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Non-alcoholic Wernicke's Encephalopathy and Magnetic Resonance Imaging Brain: Can Neuroimaging Help in Decision Making and Troubleshooting?

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Authors' contributions

This work was carried out in collaboration between all authors. Author WMN designed the study, collected patient's history and lab results, compiled the data, performed literature search and corrected initial draft of the manuscript. Author FM supervised this study, performed neuroimaging analysis and finalized the draft and Author ABA wrote initial draft. Author MB finalized the draft. All authors read and approved the final manuscript.

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Case Series

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ABSTRACT

Summary: We present 4 hospitalized patients with chronic illness without social history of alcoholism. These patients suddenly developed altered mental status and drowsiness. Clinical examination was inconclusive and patients were diagnosed as Wernicke's encephalopathy on typical Magnetic Resonance Imaging (MRI) features.
Background: Wernicke's encephalopathy (WE) is acute encephalopathy primarily caused by acute thiamine deficiency. It's a neurological emergency; thiamine replacement can prevent permanent neurological damage and even death. Chronic alcoholism is most common cause; others include

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prolonged starvation, malignancy, prolonged parenteral nutrition and bowel surgeries. Despite over a century of reports, diagnosis is not uncommonly delayed, if overlooked altogether. In Pakistan, alcohol is prohibited and majority population is non-alcoholic, clinical suspicion of WE is usually low leading to delay in diagnosis. The real challenge comes when patient has multiple comorbidities and admitted in intensive care receiving total parenteral nutrition or chemotherapy secondary to bowel surgeries or treatment of malignancy. We present 4 cases after obtaining informed and written consent. All were nonalcoholic; presented with multiple comorbidities. During hospital stay, in addition to primary complaints, these patients developed altered mental status and drowsiness. These patients were administered thiamine replacement on basis of Magnetic Resonance Imaging findings and rapid clinical response was documented. Unfortunately 1 out of 4 patients succumbed to death due to other co-morbidities; remaining recovered.

Conclusion: Non-alcoholic WE has relatively high mortality because of delayed diagnosis and lack of clinical suspicion. Mortality and morbidity decreases with an earlier diagnosis based on MRI and simultaneous prompt treatment with thiamine administration.

Keywords: Wernicke's encephalopathy; ataxia; confusion; total parenteral nutrition; Pakistan.

1. CASE PRESENTATION

1.1 Case 1

37-year-old male presented with history of abdominal firearm injury 1.5 months back. No past history of alcoholism was found. He underwent laparotomy followed by resection and anastomosis of jejunum. Later on, patient developed high output jejunocutaneous fistula and fecal collection in left paracolic gutter for which he again underwent laparotomy followed by drainage of collection, resection and re-anastomosis of bowel. Soon after, he presented with wound infection and was managed on total parenteral nutrition (TPN), fluids, and antibiotics. During the hospital stay he presented with agitation, disorientation, irritability, memory impairment and amnesia.

1.1.1 Investigations

MRI brain shows hyperintense signals on T2 and FLAIR sequences involving mamillary bodies along with contrast enhancement and diffusion restriction. Hyperintensity in periaqueductal area and around 3rd ventricle also identified. On the basis of typical MRI findings, diagnosis of TPN associated Wernicke's encephalopathy was confirmed.

1.1.2 Treatment

Thiamine B1 and other vitamins were added in his diet.

1.1.3 Outcome and follow up

Patient showed rapid recovery and was discharged with wound care and diet instructions.

1.2 Case 2

20-year-old female known case of abdominal tuberculosis presented with intestinal obstruction underwent laparotomy to relieve the obstruction. Patient does not have history of alcoholism but family history of tuberculosis was positive. 4 months after surgery, she presented with high output enterocutaneous fistula and was kept Nil per oral (NPO) followed by TPN as a part of conservative management. A month later, she presented with seizures of sudden onset and drowsiness.

