WERNICKES ENCEPHALOPATHY ASSOCIATED WITH HYPEREMESIS GRAVIDARUM

Krishnan Balagopal†,1, Sangeetha Vincent Thandiakkal**, Neetu Kurian** and Johnson Georgekutty†
†Department of Neurology, MOSC Medical College, Kolenchery, Kochi, Kerala state, India., **Department of Psychiatry, MOSC Medical College, Kolenchery, Kochi, Kerala state, India.

ABSTRACT Wernicke Encephalopathy is a neurological pathology caused by Thiamine deficiency, which usually manifests with ataxia, confusion and ophthalmoparesis. The most common cause is alcohol, but other conditions such as hyperemesis gravidarum have been described. Here, we report the case of a twenty-two-year-old Indian pregnant woman who presented to our department with Hyperemesis Gravidarum complicated with Wernicke Encephalopathy and also hyperthyroidism. She was started on Thiamine replacement, following which her symptoms improved. We discuss the typical imaging findings, clinical presentation, and treatment in such cases.

KEYWORDS Hyperemesis Gravidarum, Pregnancy, Wernicke Encephalopathy, Hyperthyroidism, Ataxia

Introduction

Wernicke’s encephalopathy (WE) is an acute neurological emergency caused due to Thiamine deficiency. It was initially described by Carl Wernicke in 1881. His initial description named the condition as polioencephalitis hemorrhagica superioris. The salient clinical features of this condition included the symptoms of ataxia, confusion and ophthalmoplegia. This was later elaborated as the syndrome of polyneuritic psychosis by Korsakoff in the year 1887. Wernicke’s encephalopathy is a common but frequently misdiagnosed syndrome due to the varying clinical presentation[1]. The classic triad of WE includes the symptoms of global confusion, oculomotor movement abnormalities and ataxic gait. The presence of one or two of the major three manifestations in the appropriate clinical setting goes in favour of the diagnosis of WE. The incidence of WE is variable and can lie between 0.2% and 2.8% of the general population worldwide. Most of the patients with WE are associated with a history of chronic alcoholism. Other causes include malnutrition, systemic malignancy, hemodialysis, and hyperemesis gravidarum, which are less commonly described[2]. We are presenting a case of a pregnant woman with HG who developed the classical clinical triad of WE along with typical imaging findings on the brain MRI.

Case report

We present a case of a 22-year-old pregnant female of 13 weeks gestational age who had been treated outside for the last one month with complaints of repeated episodes of nausea and vomiting. She had been diagnosed with Hyperemesis Gravidarum (HG) and treated with intravenous fluids, antiemetics and dextrose. She presented to the emergency with a 3 day history of altered sensorium, irrelevant talk and unsteadiness on walking. There was no history of headache or fever preceding. There was also no history of diplopia or dysarthria. She was evaluated in the emergency initially by the Psychiatry department and then transferred to the Neurology Department for further management. Clinical examination revealed patient conscious but drowsy and responding to verbal commands. Examination revealed a staring look with bilateral gaze-evoked nystagmus, dysarthria, severe gait ataxia and brisk lower limb reflexes. There was no sensory or bladder involvement. The possibility of a Wernicke’s Encephalopathy was considered given nystagmus, ataxia and altered sensorium in the setting of repeated vomiting associated with Hyperemesis Gravidarum.

Blood investigations showed elevated levels of transaminases -SGOT 175 U/L (14-36 Normal) and SGPT 305U/L (15-45 Normal).Thyroid hormone levels were deranged with ele-
Figure 1: MRI Brain T2/FLAIR sequences showing hyperintensity involving medial thalami bilaterally.

Figure 2: MRI Brain DWI/ADC sequences showing restricted diffusion in medial thalami.

Figure 3: MRI Brain FLAIR sequence showing hyperintensity involving dorsal medulla.

