Malignancy Mimicking Encephalitis – A Cause of Rapidly Progressive Fatal Dementia

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ABSTRACT

Rapidly progressive dementia (RPD) in a young patient is infrequently seen in clinical practice. The diagnosis of young patient presenting with rapidly progressive is challenging to the the neurologists as it has varied etiologies. The diffrential diagnosis is different from the typical cases of dementia. The early and accurate diagnosis of RPD depends on the comprehensive workup to diagnose the potential treatable cause of RPD.

Key Words: Cognitive Decline, Encephalitis, Malignancy

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CONFLICT OF INTEREST: None

INTRODUCTION

The diagnosis of the cause of rapidly progressive cognitive decline leading to dementia in young individuals has always been challenging but many a times not rewarding to the clinicians. Malignancies leading to cognitive impairment in the young adults are usually uncommon. The investigations of the rapidly progressive dementia are directed towards ruling out any infective, inflammatory, metabolic, traumatic and nutritional causes. The differential diagnosis becomes challenging when the investigations for the common causes are equivocal or negative and the neuro-imaging revealing the radiological features of mimicking encephalitis.

We are presenting a case of a young female with rapidly progressive cognitive impairment and multiple seizures. She was diagnosed on brain biopsy with the rare entity of intravascular lymphoma, a subtype of extra nodal large cell non Hodgkin's lymphoma. It can occasionally present with neurological symptom in the form of dementia, focal neurological deficit and seizures. The clinical diagnosis is challenging because of nonspecific presentation.

Our case report highlights that the intravascular lymphoma can present as rapidly progressive dementia in young patients and the importance of brain biopsy in suspected cases for confirming the uncommon cause. The rare presenting causes of rapidly progressive dementia should be kept in differential diagnosing while managing the patients presenting with cognitive decline.

CASE REPORT

A 37 year old right handed educated female admitted in our hospital with complaints of behavioural changes and forgetfulness of two and half month duration .She had 3 episodes of seizure in last 1 month. At the onset of disease, her family members noticed that she used to forget things after placing them, and occasionally forget to add salt in meals during cooking. She used to wear her clothes in a reverse way and come out of the washroom without tying the knot of her pants. Along with this they also noticed change in her behavior in the form of aggressiveness on trivial matters and disinhibition at several occasions. She had passed urine and stool in the open without any concern. About 1 month prior to presentation she had multiple seizure of generalized tonic clonic seizure semiology. Within two and half month of onset of symptoms she had stopped recognizing her family members with decrease speech output and was completely dependent for her Activities of Daily Living. There was no history of fever, headache, vomiting or visual symptoms. Her family members denied any history of any focal neurological deficit, myoclonus. No history of joint pain, Skin changes, HTN, DM and prior stroke. There was no history of psychiatric illness in the past in her or in the family members.

The analysis of the clinical history the patient had shown that she had multiple seizures of generalized tonic clonic seizures semiology and significant cognitive impairment involving temporal, parietal and frontal lobes. We had kept the differential diagnosis of encephalitic illness causing these deficits. The common cause being viral ie the chronic herpes simplex encephalitis.

On examination the vitals were stable. Systemic examination was non contributory. The patient was conscious but uncooperative for higher mental function. She was producing inappropriate word with impaired comprehension. Signs

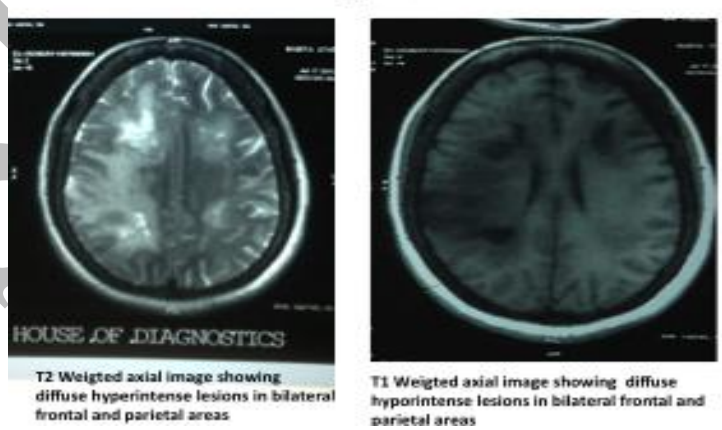
of meningial irritation were absent. Motor system examination normal. Frontal release sign were present in the form of positive bilateral grasp and snout reflex. Planters were bilaterally flexor.

