

Case report

Wernicke's encephalopathy due to hyperemesis gravidarum . . . and fetal stroke: What relationship?

Damien Biotti^{a,*}, Guy-Victor Osseby^{a,1}, Christine Durand^b, Bernard Lorcerie^c,
Stephanie Couvreur^d, Thibault Moreau^{a,1}, Maurice Giroud^{a,1}

^a Neurology Department, General Hospital, University Hospital, 21000 Dijon, France

^b Radiology Department, General Hospital, University Hospital, 21000 Dijon, France

^c Internal Medicine Department, General Hospital, University Hospital, 21000 Dijon, France

^d Obstetrical Department, University Hospital, 21000 Dijon, France

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1. Introduction

Wernicke's encephalopathy is a form of encephalopathy resulting from thiamine (vitamin B1) deficiency. It is a classical evolution, but fortunately, today, it occurs rarely in a context of hyperemesis gravidarum. When it does occur, however, there is a high risk of complications for the fetus. We report here the case of a patient who presented this syndrome, and whose fetus suffered ischemic stroke. We discuss the characteristics of this syndrome in the context of pregnancy and the associations between maternal and fetal disorders.

2. Case report

The patient was a 30-year-old woman in the 19th week of her second pregnancy. She was referred to our neurology department for a confusional syndrome with cerebellar ataxia and nystagmus that had lasted 72 h. The patient had a medical history of deep venous thrombosis complicated by pulmonary embolism in 2001 and again in 2003 during her first pregnancy. None of the examina-

tions for thrombophilia were abnormal. During the first pregnancy, the patient had already suffered from uncontrollable vomiting for the first 16 weeks, which led to a weight loss of 15 kg; she also suffered from hyperthyroidism treated with propylthiouracil.

The vomiting in the present case started when the pregnancy was discovered. It was incapacitating, did not respond to symptomatic treatment and, as a result, the patient was hospitalized several times for short periods. The patient was finally provided with medical care at home. Because of the vomiting and the patient's refusal to have a naso-gastric tube, she was rehydrated intravenously with a fluid containing glucose but not enriched with vitamins.

Five days before her admission the patient developed confusional syndrome and cerebellar ataxia diagnosed by the patient's G.P., who immediately transferred her to the neurology department. The patient was afebrile, presented temporospatial disorientation with incoherent speech. Because of severe cerebellar ataxia, the patient was unable to stand. We noticed multidirectional nystagmus. The rest of the clinical examination was normal. Wernicke's encephalopathy was suspected and the patient was treated intravenously with 1 g/d of vitamin B1.

The diagnosis was quickly confirmed by the extremely low levels of vitamin B1: erythrocyte transketolase activity was 1.35 (normal range 1.00–1.09), the thiamine pyrophosphate effect was 30 (normal range 80–165 ng/mL), and by brain MRI which revealed

* Corresponding author. Tel.: +33 380293753; fax: +33 3 80 29 36 72.

E-mail address: dbiotti@hotmail.com (D. Biotti).

¹ Tel.: +33 633785331.

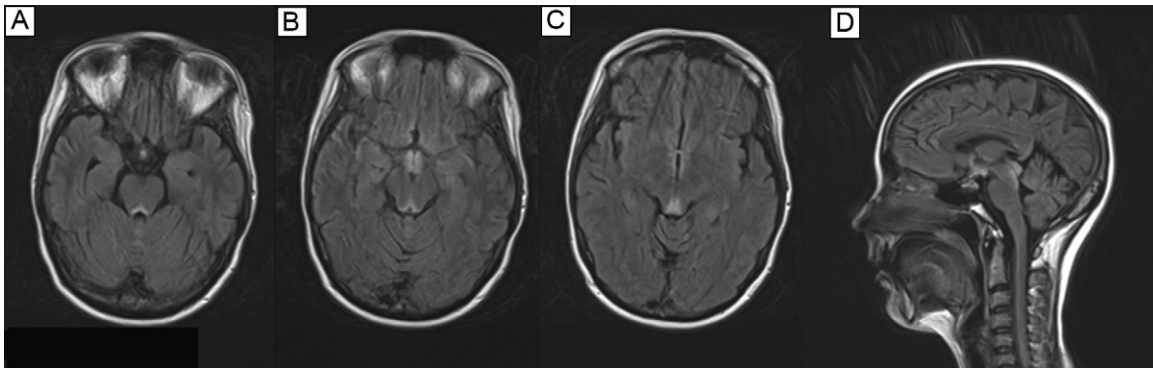


Fig. 1. Axial (A, B and C) and sagittal (D) FLAIR T2-weighted images of the brain revealing abnormal mammillary bodies and periaqueductal grey matter hyperintensities.

