al [1] reviewed 12 cases and found no putaminal abnormalities in any of them. Similarly, a review of 26 patients reported no signs of basal ganglia or cortical involvement [2, 4].

The presence of cortical damage seems to be indicative of poor prognosis and related to deep coma [1, 9]. This finding, although infrequently reported, must therefore

be promptly recognised by radiologists, as it may have significant prognostic implications (Figures 5 and 6).

Restricted diffusion, characterised by high signal on diffusion-weighted imaging (DWI) and low signal on apparent diffusion coefficient (ADC) maps, can occasionally be visible in some structures (Figures 5 and 8). One possible explanation for this finding is that thiamine plays an important role in maintaining osmotic gradients across cell membranes and in energetic metabolism, acting as a cofactor in both the Krebs and the pentose phosphate cycle. Early histopathological findings of thiamine deficiency consist of coexisting intracellular and extracellular oedema, with pathological characteristics similar to those found in hypoxic ischaemic insults [6–8]. Moreover, we can assume that areas with low signal on ADC maps represent cytotoxic oedema, and those with high signal on DWI but without low signal on ADC maps are related to vasogenic oedema, according to reports in the literature [7].

DWI findings in a given patient may be partially related to timing of MR with regard to the initial insult, in as far as early imaging may not disclose signal intensity alterations but change over time to true restricted diffusion, and subsequently to vasogenic oedema (T_2 shine-through effect). Distinct diffusion characteristics can sometimes be seen in several different structures simultaneously (Figure 8).

Blood–brain barrier disruption, characterised by anomalous enhancement, can be visible in the periaqueductal region, dorsal portion of the brainstem, cortex (Figure 9) and also in the mammillary bodies as described earlier (Figures 2 and 3). However, contrast behaviour of the lesions has been found to be highly variable in WE.

Finally, care must be taken to maintain optimal slice thickness and spacing. Given that target structures are often small, thinner slices may sometimes be necessary.

Conclusions

This review highlights the broad range of MR findings associated with WE. Greater awareness and recognition of this condition leads to early diagnosis and prompt treatment, thereby increasing the chances of full reversal of the clinical picture.

T_2 weighted, fluid-attenuated inversion recovery and DWI are the most useful MRI sequences for detecting WE. Many different anatomical structures besides the thalami, periaqueductal region and mammillary bodies may be bilaterally and symmetrically affected, such as the cranial nerve nuclei, basal ganglia and perirolandic cortex.

Contrast enhancement may also occur and is often observed in the mammillary bodies. Haemosiderin deposition can later become appreciated as T_2^* hypointensity, as originally demonstrated in the mammillary bodies in one of our cases.

Figure 3. Male patient, 17 years old, with a history of bone marrow aplasia and repeated infections, evolved with persistent vomiting for 2 months and acute onset of mental confusion. The first examination shows no abnormalities on the axial T_2^* image (a), but the axial enhanced T_1 weighted image (b) shows enhancement of the mamillary bodies (arrows). Follow-up examination was performed after 1 month: the axial T_2^* image (c) now clearly demonstrates hypointensity in the mamillary bodies (arrows), assigned to haemosiderin deposition, whereas the corresponding axial enhanced T_1 image (d) demonstrates reversal of mamillary body enhancement.

Figure 4. 27-year-old female patient with a history of depression and anorexia nervosa. She developed acutely altered mental status; MR examination was performed after 3 days. High signal intensity was noted at the caudate nuclei (arrowheads) on axial fluid-attenuated inversion recovery (a) and axial T_2 weighted images (b).

Figure 5. Same patient as Figure 4. Axial DWI (a, b) and corresponding apparent diffusion coefficient maps (c, d) show bilateral and symmetrical restricted diffusion in caudate nuclei and perirolandic cortex 3 days after onset of clinical picture.

Figure 6. Female patient, 52 years old, after surgery for rectal adenocarcinoma, submitted to chemotherapy and on total parenteral nutrition, presented acutely with vertigo, abnormal eye movements and altered consciousness. Axial fluid-attenuated inversion recovery images (a, b) show symmetrical hyperintensity in the posterior putamina (arrows in a), dorsomedial thalami (arrowheads in a) and perirolandic cortex (arrows in b).

(a)

(b)

(c)

(d)

Figure 7. Same patient as in Figure 6. Axial fluid-attenuated inversion recovery images (a–d) show symmetrical hyperintensities involving the prepositus hypoglossal nuclei (arrows in a), medial vestibular nuclei (arrows in b), facial nuclei (arrows in c), abducens nuclei (arrowheads in c), mid-brain tectum and periaqueductal grey matter (arrows in d).

Figure 8. Same patient as in Figure 6. DWI obtained 2 days after the first symptoms failed to disclose any abnormalities (not shown). Follow-up DWI (a) and corresponding apparent diffusion coefficient map (b) obtained 7 days after clinical onset show true restricted diffusion in the putamina (arrows), attributed to cytotoxic oedema, where the high signal observed in the dorsomedial thalami (asterisks) is not accompanied by low signal on ADC map (possibly due to vasogenic oedema).

Figure 9. Same patient as in Figure 6. Axial T_1 post-contrast images disclose enhancement in the periaqueductal region (thin arrow), tectal plate (large arrow) and perirolandic cortex (arrowheads).

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