PRIMARY CEREBRAL LYMPHOMA

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INTRODUCTION

Primary lymphoma of brain is an exceedingly rare tumor with incidence ranging from 0.8% to 1.5% of all intracranial tumors. Such tumors were once referred to as microgliomas.

CASE REPORT

A 60 years old lady was referred from a peripheral hospital because of weakness of left half of her body. Her daughter narrated that she has been increasingly forgetful over the past couple of months. She had been under the treatment of Psychiatrist and was on regular antidepressants. She had a past medical history of jaundice (1994) with uneventful recovery.

On neurological examination, she had a mini mental score of 8/10. Cranial Nerves examination including fundoscopy was normal. There were no signs of meningism. She had left sided upper neuron type of weakness. There was no sensory neurological deficit. Cardiovascular, abdominal and chest examination was unremarkable.

Initial investigations including full blood count and urinalysis were normal. ESR was raised at 65 mm in first hour. Biochemical profile including glucose, urea, creatinine, electrolytes and liver function tests were normal. Chest X-ray was normal. CT scan of brain revealed isodense mass in the left basal ganglion which showed enhancement after intravenous contrast administration without surrounding oedema, consistent with cerebral lymphoma (Fig.–1) .

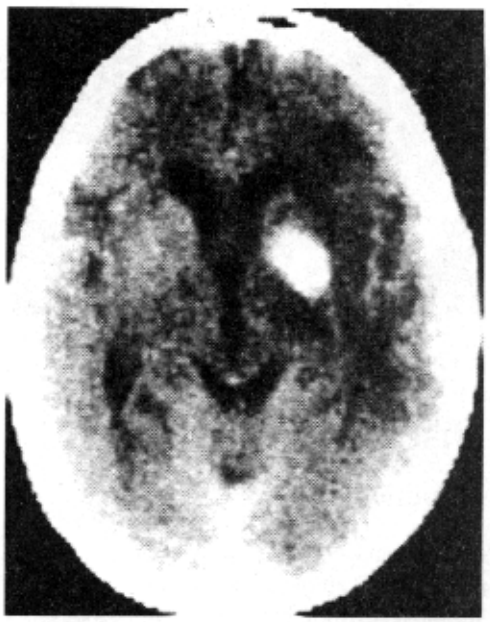

Fig. 1: Contrast CT scan brain showing hyperdense tumor with little mass effect.

CSF examination showed lymphocytic pleocytosis. CT scan of abdomen revealed no systemic involvement. Initially she was treated with dexamethasone 4 mg six hourly for seven days. A follow up CT scan brain was performed on seventh day, which showed disappearance of the lesion (Fig.–2), thus further conforming the diagnosis of cerebral lymphoma. Her case was further discussed with Oncologist and Neurosurgeon and the option of treatment with intravenous methotrexate was considered. But the family did not want any form of further active treatment. She was then discharged on steroids.

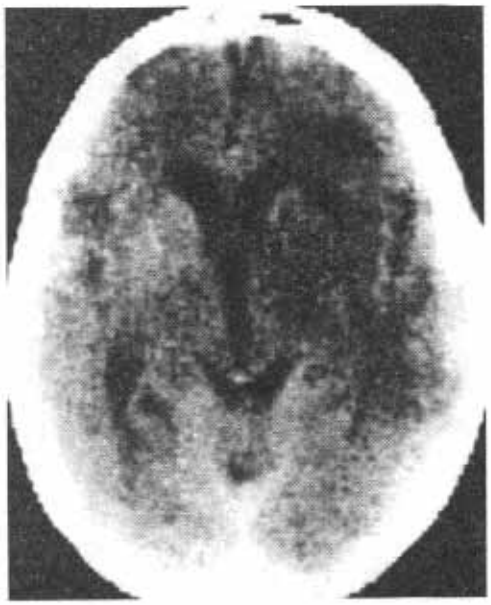

Fig. 2: Post steroid therapy CT scan.

DISCUSSION

Definition

Primary cerebral lymphomas are malignant intra-cerebral lymphomas that are similar histologically to non-Hodgkin's systemic lymphomas derived from "B" lymphocytes but occurring in the absence of recognized systemic disease.

Epidemiology

Over the last two decades the incidence of Primary Central Nervous System Lymphomas (PCNSL) has increased because of its frequency in the AIDS and other immunocompromised population. PCNSL occur with much increased frequency (3600 – fold) in patients with HIV and in patients who have immunodeficiency. It is also occurring with increasing frequency in immunocompetent population with no evident explanation.

Generally speaking these are considered as rare intracranial neoplasms accounting for 0.8 % to 1.5 % of intracranial tumors. Peak incidence is between 50 and 60 years, with a male to female ration of 3:2. However, patients with congenital immunodeficiency disorders such as Wiskott-Aldrich Ataxia, Telangiectasia or acquired disorders such as therapeutic immunosuppression are particularly at risk of developing primary intracerebral lymphomas. In patients with AIDS, primary cerebral lymphoma accounts for 6% of those with neurological complications. The common denominator present in CNS lymphomas in immunocompromised patients seems to be a dysfunction of the suppressors "T" cell system that permits proliferation and eventual neoplastic transformation of "B" cells.