hyperintensity in FLAIR/T2-Weighted images of the mammillary bodies and the periaqueductal grey matter, which is strongly associated with this syndrome (Fig. 1). For other vitamins, analysis showed deficiencies in vitamins B6, D and K. Analysis of thyroid function showed hyperthyroidism with low levels of TSH (0.020 mIU/L (0.360–3.740 mIU/L)) and an increase in T4 hormone (24.5 pmol/L (9.8–18.8 pmol/L)). Levels of thyroid peroxidase, thyroglobulin and TSH-receptor antibodies were insignificant.

MRI of the fetal brain performed as soon as the patient had been admitted revealed infarction of the right cerebral hemisphere and a large edema suggesting a recent stroke which compressed the foramina of Monro causing secondary porencephaly under pressure (Fig. 2). Fetal ultrasonography confirmed these findings with structures deviated from the midline. The biological examination was negative for infection, inflammation and thrombophilia (platelets, fibrinogen, homocysteine, antithrombin III, proteins C and S, activated protein C resistance, factor V Leiden, prothrombin mutation, lupus anticoagulants, anticardiolipin antibody and anti β 2 glycoprotein 1 antibody).

After several days of treatment, the cerebellar ataxia and the nystagmus improved, but the patient's condition evolved towards Korsakoff syndrome. The pregnancy had to be terminated and pathological examination of the fetus confirmed that the stroke was ischemic induced by occlusion of the homolateral carotid artery and affected the whole of the right hemisphere. Several areas of hemorrhagic transformation were also seen.

3. Discussion

Wernicke's encephalopathy is a classical, but fortunately rare complication of hyperemesis gravidarum. The condition is far more frequent in alcoholism-related deficiency. The association of this

syndrome with concomitant fetal stroke as found in our patient is exceptional.

Wernicke's encephalopathy is a neurological and metabolic consequence of thiamine (vitamin B1) deficiency. Its prevalence is difficult to evaluate as it is probably underdiagnosed. Nevertheless, Harper et al. [1] estimated a prevalence between 0.4 and 1.4% in France. The classical clinical triad is an association of cerebellar ataxia, oculomotor disturbances, especially nystagmus, and confusional syndrome. This triad is classical, but not always present and may be completely absent. Wernicke's encephalopathy has been reported in up to 20% of cases in autopsy series, which shows that in a high proportion of cases, the disease was not diagnosed when the patient was alive [2]. Brain MRI is the complementary examination of choice and reveals symmetrical bilateral hyperintensity on T2-Weighted images of the mammillary bodies, the thalamus, the periventricular region of V3 and V4 and the periaqueductal grey matter.

The stock of thiamine in the body will last for a maximum of 2–3 weeks, which explains the rapid and unexpected onset of this syndrome in predisposing conditions, in particular in cases of chronic alcoholism, insufficient intake, impaired absorption or hypermetabolism [2]. Without treatment the syndrome results in the death of the patient in 17% of cases or frequently leads to Korsakoff syndrome [2]. Early diagnosis and the emergency implementation of treatment with parenteral vitamin B1 are therefore essential.

