CASE REPORT

Primary diffuse leptomeningeal gliomatosis
Gliomatose leptoméningée diffuse primaire

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Introduction

Primary diffuse leptomeningeal gliomatosis (PDLG) is considered a rapidly fatal disease characterized by diffuse infiltration of the meninges by less or more differentiated...
Primary diffuse leptomeningeal gliomatosis

A 20-year-old woman attended the Department of Neurology at our hospital in June 2007 with symptoms of leg stiffness and difficulty in walking of six months’ duration. She had a history of symptoms of raised intracranial pressure (ICP) and seizures since the age of 11 years, for which she had been evaluated at a local hospital by non-contrast computed tomography (CT) and a cerebrospinal fluid (CSF) study. The CT (done on 26 January 1999) showed obstructive hydrocephalus, and the CSF study was normal. A diagnosis of Arnold-Chiari malformation was made, and she underwent a ventriculoperitoneal (VP) shunt and remained symptom-free with Carbamazepine® for two years. In May 2001, she developed recurrent symptoms of headache and weakness of the lower limbs. A contrast-enhanced CT study of the brain (done on 23 May 2001) showed a non-functioning VP shunt, but no abnormal enhancement. On repositioning the shunt to make it functional, the patient improved symptomatically but no abnormal enhancement. On repositioning the shunt, she was managed conservatively and was asymptomatic for a further five months. A CT done in January 2007 showed a normally functioning shunt (Fig. 1C) but, since then, she had developed a progressive difficulty in walking and stiffness of the lower limbs, which led to her referral to our center, a tertiary-care center for neurological diseases.

Neurological examination revealed kyphoscoliosis, downbeat nystagmus, spasticity of both lower limbs (of the right more than the left), with hyperreflexia, extensor plantar and a spastic gait. She had impaired posterior column sensations up to the ankles, and Romberg’s sign was present. Clinical examination was suggestive of a craniovertebral junction anomaly, probably an Arnold-Chiari malformation, given the long-standing hydrocephalus and second-decade onset of symptoms. Contrast-enhanced MRI of the brain and spine showed diffuse nodular leptomeningeal enhancement involving the basal cisterns and entire spinal neuraxis, with posterior scalloping of the lumbar vertebrae (Figs. 2 and 3). Tonsillar herniation and a cervicomедullary junction syrinx were noted, the former due to long-standing CSF diversion. The small syrinx was most likely due to obstruction of CSF flow at the level of the foramen magnum. She was worked-up for both infective and non-infective causes of the meningeal enhancement. CT of the chest showed no evidence of tuberculosis or sarcoidosis, and the Mantoux test was negative. Her vasculitic work up was also negative. A CSF study showed mild elevation of protein but normal sugar and cytology. No organisms were identified by staining or culture of CSF.

L4–L5 laminectomy with leptomeningeal biopsy showed no dural involvement, but the entire thecal sac was filled with a nodular, grayish-yellow lesion, which appeared to encase the cauda equina. Postoperatively, the patient did not experience any worsening of her neurological status. Histopathological examination showed features of a low-grade glioma with glial fibrillary acidic protein (GFAP) positivity and an MIB-1 labelling index of 1—2% (Fig. 4). She was not advised of any specific antineoplastic treatment due to the extensive nature of her disease and the lack of data regarding any benefit from either radio- or chemotherapy.

**Figure 1** Plain (A) and contrast (B) CT scans from August 2006 show ventricular dilatation. There are meningeal-based calcifications in the suprasellar cistern as well as post-contrast enhanced areas (B). Plain CT from January 2007 (C) shows nodular and linear meningeal-based calcification in the suprasellar cistern. The ventricles are no longer dilated following a ventriculoperitoneal shunt. Scanner sans (A) et avec injection (B) en août 2006 montrant la dilatation ventriculaire. Il existe des calcifications méningées dans la citerne suprasellaire. Des rehaussements après injection sont visibles dans la citerne suprasellaire (B). Scanner sans injection en janvier 2007 (C) montrant les calcifications méningées linéaires et nodulaires dans la citerne suprasellaire. Les ventricules ne sont pas dilatées après derivation ventriculo-péritonéale.
Figure 2  Midline sagittal MRI of the cervical spine from September 2007 shows that the cerebrospinal fluid spaces around the cord are filled with a lesion of mixed intensity in T2-weighted sequences (A), isointense in T1-weighted sequences (B) and uniformly enhanced in T1-weighted sequences after contrast administration (C). Enhancement of the suprasellar cistern is also noted. Midline sagittal MRI of the lumbar spine in T1-weighted sequence after contrast administration shows an enhancing lesion around the conus medullaris and cauda equina (D). Also, evident is the posterior scalloping of the lumbar vertebrae. Axial T1 (E), T2 (F) and T1 post-contrast (G) images show an enhancing lesion around the cord after contrast administration.

Coupe IRM sagittale médiane du rachis cervical réalisée en septembre 2007 montrant un comblement des espaces liquidiens autour de la moelle par une lésion de signal mixte en T2 (A), isointense en T1 (B) et se rehaussant de façon homogène en T1 après injection de gadolinium (C). Un rehaussement de la citerne suprasellaire est également noté (D). L’IRM sagittale médiane du rachis lombaire en T1 après injection de gadolinium montre une lésion rehaussée autour du cordon médullaire et dans le cul-de-sac dural (D). Il existe par ailleurs un scalloping des vertèbres lombaires. Les images axiales en T1 sans injection, T2 et T1 après injection montrent une lésion périmédullaire se rehaussant après injection.

in such cases. The patient underwent ventriculoperitoneal shunting for hydrocephalus, and has now survived for a period of more than 110 months without undergoing any aggressive form of therapy.

