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PRIMARY CENTRAL NERVOUS SYSTEM LYMPHOMA PRESENTING AS PARKINSONISM WITH ATYPICAL MRI FINDINGS AND ELEVATED 14-3-3 PROTEIN

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ABSTRACT

Primary central nervous system lymphoma (PCNSL) is a rare neoplasm with a incidence of 2-3% of all central nervous system malignancy. The diagnosis can be challenging especially with atypical presentations. Movement disorders can be one of the rare presentation of PCNSL. Here we present an unusual case of gradually progressing Parkinsonism with elevation of CSF 14-3-3 protein and atypical imaging findings found to have PCNL

Case report:-

A 76 year old Caucasian female referred to our center for an evaluation of the speech and intermittent speech difficulty. Initial work up revealed a contrast enhancing lesion in the bilateral putamen and head of caudate without any mass effect. Her symptoms were rapidly progressed and presented again within 6 months duration with mild dysarthria, bradykinesia, mild rigidity and reduced left arm swinging. This features were consistent with Parkinsonism. The repeat imaging showed progression of hyper intensities in the bilateral putamen. The other possibilities such as heavy metal poisoning, toxic, metabolic, inflammatory causes has been ruled out. Patient underwent stereotypic biopsy of the right caudate nucleus which reveled PCNSL. Patient underwent chemotherapy and currently in remission.

Conclusion:-

Diagnosis of movement disorders still remains clinical and rapid progression of symptoms, atypical presentation warrant further imaging and work up.

KEYWORD

14-3-3; primary CNS lymphoma; Parkinsonian disease

ARTICLE HISTORY

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BACKGROUND:

Primary central nervous system lymphoma (PCNSL) is a rare neoplasm accounting for 2- 3 % of CNS malignancies. Over the past few decades, there is an increasing incidence of PCNSL among immunocompetent patients, particularly in the age group of 60 – 70 years or older. It is recognized as an aggressive brain tumor with poor prognosis. [1] PCNSL is confined to central nervous system and often disseminated to structures within the brain, spinal cord, ocular and leptomeningeal layers. The clinical presentation varies depending on the location of tumor and immunocompetency of the patient. [2] Despite involvement of basal ganglia in CNS lymphomas, only a handful cases have been reported with movement disorders like segmental dystonia, choreoathetosis, Parkinsons disease. [3-8]

We present an unusual case of gradually progressing Parkinsonism with elevation of CSF 14-3-3 protein and atypical imaging findings found to have CNS PCNL.

Case presentation:

A 76-year-old right-handed Caucasian female with history of papillary carcinoma of thyroid, hypertension, and hypothyroidism was referred to our center for the evaluation of speech and walking difficulties of 6 months. She was initially hospitalized at a different facility for bilateral lower extremity weakness and intermittent speech problems. CT scan of the head demonstrated subtle hyperdensities in the bilateral putamen. MRI of the brain showed bilateral putamen and head of caudate T2/FLAIR hyperintensities that had non-homogenous contrast enhancement without mass effect. (Fig 1a) Magnetic resonance angiogram and venogram did not reveal any major vessel occlusions or cortical vein thrombosis. There was no evidence of carbon monoxide poisoning in the blood testing. With progressive worsening of symptoms, she was referred to our clinic for an evaluation in early summer where she was found to have mild dysarthria, bradykinesia, mild rigidity and reduced left arm swinging. Subsequent MRIs 6 months and 8 months later showed progression of the lesions with T1 ,T2 FLAIR hyper intensities and continued to show non-homogenous enhancement of bilateral putamen regions (fig 1b)(fig 1c). Serum iron studies, liver function tests, paraneoplastic, vasculitis, hepatitis

panels, toxic and heavy metal screening, HIV, vitamin levels were found to be within normal limits/negative. CSF analysis showed elevation of 14-3-3 protein (3.7 Nano gram with cut off at 2.0), normal CSF cytology and flow cytometry. She underwent stereotactic biopsy of the right caudate nucleus which showed Non Hodgkin Lymphoma, diffuse B cell type. Whole body PET scan did not show extracranial lymphoma. Patient received high dose methotrexate with remission for four months. She has recurrence of lymphoma and received whole brain radiation therapy and is in remission for past 4 months.

DISCUSSION:

Parkinsonism is a rare presentation of PCNS lymphoma although basal ganglia involvement is common. Some of the unusual features of this case are the subacute Parkinsonian symptoms, atypical imaging features, elevation of 14-3-3 protein in CSF.