Her initial routine investigations revealed normal haemogram with Hb (12.8gm %), TLC(6670 cell/cc),platelet count (2.35 lac/cc) and ESR (22). LFT (Bil-0.4mg%, SGPT-42U/L,) RFT (BU-20mg%, S.creat-0.34mg %) were normal. Serum uric acid was raised (9mg %). During the hospital stay her hemoglobin, TLC, platelet count decreased to 10gm%, 4000 cells/cc and 1.2 lac/ cc respectively. Liver function test showed increasing trend with SGPT-107 U/L, SGOT-186 U/L and GGT -1081 U/L.

CSF examination showed 3 cells with normal glucose (68mg %) and mildly raised protein (51mg %). HSV PCR, AFB and gram stain were negative. HIV ELISA, ENA profile was negative. The thyroid function test, Vit B 12 and folic acid levels were within normal limits. Ultrasound abdomen revealed mild spleenomegaly.

Neuroimaging (Fig 1 & 2) - MRI brain with contrast done which showed bilateral asymmetrical cerebral hyper intensities involving frontal, temporal and parietal lobes more on the right side. T2W image and shows hyper intensities in the corresponding areas in T1image.

Fig 1 & 2

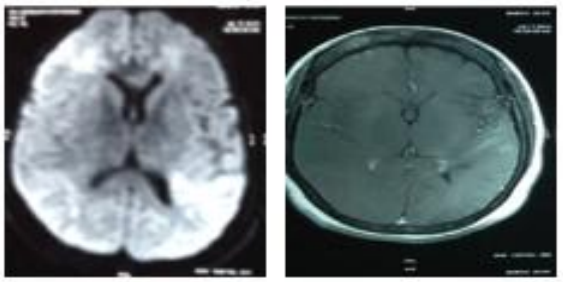


T2 Weigted axial image showing diffuse hyperintense lesions in bilateral frontal and parietal areas

T1 Weigted axial image showing diffuse hyporintense lesions in bilateral frontal and parietal areas

DWI revealed patchy diffusion restriction in bilateral cerebral lesions. Post contrast image showed subtle enhancement in right parietal region.

Fig 3 & 4



Diffusion weighted images showing restriction in the bilateral parietal and frontal areas.

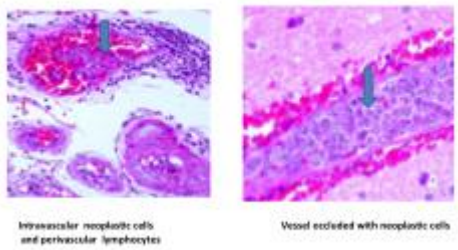
Contrast enhanced MRI showing minimal enhancement in parietal area.

Serum lactate dehydrogenase and ferritin level were raised (LDH-400 IU/L, Ferritin-301ng/ml), and fibrinogen was on higher side (407 mg/dl, Normal range: 200-400 mg/dl).

The possibilities of the encephalitic illness due to viral etiology were kept initially and as the investigations were not leading us towards the other etiological factors. The patient was kept on empirical management along with symptomatic treatment, the antiviral ie inj acyclovir and antiepileptic Inj Valproate was started. The seizures were controlled but there was no improvement in the clinical condition and she started deteriorating in her sensorium.

For further investigation, the brain biopsy was planned as the lesions were superficial. Brain biopsy confirmed intravascular large B cell lymphoma (Fig 5).Random skin biopsy was negative for malignant cells.

(Fig 5- Brain Biopsy)



Intravascular neoplastic cells and perivascular lymphocytes

Vessel occluded with neoplastic cells

Patient was started on steroids and chemotherapy ie Rituximab, Cyclophosphamide, Doxorubicin, Vincristine and Prednisone (CHOP regimen) by oncologist. The disease was rapidly progressive and patient succumbed to her illness within 2 months of diagnosis.

