

Meningeal Inflammatory Pseudotumour : A case report

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Abstract

We report the case of a meningeal inflammatory pseudotumour occurring in a 23-year-old male presenting with focal seizures and headaches. Brain imaging techniques showed a 3.5 cm left parietal meningeal tumour. Histology of the surgical specimen showed a dense lymphoid infiltrate permeating the dura mater and leptomeninges, consisting of a predominant polyclonal B cell population as confirmed by immunophenotyping and genotyping. Cultures of serum, CSF, and surgical specimen were negative and there was no serological evidence of a systemic dysimmune disease. The postoperative course was complicated by an episode of brain oedema resolving under steroid therapy. The patient, free from all medication, is asymptomatic at 3 years of follow-up. We discuss previously published cases and the nosology of intracranial inflammatory pseudotumours.

Key words : Meningeal tumour ; meningioma ; inflammatory pseudotumour ; pachymeningitis ; lymphoma.

Introduction

Meningeal tumours are most often due to neoplastic or infectious processes ; the rare cases in which neither can be demonstrated are subject to an inconsistent and confusing classification (Mirra *et al.*, 1984). Among these localised processes of undetermined etiology, a small number developing mainly in the dura mater have been described as variants of idiopathic hypertrophic pachymeningitis (Deprez *et al.*, 1997 ; Kitai *et al.*, 1997 ; Bregigeon *et al.*, 1998). A broader set of cases involving both dura mater and leptomeninges have been variously reported as intracerebral inflammatory pseudotumours, non-infectious intracerebral granulomas, or plasma cell granulomas (Llena *et al.*, 1975 ; Eimoto *et al.*, 1978 ; Castell *et al.*, 1983 ; Maeda *et al.*, 1984 ; Canella *et al.*, 1988 ; Figarella-Branger *et al.*, 1990 ; Hsiang *et al.*, 1994) reflecting both a diversity of histological findings and non-specific terminology. Although the possibility exists that some older cases might actually be lymphoplasmocytic-rich meningiomas (LPR) (WHO classification, Kleihues *et al.*, 1993), there are about thirty documented cases of intracerebral

inflammatory pseudotumours (IPT) in the literature. We report an intracerebral IPT in a 23-year-old patient in the absence of associated infectious or dysimmune disease. Immunohistological typing of the B cell infiltrate supplemented by lineage probe and PCR genotyping of B and T cells demonstrated the polyclonality of both lymphoid populations. In this patient with serological evidence of previous EBV infection, immunohistochemistry failed to disclose EBV expression in the meningeal lymphoid infiltrate.

Case Report

This 23-year-old male university student was seen in the Neurology clinic in December 1997 with recent onset of seizures characterized by transient right arm weakness and loss of dexterity with post-ictal fatigue. Prior medical history included concussions at the age of 3 and 6 years and childhood asthma. The patient also described the onset of violent headaches in 1991, apparently exacerbated by exercise — an EEG and brain CT scan performed at the time were reportedly normal, and the patient had so-called tension headaches on a regular basis since. In 1993, following a trip to Russia, he was inexplicably fatigued and febrile, but symptoms resolved spontaneously. In 1996, he reported an episode of amaurosis. Ophthalmoscopy was reportedly normal and no further investigations were performed. A family history of migraine was reported, affecting his mother, grandmother and aunt. The patient smoked half a pack of cigarettes per day.

At the time of consultation, neurological examination was strictly normal. However, a brain CT-scan showed bilateral abnormalities : a right-sided 1 cm parieto-occipital, subcortical, hypodense lesion, ill-defined, non contrast enhancing, and a left-sided parietal, hypodense, 3.5 cm tumour involving the meninges and encroached upon the underlying parenchyma, with heterogeneous contrast enhancement. Cerebral MRI performed two weeks later confirmed the left parietal meningeal tumour, hypointense on T1-weighted images,

