

## Case Report

# Paraneoplastic limbic encephalitis- forgotten etiology of altered sensorium

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## ABSTRACT

Paraneoplastic limbic encephalitis (PLE) is a rare disorder characterized by minor personality changes, irritability, depression, seizures, memory loss to frank altered sensorium. The diagnosis is difficult because clinical markers are often lacking, and symptoms usually precede the diagnosis of cancer or mimic other complications. The common causes of altered sensorium normally considered include infections, metabolic derangements, dyselectrolytemias, stroke, seizure, encephalitis etc. An oncological cause of altered sensorium is generally lower among the differentials. In absence of any overt signs of malignancy and probably due to less exposure to these cases, they generally get missed. Cancers primarily associated with limbic encephalitis are SCLC, breast cancer, thymomas, testicular malignancies, hodgkins and non hodgkins lymphoma. There have been reported cases for limbic encephalitis associated with adenocarcinoma of colon but not with adenocarcinoma of gastro esophageal junction. Our case of limbic encephalitis associated with adenocarcinoma of gastro esophageal junction is a rare entity and hence it is our endeavor to bring forth this case

**Keywords:** Endoscopic third ventriculostomy, Hydrocephalus, VP shunt, Neuroendoscopy, CSF diversion procedure, ETV

## INTRODUCTION

A case of altered sensorium is always an enigma for any specialist at whatever age and experience and of which ever speciality untill the time the final diagnosis is reached and the patient is treated. Some of the common causes include infections, metabolic derangements, dyselectrolytemias, stroke, seizure, encephalitis etc. Other than these common causes another important subsets are oncology related causes of altered behaviour. In absence of any overt signs of malignancy and probably due to less exposure to these cases, they generally get missed. Paraneoplastic encephalomyelitis is characterized by involvement of several areas of the nervous system, including the temporal-limbic regions, brainstem,

cerebellum, spinal cord, dorsal root ganglia, and autonomic nervous system.<sup>1</sup>

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## CASE REPORT

56 year old male serving soldier resident of Uttarakhand presented with history of abnormal behaviour for 4 months, headache for 3 months and inability to speak for last 15 days duration. He was apparently asymptomatic 4 months ago when his wife noticed that he had become highly irritable and had started using abusive language. There was no history of depression, delusions or hallucinations. This individual had lost around 8 kg in last four months.

He complained of dull aching holocranial headache for last three months. There was history of amnesia for recent events and had difficulty in performing simple calculations. There was a history of single episode of loss of consciousness and transient weakness of his left upper limb which recovered within 10 minutes on their own. There has been no history of any fever, cough, persistent vomiting, swelling in the body, oral ulcers or joint pain

On clinical examination he was hemodynamically stable, there was no pallor, pedal edema, lymphadenopathy or any Kayser- Fleischer rings. Neurologically his mini mental state examination (MMSE) was initially 12 which worsened. There was poor attention span. He had bilaterally VII UMN palsy associated with involvement of IX, X, XI cranial nerves. There was hypotonia in all four limbs. All reflexes were absent and bilateral plantar reflexes were extensors. Other systemic examination was unremarkable.

Based on history and clinical examination he fitted into a syndrome of chronic encephalopathy affecting frontal and temporal lobes and lower cranial nerves. With this background the possibilities considered were central nervous system vasculitis, limbic encephalitis, neurosarcoidosis or another chronic CNS infection.

Relevant investigations were carried out. His haematological and biochemical parameters were within normal limits. Cerebrospinal fluid analysis revealed mildly elevated proteins (white blood cells 80/ $\mu$ L (average, 100 WBCs/ $\mu$ L with predominant cells being lymphocytes, proteins 150 mg/dL and glucose 40 mg/dl). All viral markers including HIV were negative. His tumour markers were elevated CA125- 206 u/ml (N <35), CEA- 1206 u/ml (N2.5), CA19.9- 362 (N<37). Ds DNA and ANA were negative. Ultra sound abdomen revealed hyperechoic lesions in both lobes of liver with multiple retroperitoneal lymphadenopathy and minimal ascites. Contrast enhanced MRI revealed gyriform pattern of altered signal intensities suggestive of herpes simplex encephalitis. NCCT head revealed sub acute infarct in RT frontotemporal region, b/l insular cortex and left temporal lobe with hemorrhagic foci in left insular cortex. Electroencephalography (EEG) suggested a normal study.

In view of his preliminary findings he was managed empirically as a case of herpes simplex encephalitis with acyclovir and other supportive management. However his condition kept on deteriorating in the sense that he stopped taking food orally and his sensorium worsened over a period of week.