1.2.1 Investigations

MRI brain was performed to exclude central nervous system (CNS) tuberculosis but it shows bilateral symmetric hyperintensities on T2 and Fluid attenuated inversion recovery (FLAIR) images in periphery of 3rd ventricle, periaqueductal area, mammillary bodies and tectum. Hyperintensities in cerebellum and cerebral cortex were also appreciated.

1.2.2 Treatment

Thiamine replacement therapy was initiated.

1.2.3 Outcome and follow up

Initially the drowsiness improved but seizures went uncontrolled and patient expired due to septic shock and disseminated tuberculosis.

1.3 Case 3

37-year-old non-alcoholic male initially presented with abdominal pain and fever. CT abdomen

showed necrotic abdomino-pelvic and retroperitoneal lymphadenopathy which was causing biliary obstruction, cholangitis and pancreatitis. Further workup and lymph node biopsy showed testicular germ cell tumor with lymph nodal metastasis. Patient was managed with TPN and IV antibiotics and percutaneous transhepatic cholangiogram (PTC) to relieve biliary obstruction. Within few days of conservative treatment patient gradually developed alteration in mental status and his neurological examination depicted low Glasgow coma scale.

1.3.1 Investigations

MRI shows hyperintensities in mamillary bodies, dorsomedial thalami, tectal plate, periaqueductal grey matter and around third ventricle. Diffusion restriction was present in mamillary bodies and tectal plate.

1.3.2 Treatment

Patient received thiamine replacement

1.3.3 Outcome and follow up

Recovered progressively.

1.4 Case 4

55-year-old non-alcoholic female known case of metastatic colorectal carcinoma status post chemotherapy (13 cycles of FOLFOX, 3 cycles of FOLFIRI and 2 cycles of FOLFOX+AVASTIN) presented with drowsiness. No past history of alcohol intake was documented. Neurological examination showed cerebellar signs i.e., nystagmus and gait disturbances.

1.4.1 Investigations

She underwent MRI brain to exclude cerebellar pathology which demonstrates hyperintensities on T2/FLAIR sequences in periphery of 3rd ventricle, periaqueductal area, mammillary bodies, tectum and bilateral cerebellar hemispheres. Diffusion restriction and contrast enhancement of mammillary body was prominent finding. This patient was labeled as chemotherapy induced WE.

1.4.2 Treatment

Thiamine B1 and other vitamin were added in his diet.

1.4.3 Outcome and follow up

Gradual recovery and patient returned to normal routine within few days.

2. DISCUSSION

WE is an acute encephalopathy characterized by classic triad of confusion, ophthalmoplegia, and gait ataxia. It is primarily caused by acute thiamine deficiency which is vital for the survival of various tissues especially red blood cells and neurons as they are dependent upon glucose as their main energy source. When the stores of thiamine are depleted, these are the first cells affected.[1,2] Thiamine is a coenzyme in the pentose phosphate pathway, which is a necessary step in the synthesis of fatty acids, steroids, nucleic acids and the aromatic amino acid precursors to a range of neurotransmitters and other bioactive compounds essential for brain function. Thiamine plays a neuro-modulatory role in the acetylcholine neurotransmitter system, distinct from its actions as a cofactor during metabolic processes and contributes to the structure and function of cellular membranes, including neurons and neuroglia.[3] In addition, the administration of dextrose in the setting of thiamine deficiency can be harmful and can be associated with neurologic injury and WE [4]. Various conditions associated with WE; Most notable are chronic alcoholism, prolonged starvation, and malnutrition [5]. Other reported conditions are anorexia nervosa, [6] systemic malignancy [7], prolonged parenteral nutrition,[8] hyperemesis gravidarum [9], bariatric surgery [10] and even infants given the wrong formula.[11] The classic triad of WE is present in only one third of patients and if the history of alcohol abuse is not evident than the diagnosis is really difficult as most patients present with only one or two symptoms of the triad. The most common presenting symptom is confusion followed by ataxia and ocular dysfunction. The appropriate management is prompt intravenous or intramuscular administration of thiamine after which rapid improvement is seen [12]. MRI findings along with neurological examination can highly improve early diagnosis of WE. Contrast enhancement in mammillary bodies and thalamus is a typical finding of the disease. Zuccoli G et al reported in their study on MRI, 80% of patients had evidence of symmetric lesions in medial thalami and in periventricular region of third ventricle; 59%, in periaqueductal area; 45%, in the mammillary bodies; 36% [13]. Atrophy of mammillary bodies