Figure 4: MRI Brain FLAIR sequences showing hyperintensity involving mamillary bodies bilaterally.

vated levels of T3- 1.79 ng/ml (0.97-1.68 Normal) and T4 - 24.9 (5.53-11 Normal) with reduced TSH less than 0.015 mIU/mL (0.5-5.5 Normal). Antithyroid antibodies were within normal limits. Imaging study -MRI Brain - showed bilateral symmetric T2 FLAIR hyperintensity involving the bilateral medial thalami, mamillary body, periaqueductal region and dorsal medulla – in keeping with Wernicke Encephalopathy (Figure 1,2,3,4). Restriction of diffusion was seen in the DWI sequences in the medial thalami. EEG done showed evidence of bihemispheric slowing. Serum levels of Thiamine Pyrophosphate (TPP) were sent, which were found to be low -12 micrograms/Litre (28-85 Normal range), thus confirming the diagnosis. She was started on intravenous Thiamine replacement at 600 mg per day initially. She was also started on Carbimazole for management of associated thyrotoxicosis. She had significant improvement in sensorium and ataxia within 48 hours of starting treatment. She was able to walk without support, and the sensorium improved. She was continued on oral Thiamine at 200 mg per day. At discharge, she was conscious, oriented and able to walk with no unsteadiness. There was an improvement both in cognitive functions and in gait. She is under follow up and a repeat MRI is planned after 3 months.

Discussion

HG is responsible for many cases of hospitalization during the early months of pregnancy. The mechanism of the disease and causes are still unclear [3]. HG is a diagnosis made only when all other potential causes have been excluded. Due to episodes of repeated vomiting, these patients have evidence of electrolyte abnormalities, elevation of liver enzymes, dehydration and occasionally mental status changes. The repeated vomiting and poor feeding during HG cause both water and fat-soluble vitamin deficiency, including Thiamine, Riboflavin and Vitamin K deficiency [4]. Thiamine is a water-soluble vitamin that is absorbed all through the small intestine and also in the upper jejunum. Thiamine acts as a cofactor for many enzymes in the body. These include transketolase, alpha-ketoglutarate dehydrogenase, and pyruvate dehydrogenase, all of which play a major role in carbohydrate metabolism. During HG, there occurs a significant reduction in the Thiamine reserves, and the absorption of Thiamine is also affected due to vomiting and poor oral intake. Wernicke Korsakoff syndrome arises due to thiamine deficiency. It is common among alcohol abusers, but it also appears in cases of malnutrition, malignant tumour, gastrointestinal dysfunction, pregnancy, and hyperthyroidism, and in patients who undergo hemodialysis. WE following hyperemesis gravidarum usually occurs at 14 - 16 weeks of gestation, following more than three weeks of vomiting. Administration of Thiamine 100 mg of intravenous or intramuscular thiamine in HG patients with persistent or severe vomiting can be done to prevent them from developing WE [5]. The WE diagnosis is based on the timely recognition of the clinical manifestations and rapid reversal of symptoms with thiamine treatment. Deter-
ministration of blood transketolase activity and thiamine pyrophosphate(TPP) is a fairly accurate reflection of the thiamine status in the body. Thiamine pyrophosphate is a coenzyme that is found predominantly in the brain. It is an important cofactor for enzymes involved in the pentose phosphate pathway and other vital pathways. The deficiency of thiamine affects energy metabolism, especially in tissues with high thiamine turnover, such as neural cells. This can result in widespread cell death from necrosis or apoptosis. TPP levels were found to be low in our patient, which further supported the diagnosis. Elevated liver enzymes are seen commonly in patients with WE, as was seen in our patient also. The thyroid derangement seen here could be a form of gestational hyperthyroidism, as has been described. Hyperemesis gravidarum prevalence ranges from 0.3–1% of all pregnancies. A significant proportion of affected women also manifest biochemical features of gestational hyperthyroidism. Beta HCG(Human Chorionic Gonadotropin) shares a common subunit with the glycoprotein pituitary hormone TSH. Because of this structural similarity, it can activate the TSH receptor when present at high levels. Gestational hyperthyroidism is, therefore, typically a transient phenomenon and tends to resolve as HCG levels fall in the second trimester [6]. The classic triad of WE is seen more commonly in patients with HG as compared to those with WE from other causes, including alcoholism. Altered sensorium and global confusion is the most common finding followed by ophthalmoplegia and gait ataxia. Patients with WE show a definite pattern of extensive damage in the subcortical regions of the brain. This includes the involvement of the thalamus, mammillary bodies, midbrain, and other brainstem structures. Reversible cytotoxic oedema is noted in the subcortical region and predominately seen in the T2/FLAIR and diffusion-weighted imaging (DWI) sequences [7]. Wernicke’s Encephalopathy is a medical emergency that can be potentially fatal but completely reversible. Mortality ranges from 10% to 20%, and many survivors are left with persistent neurologic deficits despite appropriate treatment. Whenever there is a clinical suspicion of Wernicke encephalopathy due to hyperemesis, intravenous Thiamine should be administered immediately. Guidelines by various bodies, including the European Federation of Neurological Societies (EFNS), postulate that thiamine should be given 200 mg thrice daily via intravenous route and started before any carbohydrate. Thiamine should be continued until there is no further improvement or change in signs and symptoms. If patients with Wernicke’s encephalopathy are diagnosed late and receive delayed treatment, it can be potentially fatal and cause several problems, including neurologic sequelae in the mother and preterm birth, intrauterine growth retardation in the fetus [8]. A very low threshold of suspicion and quick and timely intervention are keys to preventing significant neurological disability.

