Wernicke's Encephalopathy with Incidental Pituitary Haemorrhage in Hyperemesis Gravidarum

Sir,

Wernicke's Encephalopathy (WE) is due to deficiency of thiamine. It is seen in situations of nutritional deficiency like chronic alcoholism, hyperemesis of pregnancy, systemic malignancy, bariatric surgery, haemodialysis, prolonged intravenous feeding, refeeding, and acquired immunodeficiency syndrome. Approximately, 80% of patients with untreated WE develop Korsakoff syndrome, characterized by memory impairment and confabulation.[1] We describe a case of WE with incidental pituitary haemorrhage in a patient with hyperemesis gravidarum.

A 19-year-old Primigravida, 16 weeks gestation, presented with complaints of swaying while walking, abnormal eye movements, and difficulty reading for two days. She had severe nausea and vomiting from the first trimester requiring multiple admissions to the general hospital. She was mostly confined to bed with extreme fatigue. She weighed 60 kg before pregnancy and 45 kg on admission. On clinical examination, vitals and general examination were normal. She was well oriented. Ocular examination showed primary position upbeat nystagmus more prominent in up gaze; extraocular movements were complete, pupils 3 mm in size reacting to light. Fundus optic disc was

hyperaemic with mild oedema, peripapillary haemorrhages, tortuous veins, and normal macula [Figure 1a and 1b]. Visual acuity was 6/36 in both eyes; she could count the number of letters but not identify them as she couldn't fixate due to nystagmus. On motor examination, she had normal tone, power, and deep tendon reflexes in all limbs. Finger-nose-finger coordination was normal but was severely ataxic on standing and walking. Anatomical localization considered were 1) upbeat nystagmus due to lesions of projections from anterior semicircular canals to oculomotor neuron complex, i.e., superior rectus and inferior oblique subnucleus, in brainstem paramedian region and 2) gait ataxia due to a lesion of cerebellar vermis or its connections. Differentials were 1) posterior circulation stroke, 2) brainstem demyelinating lesion, 3) mass lesion with acute haemorrhage, 4) nutritional thiamine deficiency, and 5) drugs or toxins ingestion.

Lab parameters revealed Haemoglobin 12.9 grams%, normal blood counts, hypokalaemia 2.4 mEq/L, raised transaminases SGPT 224 IU/L, SGOT 92 IU/L, serum total protein 5.790 gm/dl, albumin 3.25 gm/dl, globulin 2.5 gm/dl, INR test 12.4 sec, control 13.8 sec, APTT test 26.9 sec, and control 28 sec. Ultrasound abdomen showed markedly distended gall bladder with calculi and echogenic sludge. She came with a 1.5 Tesla Magnetic Resonance Imaging (MRI), and it showed subtle flair hyperintensity involving bilateral medial thalami and mamillary body [Figure 1c]. The patient refused Lumbar Puncture. Anti-nuclear antibody was negative. In the presence of hyperemesis gravidarum, upbeat nystagmus, ataxia, and MRI with medial thalamic and mamillary body hyperintensity, a diagnosis of thiamine deficiency was made.

She was placed on IV thiamine 200 mg tds, and electrolytes were corrected appropriately. Urine culture yielded E. coli and started on the sensitive antibiotic nitrofurantoin. The nystagmus amplitude reduced substantially in two days, and the reading improved. Second imaging MRI 3Tesla after four days showed medial thalamic hyperintensity and, in addition, diffuse pituitary gland enlargement with haemorrhage into the posterior aspect of the anterior pituitary, suggestive of pituitary apoplexy [Figure 1d]. On hormonal assay, FT4 was low, 0.792 ng/dl (0.89–1.76), TSH 0.59 IU (0.25–5), and S.Cortisol 17.6 ug/dl (6.22–19.4) were normal. She was placed on thyroxine 25 ug. Thiamine after one week was continued orally. In two weeks, her gait improved significantly, and she could walk with minimal support. Optic disc oedema and peripapillary petechial haemorrhages almost resolved, upbeat nystagmus became less pronounced, and lab parameters improved with normal transaminases and electrolytes.