is a highly specific finding in autopsy of chronic WE and Korsakoff syndrome and is present in up to 80% of cases. In another study, the most obvious neuroradiological sign of acute WE, regardless of etiology, is bilateral hyper intensity on late-echo MRI, occurring in mammillary bodies, thalamus, periventricular gray matter, inferior and superior colliculi. [14] Also most distinctive neuroimaging findings of acute WE are represented by bilateral symmetric hyperintensities on T2 and Fluid attenuated inversion recovery (FLAIR) images in periphery of 3rd ventricle, periaqueductal area, mammillary bodies and tectum (Figs. 1-6). [15,16]

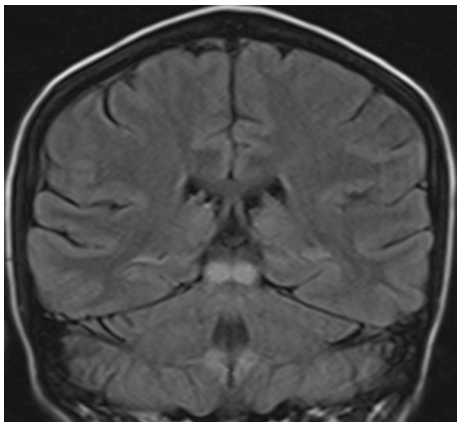


Fig. 1

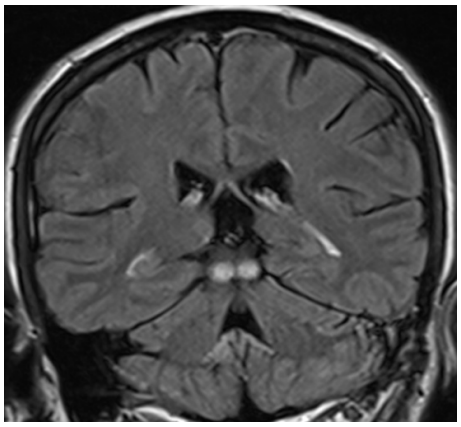


Fig. 2

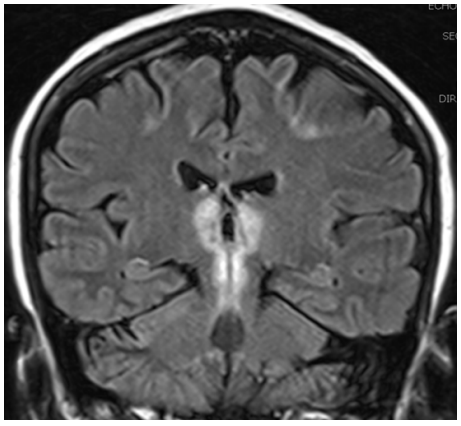
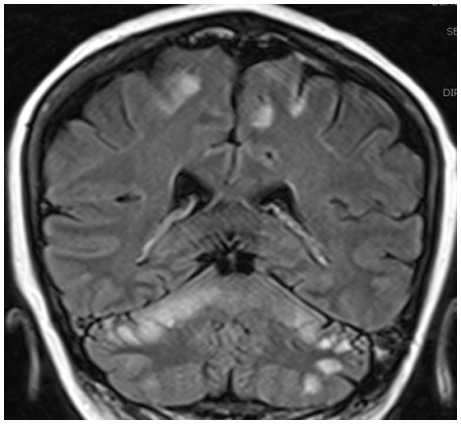


