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Paraneoplastic Limbic Encephalitis in Non-Hodgkin's Lymphoma

Case Report

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Abstract

Limbic encephalitis can be either non-paraneoplastic or paraneoplastic manifestation of various malignancies such as carcinoma of lung (small cell), ovary, breast, testis, GI tract, hepatobiliary etc. Patients usually present with acute or subacute onset of delirium, seizures, dementia, personality changes, etc. Differentiation between non-paraneoplastic and paraneoplastic limbic encephalitis is done by exclusion of malignancy. PET CT scan helps in detection of occult primary. Presented here is a case of paraneoplastic limbic encephalitis secondary to High grade B cell Non-Hodgkin's lymphoma..

Introduction

Paraneoplastic limbic encephalitis is a type of paraneoplastic neurological syndrome (PNS). It a non-metastatic manifestation that does not occur secondary to any of associated complications such as metabolic derangement, infection, nutritional imbalance or ischemia. It is a cancer associated immune mediated disorder of the nervous system that may precede the detection of malignancy by several months. [1] The most commonly associated malignancies are that of lung cancers, testicular tumours and breast cancers.

Non paraneoplastic limbic encephalitis is an autoimmune disorder associated with antibodies to neuronal cell surface or synaptic receptors. Common presentations include personality changes, irritability, depression, seizures, confusion, memory loss, etc. CSF usually shows elevated proteins, lymphocytes, immunoglobulin G. CSF workup for limbic encephalitis may or may not be indicative of an auto immune process.

Case report

A 68 year old male, presented with a seizure and postictal delirium. There was preceding weight loss of 7kgs in 1 month. Clinical examination revealed normal vital signs and obtunded mental status. Rest of the examination was unremarkable.

MRI brain showed focalaltered signal in the genu of corpus callosum with restricted diffusion and asymmetric increased T2 hyperintense lesion in theleft mesial temporal lobe. FDG PET-CT scan was done to look for occult primary. Brain images showed increased FDG uptake in the genu of corpus callosum, left mesial temporal lobe and caudate nucleus. The amygdala, head, body and tail of hippocampus also showed increased FDG uptake (findings suggestive of limbic encephalitis). The wholebody images showed an FDG avid lesion in the parotid and multiple FDG avid hypodense liver deposits. MRI of liver revealed lesions in segments V, VII and VIII in the right lobe, smaller lesions in the left lobe of liver with restricted diffusion. Thus, a diagnosis of limbic encephalitis with occult primary in left parotid was proposed with liver metastases. However, histology from parotid lesion showed a benign lesion (Warthin's tumor). Liver biopsy was then done to reveal a diagnosis of Highgrade B- cell lymphoma (Figure 1-4).

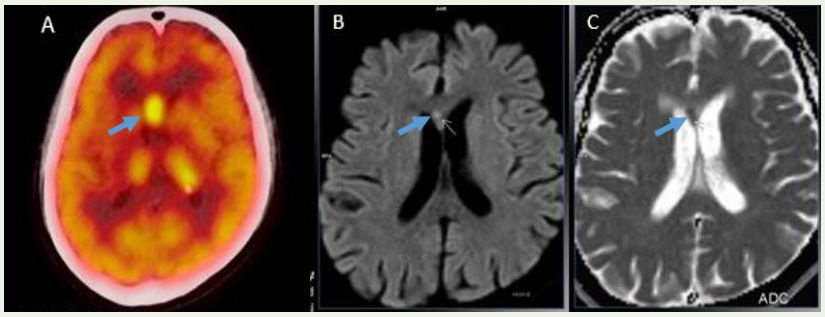

Figure 1: Image A: FDG PET-CT scan showing a hypermetabolic focus in the genu of corpus callosum. Image B and C: DWI demonstrating a lesion in the genu of corpus callosum with restricted diffusion.