DISCUSSION

Intravascular lymphoma is a rare subtype of malignant extra nodal large cell lymphoma [1].It is of B cell origin in 90% of cases. Pathologically it is characterized by growth of lymphoma cells in the lumen of small vessels specially capillaries. IVL was first described in 1959 by Pflegger as "angio endotheliomatosis proliferans systemisata" who thought it to be endothelial origin.[2] Any organ of the body can be involved. Lymphomatous origin was confirmed by Wick in 1986. [3] It usually affects elderly patients with age >60 years without any gender preference. Patients present with non specific symptoms in the form of fever, fatigue and decrease appetite without lymphadenopathy. Our patient did not have any of these symptoms. Haemophagocytic and cutaneous variant are seen and diagnosis is made by organ biopsy. In our case the diagnosis was made with brain biopsy of the lesions which were mimicking encephalitis clinically and radiologically.

Intravascular lymphoma is a rare type of malignant lymphoma. According to the WHO classification it is classified as a subtype of extra nodal diffuse large B cell lymphoma. It is characterized by selective growth of tumor cells in the small vessels specially capillaries.[4]

Two variants of intravascular lymphoma has been described .Haemophagocytic syndrome which is usually seen in Asian patients and the Classical variant or cutaneous variant which is described in European patients .Patients with haemophagocytic syndrome presents with hematological abnormalities in the form of anemia ,decrease red blood cell count ,leucocytopenia thrombocytopenia and hepatosplenomegaly.[5]Classical syndrome present with cutaneous and neurological manifestation.[6] Neurological presentation may be initial manifestation in 25% of patients in the form of altered sensorium, focal neurological deficit, dementia, seizure. [7] Other organs that can be involved are lungs, kidneys, and liver with symptoms related to the involved organ. Our patient

had presented with pure neurological syndrome while other organ involvement was absent.

Organ biopsy is necessary for diagnosis of intravascular B cell lymphoma (IVLBCL) .Random skin biopsy from the uninvolved site may help in diagnosis. The skin biopsy in our case was negative .Other findings that may suggest possibility of IVLBCL are decrease blood cell count, raised lactate dehydrogenase level. There was evidence of the decrease in the blood counts in our patient. The Clinical outcome was poor before the rituximab arrival. Three year survival with CHOP (Cyclophosphamide, Doxorubicin, Vincristine, Prednisone) was 33% which was improved after addition of rituximab (R-CHOP) to 66% at 2 years. [8]Some studies have shown good efficacy of autologous stem cell transplant in patients with IVLBCL.

CONCLUSION

Our case showed that rapidly progressive dementia can be the presenting feature of this rare disease which has presented like encephalitic illness . The case highlights the importance of early brain biopsy in suspected cases for early diagnosis and timely intervention to improve the outcome.

REFERENCES

1. Sandera M, Holguin M. Intravascular lymphoma: case series and review of the literature. Blood 2005; 106:4687

2. Pfleger L,Tappeiner J. [On the recognition of systematized endotheliomatosis of the cutaneous blood vessels (reticuloendotheliosis?].Hautarzt 1959; 10:359–63.

3. Wick MR, Mills SE, Scheithauer BW, Cooper PH, Davitz MA, Parkinson K. Reassessment of malignant "angioendotheliomatosis".Evidence in favor of its reclassification as "intravascular lymphomatosis". Am J Surg Pathol 1986; 10: 112–23.

4. Nakamura S, Ponzoni M, Campo E. Intravascular large B-cell lymphoma. In: Swerdlow SH, Campo E, Harris NL, et al, eds. WHO classification of tumours of hematopoietic and lymphoid tissues. Lyon, France: IARC Press, 2008: 252–53.

5. Ponzoni M, Ferreri AJ, Campo E, et al. Definition, diagnosis, and management of intravascular large B-cell lymphoma: proposals and perspectives from an international consensus meeting. J Clin Oncol 2007; 25(21):3168–73.

6. Ferreri AJ, Campo E, Seymour JF, et al. Intravascular lymphoma: clinical presentation, natural history, management and prognostic factors in a series of 38 cases, with special emphasis on the 'cutaneous variant'. Br J Haematol 2004; 127: 173–83.

7.Shimada K, Matsue K, Yamamoto K, et al. Retrospective analysis of intravascular large B-cell lymphoma treated with rituximab-containing chemotherapy as reported by the IVL study group in Japan. J Clin Oncol 2008; 26: 3189–95.

8. Ferreri AJ, Campo E, Ambrosetti A, et al. Anthracycline-based chemotherapy as primary treatment for intravascular lymphoma. Ann Oncol 2004; 15: 1215–21.

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