

WERNICKE'S ENCEPHALOPATHY IN GENERAL NEUROLOGICAL PRACTICE: SHORT CONSIDERATIONS ON THE NEED FOR REVISION (I)

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Wernicke's encephalopathy (WE) is associated with thiamine (vitamin B1) deficiency and has classically been described as acute onset of nystagmus, ophthalmoplegia, ataxia and global confusion, usually occurring together. Much progress has been done in the past years in completing the WE characteristics and patterns of occurrence, however several issues are not cleared, and further work is needed. The main issue remains the recognition of the patient at risk for developing WE. The present article aims to note some of the characteristic but less retained features of WE, as new data in the MRI era. Hereby, some false 'myths' concerning WE as the omnipresence of the acute onset or of the clinical constellation must be corrected, and this can have important implications in the management of WE patients.

1. WE AS SOLELY AN 'ACUTE' CONDITION

For the general neurologist, it is important to emphasize that WE can be prevented and treated successfully before the onset of irreversible brain damage. Considered initially as an acute disorder, it is thought that patients can suffer recurrent episodes of WE, some of which might be subclinical, leading to a more chronic form of the disease. Not so rare, some of these patients develop a severe amne-

sic syndrome (Korsakoff's). Harper's and other autopsy studies have shown that the diagnosis of WE and KP is not made during life in 80% of the cases (!). This work demonstrated that the diagnosis is only made clinically in about 1-20% of cases prior to autopsy. This means that it is virtually impossible to establish accurate prevalence rates of WE in various populations without significant numbers of autopsies. However, review of the clinical findings in cases of WE that have been diagnosed at autopsy show a consistent pattern of signs and symptoms. The patterns appear to be similar regardless of whether the thiamine deficiency is related to nutritional problems alone or associated with alcohol misuse.

2. THE 'TRIAD' AS SOLELY CLINICAL APPEARANCE OF WE

Based on the original description by Wernicke (1881), the triad consists of an abrupt onset of a confusional state, impairment of consciousness, ataxia and eye signs (nystagmus and ophthalmoplegia). However, as Wernicke himself described in initial cases, other important clinical signs and symptoms are often present before the later 'classical' signs who, in turn, may not always be as prominent and striking as generally believed. Stupor and

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coma have been said to be rare in WE, but they can develop rapidly and can associate with severe outcome. Also, some stated that mild, moderate and severe phases of WE have distinctive signs, who can be reversed in approximately the same chronological order following treatment: mild WE is characterized by anorexia, nausea, vomiting and eye signs; moderate WE by emotional changes and memory loss, while the severe WE by confusion, confabulation and coma. Neurologists have come to rely too much on the 'classic triad' of signs for diagnosing WE which occurs only in 10% of patients, although it has been known for many years that other indications suggest that the patient is at risk.

3. THE PATIENT AT RISK: TO BE RECOGNIZED BEFORE OR DURING WE

The responsibility of the clinician is to identify patients at risk of WE as early as possible and to institute effective prophylactic therapy, since approximately 10% of them die in the acute phase and between 56–86% may develop Korsakoff's when given no or inadequate parenteral thiamine.

In 1997, Caine et al. developed operational criteria to differentiate between WE alone or in combination with Korsakoff's psychosis or hepatic encephalopathy. The WE criteria included two of the following signs: dietary deficiency; oculomotor abnormalities; cerebellar dysfunction; either altered mental state or mild memory impairment. The authors showed that using these operational criteria, an antemortem identification of WE with a high degree of specificity can be obtained, but this can be achieved accurately only in the absence of hepatic encephalopathy.

In practice, the early prodromal symptoms of thiamine deficiency have to be taken in conjunction with other predisposing factors to WE, in order to identify patients who need parenteral thiamine prophylaxis. Factors predisposing to thiamine deficiency are weight loss in past year, reduced BMI (Body Mass Index), high carbohydrate intake in the settings of poor nutritional status, recurrent vomiting in the past month, co-occurrence of other nutritionally related conditions (polyneuropathy, amblyopia, pellagra, anaemia). In alcoholics, factors predisposing to neurotoxicity are the genetic predisposition to alcohol dependence, amount and frequency of alcohol use and severity of dependence, frequent episodes of acute intoxication, withdrawal syndromes, alcohol-related liver damage. The cli-

nician must be aware of early signs-symptoms of thiamine deficiency, as loss of appetite, nausea/vomiting, fatigue, apathy, giddiness, diplopia, insomnia, anxiety, difficulty in concentration, loss of memory.

It is important to note that always the unbalanced diet is a main setting and predisposing factor for WE occurrence. This explains also why WE occur not only in alcoholics.

Radiology can not offer a solution to find patients at risk, but in 2005 Guerrini et al. have identified an abnormal gene present in some patients with WE which is involved in thiamine transport and perhaps may offer the basis of a diagnostic test in the future.

The extent to which the early signs of thiamine deficiency reflect biochemical changes in the body, and when they begin to affect the human brain, remain speculative. Langlais and Zhang have shown in rat that a single episode of thiamine deficiency can selectively damage cortical white matter tracts, while at the same time sparing the thalamus or mammillary bodies, and may be responsible for the behavioral changes observed in alcoholic patients without WE.

4. WE IN ALCOHOLICS: PARTICULARITIES OF MANAGEMENT

Although much has been learnt about WE natural history and pathophysiology, early diagnosis still depends upon clinical judgment and experience. The combination of thiamine deficiency and alcohol misuse is a common association, some studies giving a 90% incidence of alcohol misuse in WE patients. It is important to identify this association with alcohol because it appears to increase significantly the amount of thiamine required to treat the patient successfully compared to individuals with a predominantly nutritional thiamine deficiency. It is also necessary, when alcohol misuse is involved, to give the thiamine parenterally because of alcohol-related malabsorption of thiamine across the intestinal mucosa. It is not known if brain thiamine transport systems are similarly affected, even so some suggested. Also, alcohol neurotoxicity can interfere with the effective utilization of thiamine, so preventing the amnesic aspects of WE and Korsakoff's requires prophylactic thiamine replacement together with stopping of alcohol intake at the earliest possible time.

As new techniques of neuro-imaging are developed and resolution increases, anatomical structures

like the mammillary bodies can now be visualized, thus aiding the clinical diagnosis of WE. Also, it must be emphasized that WE can occur frequently in non-alcoholics, thus being under diagnosed. Finally, the lack of studies on the duration, mode of administration and pharmaceutical form of thiamine to be used in WE treatment or prophylaxis

must also be recalled. The imagistic aspects of WE in alcoholic and non-alcoholic populations, as the clinical and paraclinical features of the non-alcoholic WE and the practical issues regarding treatment will be discussed in the second part of this short review.

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