Primary CNS lymphoma commonly presents with rapidly progressive neurological deficits from solitary hemispheric masses (in immunocompetent individuals), occasionally stroke and cranial nerve deficits, progressive encephalopathy (in immunocompromised patients). [9-11] our patient presented with bradykinesia and rigidity and fulfilled the diagnostic criteria for Parkinsons disease proposed by Hughes AJ and et al [12]. However the red flags in our patient included abnormal MRI which prompted further work up that included serology and CSF analysis for alternative diagnoses which can present with Parkinsonism. Previous authors who presented cases with Parkinsonism as a symptom of basal ganglia lymphoma suggested interruption of striatal post synaptic dopamine receptors.[5,6] Unique features of our patient are that she did not have classic MRI findings of a CNS lymphoma but later evolved to classic MRI findings with T1 and T2 Flair hyperintesities with homogenous contrast enhancement. [13] Also her CSF cytology and flow cytometry was negative for lymphoma but her 14-3-3 protein was elevated with Jacob Cruedzfeldt disease in differential diagnosis. 14-3-3 is found in neuronal cytoplasm, glia, and synaptic membranes of the brain. It plays a crucial role on signal transduction, neurotransmission, and cell differentiation and is released into CSF when there is extensive neuronal damage. False-positive results can be seen in patients with herpes simplex encephalitis, hypoxic brain damage, and atypical encephalitis, intracerebral metastases of a bronchial carcinoma, metabolic encephalopathy, and progressive dementia of unknown cause. [14] In our case it is false positive for PCNSL which is also rare and was reported only in a few other HIV cases with PCNSL.

CONCLUSION:

Parkinsonism is a clinical syndrome with a broad differential. The etiology of Parkinsonism is largely clinical based on a thorough history and clinical exam. Imaging studies are not always warranted. Our case is unique in that she had a subacute Parkinsonism with extrapyramidal signs for more than 6 months. She potentially could be diagnosed with Parkinsons disease based on queen square brain bank criteria. However her imaging findings propelled further diagnostic testing leading to a diagnosis of Primary CNS lymphoma. This case emphasizes the importance of considering imaging studies early on in selected Parkinsonian disorders to look for alternative diagnoses.

List of abbreviations:

PCNS- Primary CNS lymphoma , HIV- Human immunodeficiency virus , CSF-Cerebrospinal fluid MRI-Magnetic resonance imaging, PET- Positron emission topography, CT- Computerized Topography.

Images

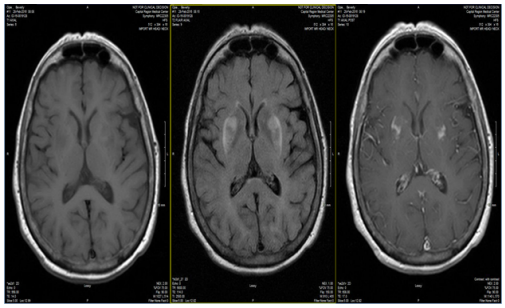
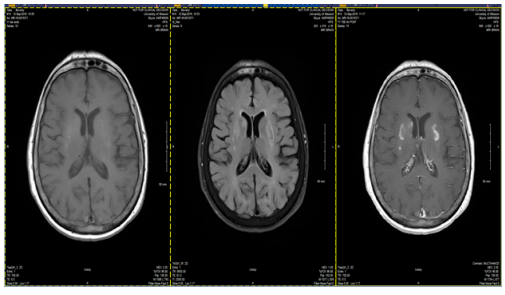


Fig 1: First MRI of patient (8 months before diagnoses)
Fig 1 A: Isointense to slightly hypointensity in bilateral putamen in T1 sequence.
1 B: T2 FLAIR sequence showing bilateral putamenal hypeintensities, fairly symmetric.
1 C: Post contrast MRI showing mild heteregenous enhancement of bilateral putamen regions.



(Fig 2) Similar MRI 6 months after symptoms onset

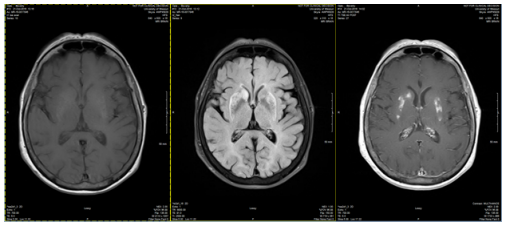


Fig 3A, B, C: MRI shortly before tissue diagnoses confirming PCNSL. T1 and T2 FLAIR sequence of MRI showing hyperintensities in bilateral putamen and right caudate of basal ganglia. Also note similar non homogenous contrast enhancement of bilateral putamen and caudate nucleus of basal ganglia.

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