Pathology

Macroscopically, PCNSL range from a well demarcated or ill defined solid, partially necrotic tumor to multifocal infiltrates. 60 % occur in the cerebral hemisphere while the rest occur in the cerebellum, brain stem and rarely in the spinal cord. Multicentricity occur in 25 % of cases. In the cerebral hemisphere, they occur in the basal ganglion and periventricular region with subependymal extension. Vitreous, uveal and retinal (ocular) involvement occurs in 20 %[1]. Two thirds of the ocular lymphomas will have cerebral involvement within one year. Leptomeningial involve-

ment is more common with secondary lymphomas rather than primary cerebral lymphomas.

Histology

PCNSL are diffuse rather than nodular and display a range of cytologic differentiation from small cell to mixed form and large cell type. They are almost always B-cell in origin and are aggressive in behavior[4]. Since the brain is devoid of lymphatic tissue, it is uncertain how this tumor arises; one theory holds that it represents a systemic lymphoma with a particular strong proclivity to metastasize to the CNS. However, what should be noted is that systemic lymphomas of the usual kind only rarely metastasize to the brain.

Clinical Findings

Hemispheric PCNSL usually cause behavior disturbance, personality changes, confusion, dizziness and focal cerebral signs rather than headache or other signs of raised intracranial pressure. Rarely pia arachnoid may be infiltrated and a purely meningeal form that involves the peripheral and cranial nerves may present which is known as "Neurolymphmatosis". It presents with painful, mainly motor radiculopathies. There have been cases reported with flaccid paraperesis and back and scaiatic pain, due to infiltration to the cauda equina, nerve roots and contiguous meningeal. Perivascular and meningeal spread results in shedding of cells into the CSF.

Imaging Findings

Non contrast CT shows them as seep seated, slightly hyper dense poorly defined lesions that often are in contact with the ventricular ependyma. Non contrast MRI shows them as poorly defined, hypo or isodense lesions in T1 WI and T2 WI relative to the grey matter. Enhancement in both CT and MRI studies is the rule and is more commonly homogenous. Oedema and mass effect may be inconspicuous. Bilateral lesions may occur in 24 %. Characteristic is the disappearance of the lesion of complete or transient resolution enhancement in response to corticosteroids.[3] The radiologic appearance in case of AIDS patients is less predictable and very difficult to distinguish from that of toxoplasmosis and other processes with which lymphoma often coexist.

CSF

It may show lymphocytic and mononuclear pleocytosis[2]. The immunohistochemical examination shows monoclonal lymphocytes or an elevated beta microglobulin. These findings point to Leptomeningial spread of the tumor. However, frequently the diagnosis is not possible from just cytologic examination alone.

Histologic Diagnosis

Since surgical resection is ineffective except in rare instances because the lesions are deep seated and often multicentric, streotactic needle biopsy is the preferred method of establishing the diagnosis.

Management

Different regimens have been tried. Standard lymphoma therapy has been tried with poor results, probably because of poor blood brain barrier penetration[4]. Combination of methotrexate, intrathecal therapy, radiation and high dose cytarabin or just methotrexate and radiation appears to be associated with high survival rates but substantial neurotoxicity.[5] A substantial fraction of patients developed ataxia dementia syndrome that required institution care in one study. Cranial irradiation and corticosteroids often produce a partial, or rarely, complete response but tumors recur in more than 90 %. The median survival of patients treated with this regimen is 10 -18 months and less in those with AIDS or other immunocompromised states.

The preferred treatment protocol is adopted from the "New approach to brain tumor therapy (NABTT)" consortium. This basically involves giving intravenous methotrexate[6] in a dose of 8 gm/m.[2] This is rarely associated with leukoencephalopathy or dose limiting myelosuppression. The above dose is repeated at a 14 days interval. Monthly gadolinium enhanced MRI is used to monitor response to induction. In patients who achieve a complete remission after a minimum of two treatments are administered at 14 days interval, followed by one treatment, each month for 11 more treatments. In patients who maintain complete remission, treatment is discontinued thereafter. Patients who achieve partial remission or stable disease are treated with 8 cycles of methotrexate every 14 days. Patients who relapse shortly after the conclusion of the therapy or progress during the therapy are treated with brain irradiation or supportive care. In patients who relapse after one year of therapy, re treatment with methotrexate may be the alternate to radiation therapy.

Evaluation for re-treatment include diagnostic biopsy, lumbar puncture if not contra-indicated for cytologic examination and neuro-opthalmologic evaluation. Because methotrexate is excreted in the urine, patients with renal dysfunction and serum creatinine level of greater than 2 mg/dl are not candidates for this treatment. Similarly, because methotrexate accumulates in effusions, the presence of ascites and pleural effusion are relative contraindications to this therapy[7]. During induction the urinary pH should be maintained greater than 7 and the patient should be well hydrated. This involves administration of 5 % Dextrose plus 10 mEq KCl + 50 mEq $NaHCO_3$ / L to achieve urinary output of 2.5 $L/m^2/24$ hours. Methotrexate is administered if the urine output is greater than 100 ml/hour and urine pH is greater than 7 which have been monitored for 4 consecutive days. For urine output of lesser than 100 ml/hour, the rate of intravenous fluids is increased by b25 % to 50%.

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