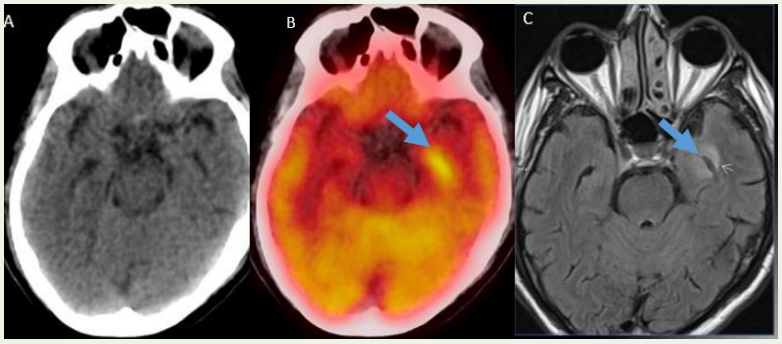

Figure 2: Image A and B: FDG PET scan shows increased FDG uptake in the left mesial temporal lobe. Image C: MRI Brain showing T2 hyperintensity in the corresponding area. Image B and C: DWI demonstrating a lesion in the genu of corpus callosum with restricted diffusion.

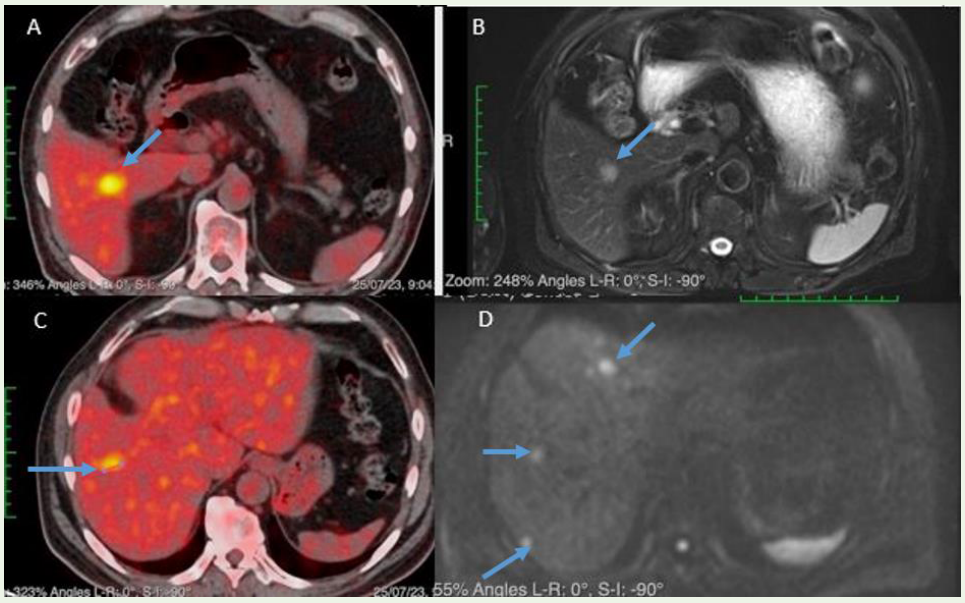

Figure 3: Image A and C: FDG PET-CT scan showing hypermetabolic liver lesions. Image B and D: MRI Liver (High B) scan showing multiple liver lesions with restricted diffusion.

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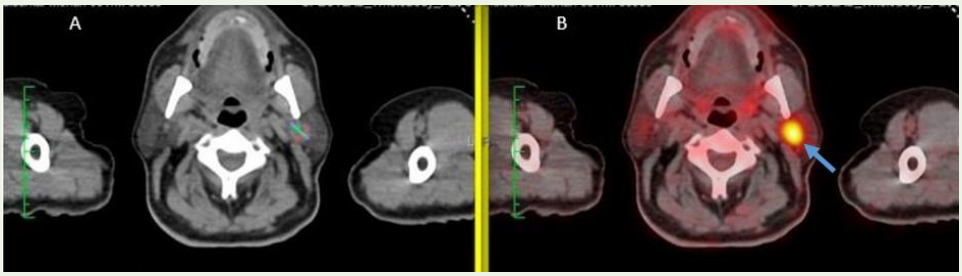

Figure 4: Image A and B: FDG PET-CT scan showing an FDG avid lesion in the left parotid gland.