Fig. 3



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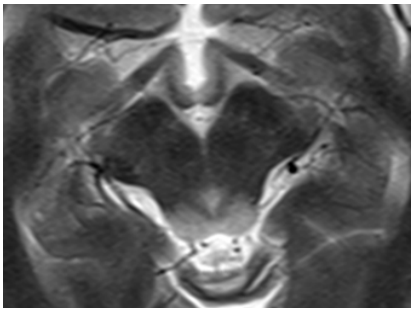

Fig. 5

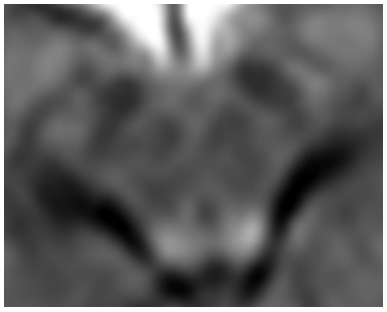

Fig. 6

Figs. 1-6. MRI brain shows bilateral symmetric hyperintensities on T2 and fluid attenuated inversion recovery (FLAIR) images in periphery of 3rd ventricle, periaqueductal area, mammillary bodies and tectum. Hyperintensities of some atypical areas like cerebellum and cerebral cortex are also appreciated. Diffusion restriction and contrast enhancement of mammillary body is also a prominent finding

Hyperintensities of some atypical areas like cerebellum, cranial nerve nuclei, and cerebral cortex are also most important and effective tool in the diagnostic assessment of WE. Alcoholic patients can show atrophy of the mammillary bodies and the cerebellar vermis as a result of previous WE attacks on MRI. No atrophy, instead, is found in nonalcoholic patients; in their case, signal intensity alterations represent the first result of thiamine-related metabolic pathway dysregulation [17]. Multiple case reports and case series have been reported about WE in international literature with prominence on chronic alcoholism. In this case series, we have emphasized WE in Pakistani population where alcohol is prohibited. This condition is often underestimated because literature has more emphasized this condition with chronic alcoholism. In addition our patients often presents with multiple co morbidities and are usually terminally ill so diagnosing this condition timely may safe patients life and prevent permanent neurological damage. Clinical examination is also not very helpful in these patients as majority patients present with drowsiness or even coma. Eventually the only lifesaving tool is Magnetic Resonance Imaging which can diagnose this condition followed by thiamine replacement. Unfortunately 1 out of 4 patients succumb to death due to delayed in diagnosis and other co morbidities. And we lately identified that our TPN mixture does not contain Thiamine. Taking this into consideration, we can conclude that nonalcoholic WE has high mortality when there is delay in diagnosis or left untreated or vice versa it has least mortality and morbidity if diagnosed early and promptly treated.

3. CONCLUSION

Wernicke's encephalopathy should be considered in all patients with acute delirium and ataxia. Chronic alcoholism is not the only risk factor for WE. History of TPN, multiple bowel surgeries and chemotherapy are more important risk factors for WE in non-alcoholic population. Thiamine supplementation is recommended in patients with increased risk as early diagnosis is important because it prevents permanent neurological damage or even death. In addition rapid recovery is also a rule in early stage. MRI findings along with signs and symptoms highly improve the diagnosis but in cases MRI is the only indicator of Wernicke's encephalopathy when clinical picture is non-conclusive or confusing as in our cases.

4. LEARNING POINTS/TAKE HOME MESSAGES

- In countries like Pakistan where alcohol is prohibited by law; Clinical suspicion of Wernicke's encephalopathy is usually low which leads to delay in diagnosis or even death if remain undiagnosed.
- Clinical suspicion or diagnosis of Wernicke's encephalopathy always remains a diagnostic challenge.
- If patient is chronically ill, malnourished or receiving TPN or had other co morbidities than relying on MRI brain findings rather than clinical diagnosis is better choice.
- Timely thiamine replacement therapy plays life saving role and reduces the risk of permanent neurological deficit.

CONSENT

As per international standard or university standard written patient consent has been collected and preserved by the authors.

ETHICAL APPROVAL

Not applicable due to retrospective data collection.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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