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PRIMARY DIFFUSE LEPTOMENINGEAL GLIOMATOSIS – AN ENIGMA

Pathology

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ABSTRACT

A 52-years-old male was diagnosed with primary diffuse leptomeningeal gliomatosis (PDLG), which is a rare meningeal neoplasm without any evidence of primary tumour in the parenchyma of the brain or spinal cord. Since the initial reporting by Bailey in 1936, less than 80 cases have been reported. The patient had initially presented with progressive alteration of sensorium of one month with blurring of vision. MRI revealed multiple meningeal deposits, without any brain or spinal parenchymal lesion. Histology of stereotactic biopsy showed an anaplastic astrocytoma displaying immunoreactivity for glial fibrillary acidic protein, representing the glial component, against a backdrop of meningeal tissue highlighted by vimentin-immunoreactivity without epithelial membrane antigen-immunoexpression. Though the patient was offered radiotherapy, but after 3 cycles he succumbed to the illness. The present case highlights an unusual location of a common CNS neoplasm, which should be considered as a differential diagnosis of meningeal lesion including treatment-resistant tubercular meningitis.

KEYWORDS

Gliomatosis, leptomeninges.

INTRODUCTION :

Leptomeningeal gliomatosis is a rare neoplasm similar to gliomatosis cerebri that is characterized by widespread infiltration of the subarachnoid space by a diffusely infiltrating glioma. It may commonly occur as meningeal infiltration of an intra-axial glioma (secondary leptomeningeal gliomatosis) or rarely, originate from an ectopic glial rest within the leptomeninges (primary leptomeningeal gliomatosis).[1] Primary diffuse leptomeningeal gliomatosis (PDLG) is an extremely rare entity distinguished by diffuse and multifocal involvement of the meninges by a glioma, with majority being detected only on postmortem examination. We hereby report another case of PDGL with morphological appearance of an anaplastic astrocytoma with tumultuous clinical course and fatal outcome.

CASE REPORT :

This 52-years-old male presented with right sided hemiparesis along with blurring of vision and slurring of speech. Magnetic resonance imaging (MRI) brain revealed multiple meningeal lesions involving supratentorial and infratentorial compartments including bilateral cerebellum and brain stem, III ventricular outlet and left cavernous sinus region (Fig1 A-B). Brain and whole body positron emission tomography (PET) scan revealed multiple foci of FDG avidity in brain parenchyma. Cerebrospinal fluid (CSF) was negative for malignant cells. Histopathology of stereotactic biopsy showed a meningeal based neoplasm in the form of an anaplastic astrocytoma (WHO grade III) with nuclear pleomorphism and frequent mitoses without any vascular proliferation or necrosis (Fig 2A]. The meningeal component was positive for vimentin-immunoreactivity while the glial component was immunopositive for glial fibrillary acidic protein (GFAP) (Fig 2B) and immunonegative for cytokeratin and epithelial membrane antigen (EMA). MIB1 labeling index was around 5% (Fig 2C).

Patient was offered definitive radiotherapy along with concurrent chemotherapy. After receiving 24 Gy/12 cycles of whole body radiotherapy along with concurrent chemotherapy, there was a sudden deterioration in his sensorium alongwith polymorphonuclear leucocytosis. Non-contrast enhanced computerized tomography (NCCT) brain revealed multiple areas of hyperdensities in bilateral basifrontal region (left more than right) that was associated with left sided compressions at ventricles along with midline shift. MRI brain showed extensive meningeal nodules around both cerebral and cerebellar hemispheres as well as right side of medulla. The largest was seen in the left supra- and parasellar regions that caused narrowing of the cavernous segment of left internal carotid artery (ICA) and M1 segment of left middle cerebral artery (MCA) precipitating acute ischemic infarcts in left parietal region. Unfortunately within 3 months of diagnosis the patient succumbed to the illness.