Discussion

Paraneoplastic syndrome is a set of signs and symptoms that are expressed in the presence of a malignancy. The symptoms develop when a malignant tumor causes changes in the body that are not directly caused by cancer itself. Paraneoplastic syndromes may affect different organ systems, most often the endocrine, neurologic, rheumatologic, dermatologic and hematologic systems. The most commonly associated malignancies include small cell lung cancer, breast cancer, gynecologictumors and hematologic malignancies. [2]

Paraneoplastic encephalomyelitis is a group of neurological manifestations associated with cancer related inflammation of the brain or spinal cord or both. Autoantibodies targeting intracellular epitopes are thought to cross-react between cancer and central nervous system proteins, glycoproteins, and complex carbohydrates. Associated diseases can include limbic encephalitis, encephalomyelitis, subacute cerebellar degeneration, opsoclonus myoclonus, optic neuritis and rapidly progressive sensory polyneuropathy. [3]

Limbic encephalitis is of two broad types: Infectious and autoimmune limbic encephalitis.[4]

Infectious encephalitis (IE) and autoimmune encephalitis (AE) are symptomatically similar, however essentially different in pathogenesis.

Infectious limbic encephalitis is the inflammation of the limbic areas of the brain preceded by an infection (mostly bacterial or viral).

Autoimmune encephalitis refers to acute to subacute, progressive inflammation of the brain associated with antibodies against neuronal cell surface and synaptic protein. [5]

Autoimmune encephalitis is further divided into paraneoplastic and non-paraneoplastic.

Non-paraneoplastic limbic encephalitis is an inflammatory process which is due to antigen-specific cellular and humoral immune responses directed towards CNS neurons (more specifically neuronal surface antigens or extracellular antigens).

Paraneoplastic limbic encephalitis is a rare paraneoplastic syndrome that affects the mesial temporal lobe and presents with cognitive dysfunction, seizure, change in personality, irritability, hallucinations, disorientation, and/ or disruption of consciousness and short-term memory loss in presence of, or preceding a malignancy. 50% of patients will have lung cancer, 20% will have testicular tumours, and 8% will have breast cancer.[6] IgG antibodies in the serum and CSF directed against intracellular neuronal antigens (unlike non-paraneoplastic) are expressed by tumour cells and are called onco-neuronal antibodies [7].

After thorough clinical examination, imaging plays a crucial role in aiding the diagnosis of limbic encephalitis. MRI with contrast is considered to be the most sensitive imaging modality. Limbic encephalitis mostly involves the mesial temporal lobes and limbic systems and is demonstrated by cortical thickening and increased T2/ FLAIR signal intensity of these regions. Bilateral involvement of the structure is more common than unilateral.Whereas, FDG PET scan will show increased metabolic activity in the corresponding areas [8].

There are only a few case reports of Lymphoma presenting as limbic encephalitis. Senthil Rajappa, et al. explained paraneoplastic limbic encephalitis secondary to primary renal lymphoma [9].

Dögel D, et al. [10] and Thuerl C, et al. [11] published case reports of Non-Hodgkins lymphoma presenting with paraneoplastic limbic encephalitis.

Soto-Rincón CA et al. [12] have reviewed Ian Carr's article wherein the association between memory loss and Hodgkin's lymphoma has been given the eponym of Ophelia syndrome.

Our patient was suspected with occult primary in the parotid gland. However, the histology from parotid lesion showed Warthin's tumor.Liver biopsy was then done to reveal a diagnosis of High grade B- cell lymphoma.

Thus, concluding that the neurological manifestations were a set of paraneoplastic symptoms secondary to High grade B- cell lymphoma.

Acknowledgement

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