Conclusion

WE is one of the rare neurological complications seen in pregnancy complicated by Hyperemesis gravidarum, where a delay in diagnosis and treatment can be costly. Therefore, in pregnant women with frequent vomiting and any neurological changes, WE should be considered and promptly treated. Quick recognition and treatment is needed to prevent permanent neurological deficits.

Abbreviations

- WE-Wernicke’s Encephalopathy
- HG-Hyperemesis Gravidarum
- MRI-Magnetic Resonance Imaging
- DWI-Diffusion Weighted Imaging
- FLAIR-Fluid Attenuated Inversion Recovery
- EEG-Electroencephalogram
- HCG-Human Chorionic Gonadotropin
- TSH-Thyroid Stimulating Hormone

Funding

This work did not receive any grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of Interest

There are no conflicts of interest to declare by any of the authors of this study.

References

1. Toth C, Voll C. Wernicke’s encephalopathy following gastropasty for morbid obesity. Can J Neurol Sci. 2001;28:89-92
2. Galvin R, Brathen G, Ivashynka A et al. EFNS guidelines for diagnosis, therapy and prevention of Wernicke encephalopathy. Eur J Neurol. 2010;17:1408–1418.
3. London V, Grube S, Sherer DM, Abulafia O. Hyperemesis gravidarum: a review of recent literature. Pharmacology. 2017;100:161–171.
4. Lee NM, Saha S. Nausea and vomiting of pregnancy. Gastroenterol Clin North Am. 2011;40:309–334.
5. Oudman E, Wijnia JW, Oey M, van Dam M, Painter RC, Postma A. Wernicke’s encephalopathy in hyperemesis gravidarum: A systematic review. Eur J Obstet Gynecol Reprod Biol. 2019 May;236:84-93.
6. Justin C, Annamalai A, Pricilla G, Muralidharan K, Srinivasan K, Gurnell M. More than just morning sickness. QJM. 2013;106(12):1123-1125.
7. Suzuki S, Ichijo M, Fuji H, Matsuoka Y, Ogawa Y. Acute Wernicke’s encephalopathy: comparison of magnetic resonance images and autopsy findings. Intern Med. 1996;35:831–834.
8. Kantor S, Prakash S, Chandwani J, Gokhale A, Sarma K, Albahrami MJ. Wernicke’s encephalopathy following hyperemesis gravidarum. Indian J Crit Care Med. 2014;18(3):164-166.