DISCUSSION:

PDLG is an uncommon neoplasm that may occur in two forms, viz. as a nodular solitary tumour or as a diffusely infiltrating form, with widespread involvement of the cranial and spinal leptomeninges. [2] A high-grade glioma generally heralds a poor survival for the patient, owing to lack of standardized therapeutic regimes.[3-4]

PDLG is an uncommon neoplasm with only around 80 cases documented in the literature till date.[5] Though the index case was 52 years old, but the mean age reported is around 35 years without any gender predominance. The patient typically presents with neurological symptoms primarily related to increased intracranial tension, multiple cranial nerve palsies and seizures, with rare cases manifesting with hemiparesis, like that of the present case. In addition few have also demonstrated behavioural changes, gait disturbances, visual loss, meningeal signs and coma.[2]

Examination of the CSF typically reveals increased protein levels with low or moderate pleocytosis without any malignant cells, akin to the above case.[6] Neuroimaging studies reveal ventriculomegaly with diffuse or focal leptomeningeal contrast enhancement, as was noted in this patient. In addition spinal involvement may be noted with or without contrast enhancement of the basal cisterns, cerebellum, brain stem and convexity.[2,7]

The differential diagnoses of PDLG encompass various infectious, inflammatory, granulomatous, and neoplastic pathologies. In the endemic areas it may simulate tuberculous meningitis, and display resistance to therapy when offered antitubercular drugs.[7]

Overall the mainstay of surgery is to (a) obtain an accurate diagnosis, and (b) to reduce intracranial pressure. In order to achieve the latter some patients are subjected to CSF diversion procedure in the form of ventriculoperitoneal or other alternative route shunting.[2]

Since PDLG may exhibit varying and non-specific clinical features, time course, and progression of illness, achieving a definitive ante mortem diagnosis may be a daunting task. Definitive tissue diagnosis is obtained by evaluating the tissue obtained by stereotactic biopsy for the following parameters, as suggested by Cooper and Kernohan: (a) lack of any extramedullary meningeal neoplasm attached to the neural parenchyma; (b) absence of primary neoplasia within the central neuraxis, and (c) presence of distinct leptomeningeal encapsulation around the neoplasm.[8]

The common histological subtypes of PDLG are high-grade astrocytomas, oligodendrogliomas and gliosarcomas, with a solitary

case reports documenting pilocytic astrocytoma. Apart from gliomas, leptomeninges may also have unusual tumours like ependymoblastoma, primary neuroectodermal tumor (PNET), melanocytoma, and lymphoma occurring as a primary neoplasm, which warrants detailed immunohistochemistry studies for definitive diagnosis.[7]

Owing to the small number of cases the genetic basis of PDLG is not well comprehended. However some authors have described association with loss of p53 and phosphatase and tensin homolog gene tumor suppressor gene, while others have linked it to mutation of neurofibromatosis 1 (NF1) gene.[7]

Management of PDLG includes craniospinal irradiation and chemotherapy. Beauchesne et al observed complete clinical and radiological remission for 15 months after a course of corticospinal tract radiation with chemotherapy.[9] Hansen et al noted that radiotherapy in combination with temozolomide tends to prolong the median survival time to 15 months in comparison with 5 months with radiation alone.[3] Owing to the lack of sufficient data, the index case was offered radiotherapy only and unfortunately succumbed to the illness within three months of diagnosis. It is thus apparent that PDLG with anaplastic astrocytoma has a more aggressive clinical course when compared to a similar tumour in the intraparenchymal location, possibly due to lack of any standardized therapeutic protocol.[3]

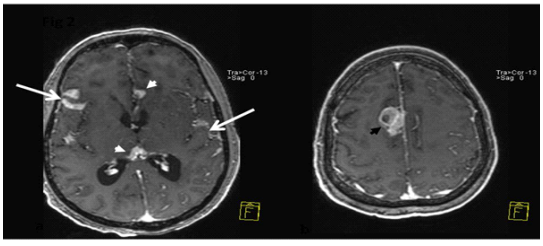

Fig 1 (A-B). Post-contrast Axial reformatted T1 weighted MR images of the brain at the level of the sylvian fissures (A) and the cerebral convexities (B) reveal well-defined enhancing lepto-meningeal plaques in the sylvian fissures (white arrows), right parafalcine region (black arrowhead) and in the inter-hemispheric fissure (white arrowheads)

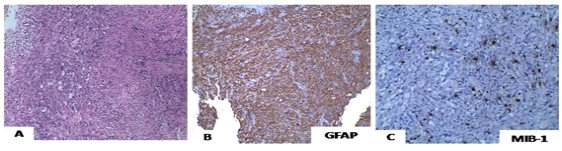

Fig 2 (A-C). Meningeal based tumour showing features of high grade diffusely infiltrating glioma (A : H&E x 100) displaying immunoreactivity for glial fibrillary acidic protein (B: GFAPx100) with proliferation of 5% by MIB-1 (C: MIB-1x200).

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