Vomiting and nausea, related to Human Chorionic Gonadotropin (hCG) levels, are very frequent in the early weeks of pregnancy. Hyperemesis gravidarum occurs in 0.3–1% of pregnancies [3] and is the pathological form of the condition with severe, long-lasting and uncontrollable vomiting, which often requires periods of hospitalization. It is also the cause of many complications principally metabolic in nature. This pathology most often appears at the

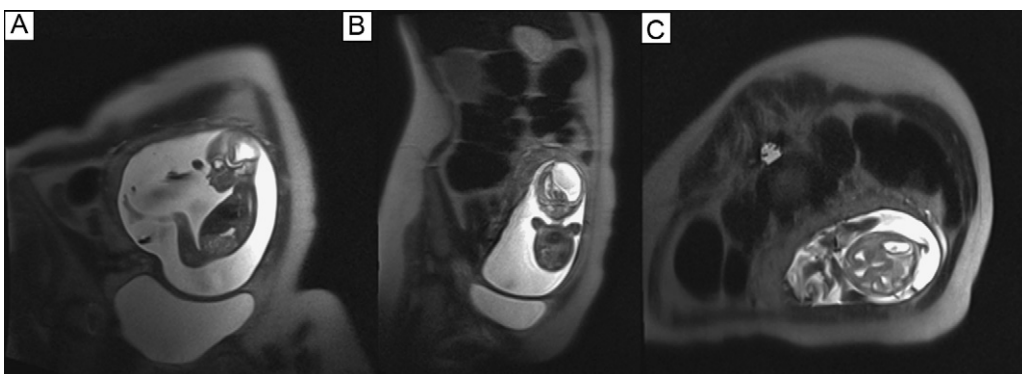


Fig. 2. T2-weighted images of the fetus. In the brain we observed an aspect of large porencephaly under pressure; the maximum ventricular dilatation measured 31 mm. The right hemispheric structures had almost completely disappeared with a mass effect and deviation of the midline structures to the left.

beginning of the pregnancy and is frequently associated with a history of psychiatric, digestive or endocrine disorders; recurrence during the second pregnancy is seen in around 15% of cases. Hyperemesis gravidarum is associated with considerable morbi-mortality; Wernicke's encephalopathy is the principal complication in motherhood and responsible for up to 50% of fetal deaths via direct or indirect mechanisms [4]. Fetal loss could even be the first sign of Wernicke's encephalopathy. Chiossi et al. [4] showed that on average Wernicke's encephalopathy occurred after 7 weeks of vomiting and in around the 14th week of pregnancy. Moreover, pregnancy is a high-risk period for thiamine deficiency because of the hypermetabolism induced by the pregnancy and because of the risk of vomiting and digestive disturbances that may increase vitamin losses and reduce intake. Hypermetabolism due to physiological pregnancy-related hyperthyroidism may also evolve towards another risk factor, true thyrotoxicosis. Certain series of hyperemesis gravidarum report up to 2/3 of patients with associated hyperthyroidism, as was the case in our patient [5]. Apart from cases of auto-immune hyperthyroidism, which may also be seen, the most frequently reported mechanism able to explain hyperthyroidism is a cross-reaction between hCG and thyrotropin, which induces stimulation of the thyroid gland [3].

The second point of interest is the possible consequence of maternal Wernicke's encephalopathy on the fetal brain. No data are available in the literature. We know that high fetal mortality is described but there are no specific explanations on the possible increased risk of hemorrhagic or ischemic fetal stroke. In our case, we found right hemisphere infarction on the fetal brain MRI. It is tempting to try to establish a link between the mother's condition and that of the fetus. Indeed, even though it was difficult to date the stroke, the fact the patient could no longer feel her baby moving could suggest that the stroke had occurred shortly before.

Finally, the management of hyperemesis gravidarum is essential. A recent review of the literature [3] underlined the interest of

dietary hygiene, such as modifications in diet (certain foods may trigger vomiting), in the mildest forms of the disease or the use of relaxation techniques. Nevertheless, in the more severe cases more stringent measures including hospitalization may be required. Oral and sometimes parenteral nutrition and rehydration are necessary to improve the clinical status of the mother and fetus, in which case glucose solutions should be avoided as they may trigger the onset of Wernicke's encephalopathy. Finally, antiemetics may be used as they are effective, safe and are associated with reduced fetal morbidity.

Suspected Wernicke's encephalopathy is a medical emergency. Oral supplementation is no longer indicated and the intravenous or intramuscular route must be used. There is no consensus regarding the duration of treatment or the recommended daily dose [2].

4. Conclusion

We report the case of a patient with Wernicke's encephalopathy in the context of hyperemesis gravidarum in whom imaging unexpectedly revealed concomitant fetal stroke thus raising the possibility of a relationship between these two cerebral diseases.

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