Discussion

PDLG is a tumor, in which glial neoplastic cells diffusely infiltrate the leptomeninges, but with no evidence of a primary neoplasia within the neuraxis [3]. A recent review by Yomo et al. [4] described 45 reported cases of PDLG in the age range of one to 80 years with no gender predilection. The most common symptom reported in their study was intracranial hypertension complicated by hydrocephalus. The clinical features were, however, usually confused with tuberculous or fungal meningitis. According to this review, the CSF assays in these patients usually indicated a marked increase in proteins with moderate pleocytosis and a normal or low glucose level. The study concluded that MRI with FLAIR sequences is useful for an early diagnosis of PDLG, but that a meningeal biopsy is the only definitive diagnostic investigation. In another literature review by Debono et al. [5], a total of 30 PDLG cases were reported. The age of the patients ranged from nine to 71 years (mean age: 35) with no gender predilection. Raised intracranial pressure was again the most common presentation. Ventriculomegaly was seen in 50% of patients with focal or diffuse contrast-enhancing leptomeningeal thickening. Spinal cord involvement was observed in 58% and the lesions were either diffuse or involved any one level. This review stressed the importance of contrast-enhanced MRI for diagnosing the condition.

Similar to earlier reports, our patient was also admitted with complaints of raised intracranial pressure. The initial clinical presentation and imaging findings made the clinician suspect Arnold-Chiari malformation. She underwent VP shunting for the hydrocephalus and was asymptomatic for the next three years. Contrast-enhanced CT done at this time did not reveal any enhancing lesion; this led the clinician to exclude the possibility of a mass lesion as the cause of the hydrocephalus. The next CT scan done seven years into the illness, however, showed suprasellar enhancement and leptomeningeal calcification. The absence in the earlier CT of the enhancement that showed up in the subsequent CT is an interesting finding. This is similar to the case of intracerebral glioma, which shows enhancement in
Figure 4  A Photomicrography shows the classical features of a low-grade astrocytic neoplasm, comprising stellate-shaped cells supported by a glial fibrillary matrix (HE × 200). B Immunostaining shows that the majority of cells are GFAP-positive (Avidin Biotin Complex × 200).

subsequent imaging studies especially when the grade of neoplasm changes. The repeat CSF study showed only mild protein elevation, which is probably why the clinician did not consider an infective or neoplastic pathology. This meant that the diagnosis of PDLG was missed for eight years. After admission of the patient to our hospital, the same clinical possibility of Arnold-Chiari malformation was considered. However, as suprasellar enhancement was noted in a previous CT scan, it was decided to do contrast-enhanced MRI of the brain.

The brain MRI showed diffuse nodular leptomeningeal enhancement in the basal cisterns and the entire spinal neuraxis, similar to that observed in earlier reports [6]. There was no enhancement in the cerebellum or brainstem. MRI brain findings from a previous study reported ventriculomegaly and contrast-enhancement of the basal cisterns, cerebellum, brainstem and convexity, with cranial base infiltration and extension to the sinuses and dura. In the spinal cord, the predominant involvement was diffuse or focal contrast-enhancing leptomeningeal thickening [5]. A similar appearance has also been seen in chronic meningitis [7]. In our findings, the lumbar vertebral bodies showed posterior scalloping, suggesting the long-standing nature of the lesion. Another interesting MRI finding was the meningeal-based calcification. Given the MRI diagnosis of chronic meningitis, we considered the possibility of old calcified granuloma as the cause of the calcification. However, as the biopsy was suggestive of a primary low-grade glioma with astrocytes and oligodendrocytes, the leptomeningeal calcification could be attributed to tumor calcification. This case report highlights the need for a high index of suspicion in patients with hydrocephalus in diagnosing this condition.

The etiology of PDLG remains unclear. Cooper and Kernohan speculated that neoplastic cells of a meningeal glioma presumably arise within heterotopic leptomeningeal glial nests, which can be found in the subarachnoid space, in approximately 1% of non-selected necropsies, most commonly around the medulla oblongata, and in 25% of autopsies with developmental neurological abnormalities [3].

There is no specific or optimal treatment schedule for PDLG, and its therapy has been highly variable among reported cases. Treatment for hydrocephalus consists of only external drainage or a ventriculoperitoneal shunt. Specific therapy mainly consists of whole CNS irradiation or chemotherapy (intrathecal or intraventricular), or a combination of both, which has proved effective for some patients [4,5]. The prognosis of PDLG is thought to be poorer than the solitary form, with the longest survival time of a patient being 78 months [8] and the shortest being only six weeks [9]. Our patient has survived for more than 110 months without aggressive therapy, indicating that longer survival is possible, especially in patients with lower grades of neoplasm. However, in contrast to our patient, the patients in the literature who survived for longer periods had all undergone aggressive treatment in the form of chemo- and radiotherapy [10]. As there was a low MIB index and prolonged survival without any specific treatment, our patient was neither started on chemotherapy nor subjected to irradiation. It was decided to manage this patient conservatively.

References