Carl Wernicke, in 1881, first described WE. Wernicke's Encephalopathy is a clinical diagnosis based on the appearance of characteristic clinical features in the setting of nutritional deficiency or high metabolic demands. The clinical triad of ophthalmoplegia, gait ataxia, and acute confusion classically describes it, and the complete triad is seen only in 10%.[1]

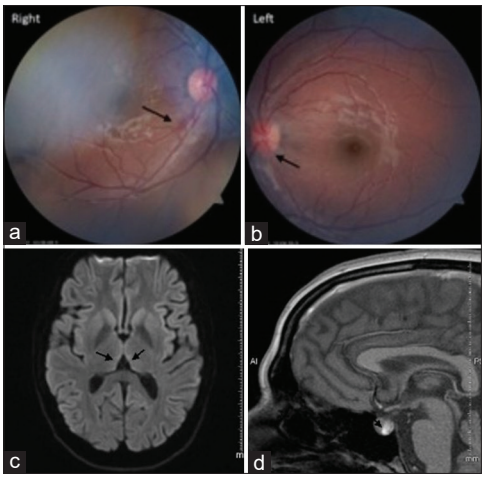

Figure 1: (a) Right fundus, superficial haemorrhage along the inferior temporal arcade. (b) Left fundus disc hyperaemic with mild oedema. (c) MRI Brain flair, medial thalamic hyperintensity, and (d) MRI Brain T1 shows haemorrhage into the posterior aspect of the anterior pituitary

Our patient had spontaneous upbeat nystagmus with stance and gait ataxia. She had no cognitive impairment and no ophthalmoparesis. In Wernicke's, the most common ocular finding is horizontal gaze-evoked nystagmus. Primary position upbeat nystagmus is also described due to lesions in the caudal medulla in the perihypoglossal region (intercalatus and Roller nuclei).[2] Other sites of upbeat nystagmus include pontomesencephalic and anterior vermis lesions.[3] Mechanisms of upbeat nystagmus include 1) imbalance of vestibular–ocular pathway, 2) dysfunction of vertical neural integrator involved in gaze holding, and 3) impairment of upward pursuit. Optic disc oedema and retinal haemorrhages are rare findings postulated due to impaired mitochondrial function in retinal ganglion cells and capillaries. The second of the triad, gait ataxia, is due to preferential damage to the superior cerebellar vermis and contributed by concomitant peripheral neuropathy or vestibular dysfunction.[2] (3) Acute confusion, the last of the triad, is due to the involvement of midline thalamic nuclei and mamillary body.

Diagnosis is based on a high degree of clinical suspicion in appropriate clinical settings and supported by imaging findings. Magnetic Resonance Imaging imaging is characterized by bilateral symmetrical T2 hyperintense lesions in the medial thalami, hypothalamus, midbrain tectum, periaqueductal gray, and mammillary bodies.[4] The absence of MRI signal intensity alterations does not exclude the diagnosis of Wernicke's. Magnetic Resonance Imaging has a low sensitivity of only 53% but high specificity of 93% for the diagnosis of WE.[5]

Our patient had subtle medial thalamic and mamillary body hyperintensity and pituitary haemorrhage. In literature, micropetechiae are often described histologically in affected regions. The first name was superior hemorrhagica polioencephalitis by Wernicke.[6] In 1965, William

Rosenblum described haemorrhage of any type in 60% of 43 cases.[6] In a nine-year study in Australia, of 131 cases of WE diagnosed pathologically, 5% showed periventricular haemorrhage.[7] The pituitary haemorrhage in our patient was asymptomatic with normal hormonal workup. So, it is most likely incidental.

The presumptive diagnosis of WE can be confirmed by High Performance Liquid Chromatography, but a normal level does not exclude it.[8] European Federation of Neurology guideline recommends thiamine to be given for suspected or manifest WE, 200 mg thrice daily, preferably intravenously, before any carbohydrate.[8] In conclusion, WE is a reversible neurological emergency often presenting with the incomplete triad requiring a high degree of clinical suspicion to diagnose.

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Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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