In view of his rapidly worsening condition he was further investigated. CECT abdomen was done which revealed multiple hyperechoic lesions in liver with central hypodensity and peripheral enhancement with largest lesion in segment VI with periportal lymphadenopathy. UGIE revealed ulcero proliferative growth starting from lower end of esophagus involving cardia and extending into fundus. Biopsy of the growth revealed it to be a case of poorly differentiated adenocarcinoma. Whole body PET revealed metabolically active soft tissue thickening in stomach wall with SUV(9.6). Extensive hyper metabolic liver lesions were noted. FDG avid bilateral supraclavicular and abdominal lymph nodes. CSF anti Hu antibodies were subsequently found to be positive (4,592 U/ml) which is normally undetectable.

Based on these findings final diagnosis of metastatic gastroesophageal adenocarcinoma with paraneoplastic limbic encephalitis was made. He was started on epirubicin, oxaloplatin and cepecitabine based chemotherapy. In spite of initiation of chemotherapy and other supportive measures patient succumbed to his illness after 4 weeks.

## DISCUSSION

Paraneoplastic syndromes are a group of clinical disorders which are associated with malignant disease though not directly related to the physical effects of primary or metastatic tumour.<sup>1</sup> They are produced due to either overproduction or underproduction of some active metabolites from the tumours or host response to the tumour which results in the syndrome.<sup>2</sup> Many times paraneoplastic syndrome may be the first sign of a malignant disease and its recognition may be critical for early detection and prompt management. Though most of these symptoms get treated with the treatment of malignancy however many of these are associated with immunological disorders and may not necessarily respond to the treatment of the malignancy. Paraneoplastic syndrome are further divided into endocrinal, renal, cutaneous, haematological and neurological types. Among the neurological paraneoplastic syndromes, the most misdiagnosed syndrome is that of limbic encephalitis.<sup>3</sup> Cancers are primarily associated with limbic encephalitis SCLC, breast cancer thymomas, testicular malignancies and few cases of hodgkins and non hodgkins lymphoma.<sup>3</sup> Humayen Gultekin case study of 50 patients with PLE found that lung is the most common site of cancer followed by testis and then breast.<sup>2</sup> However our patient presented with PLE associated with adenocarcinoma of GE Junction which in itself a rare entity.

The diagnosis of PLE require neuropathological confirmation or presence of all the four of following (i) Compatible clinical picture (ii) interval of <4 years between onset of symptoms and diagnosis of cancer (iii) exclusion of other neuroncological complication and (iv) either one of the following: CSF with inflammatory changes with negative cytology; MRI showing temporal lobe abnormalities; EEG showing epileptic temporal lobe activities.<sup>3</sup> Our patient fulfilled this criterion.

The overall prognosis in patients with these disorders is highly variable, depending on the underlying limbic encephalitis has a very wide range of manifestations, it can manifest as a rapidly progressive psychotic symptoms as happened to our patient when he started using abusive language, to other features like memory loss and focal seizures. It is very easily mistaken for herpes simplex encephalitis and many times are treated for the same without any improvement. The main pathophysiology behind it is formation of autoantibodies against Hu present in serum and cerebrospinal fluid. Anti Hu antibodies are generally seen in small cell lung carcinoma. Other onconeural antigens studied are ANNA3 and PCA2.<sup>5</sup> In testicular carcinoma there is presence different type of antibody called as Ma2.<sup>4</sup> However the absence of anti-Hu antibodies does not rule out the presence of an underlying SCLC in patients with a clinical diagnosis of LE. Patients with LE and SCLC who are without anti-Hu antibodies are less likely to develop paraneoplastic encephalomyelitis (PEM) and seem to improve more often after treatment of the cancer than those who present anti-Hu antibodies.<sup>6</sup> In most cases if the CSF is acellular and there is no evidence of cancer, VGKC-Ab is the likely culprit and if the CSF is cellular, a paraneoplastic syndrome is more likely. Depending on the antibody, the neurologic symptoms may resolve with treatment of the cancer and/or immunosuppressive therapy or the neurological symptoms may be permanent even if the cancer is cured.<sup>7</sup>

Since treatment of the tumour is the best way of either stopping progression or reversing the neurologic symptomatology for most paraneoplastic syndromes, an extensive search for a tumour should include imaging of the entire body by CT or MRI or PET scan can be used.<sup>8</sup> A trial with immunotherapy can be considered, however their role is still controversial.

Tumor and its stage as well as the severity of the neurologic syndrome. Some patients make a complete recovery, while others die or have permanent neurologic sequelae. Delay to diagnosis and treatment has been associated with a worse prognosis.<sup>9,10</sup> The delay in diagnosis and treatment could be the cause of mortality in our case.

## CONCLUSION

It has been an endeavor to bring a case of altered sensorium due to a rare case of limbic encephalitis associated with Adenocarcinoma of gastroesophageal junction with an idea to sensitize all of us to be aware of such an entity while evaluating a case of altered sensorium.

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