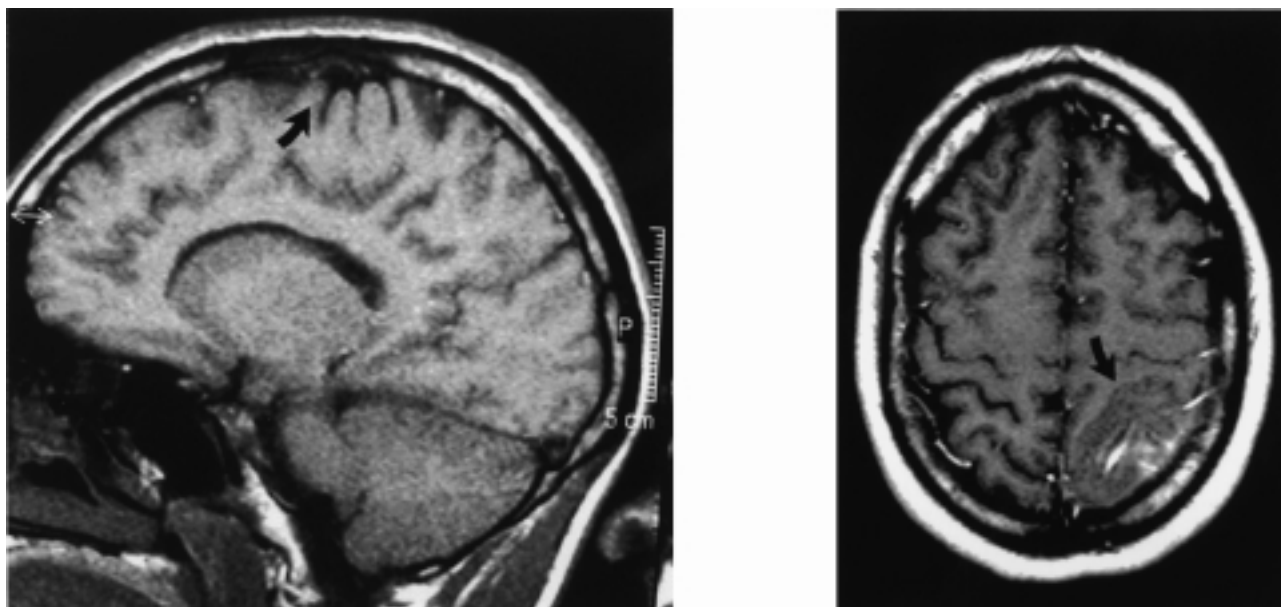


FIG. 1. — Pre-operative cranial MRI : T1-weighted image after gadolinium-DTPA injection. a) : hypointense meningeal tumour encroached upon the dura mater, slightly depressing the neighbouring cerebral cortex, with minor contrast enhancement (arrow), sagittal plane b) isointense signal in the parietal cortical and subcortical parenchyma, with no contrast enhancement (arrow), axial plane.

hyperintense on T2 sequences, with minor heterogeneous Gadolinium enhancement (Fig. 1a). The underlying parietal parenchyma appeared isointense on T1 sequences and hyperintense on T2, with no contrast enhancement (Fig. 1b). No abnormal signal was identified in the right hemisphere.

Lumbar puncture was performed and opening pressure was normal. The CSF had normal protein and glucose levels and a cell count of 27 lymphocytes/mm. Serology was positive for echovirus, EBV, coxsackie virus, and measles IgG and negative for borreliosis, toxoplasmosis, syphilis, CMV, HSV, HIV, and poliovirus.

The left meningeal tumour was resected one week later. Intraoperatively, the lesion appeared as a yellowish well-circumscribed tumour located mainly in the leptomeninges with a broad dural insertion. Despite pial adherence, a complete resection could be carried out through a natural plane of dissection between the tumour and the cortex. There was neither diffuse nor nodular thickening of the surrounding dura mater, and no remodelling of the overlying bone. Histological examination described an inflammatory pseudotumour, later confirmed by immunocytochemistry and genetic analysis. There were no operative complications. Immediate post-operative MRI confirmed complete resection of the meningeal lesion, with discrete remaining oedema of the underlying left parietal parenchyma. Bacterial and fungal cultures of the surgical specimen were negative. The patient was prescribed corticosteroids and anti-epileptic medication and discharged.

Three weeks later the patient was re-admitted for a seizure consisting of expressive aphasia, right hemiparesis and loss of dexterity and deviation of the

head to the right, with significant post-ictal fatigue. Brain MRI showed extensive left parietal parenchymal oedema, facing the operative site, and no residual tumour (Fig. 2a and 2b). Clinical and radiological features dramatically improved over a 3-week course of corticosteroids and normalised completely by the fifth postoperative month. The patient had no further seizures and he is in good health 3 years later without medication.

PATHOLOGICAL FINDINGS

The lesion consisted of a dense inflammatory infiltrate, located in both the leptomeninges and dura mater. In places, primary or secondary follicles were formed with large germinal centres (Fig. 3a). This lymphoid population was composed of plasma cells, small lymphocytes, and blast cells with immunoblastic or centroblastic features (Fig. 3b). Histiocytes were admixed in small number with the occasional formation of epithelioid granulomas in the absence of fibrinoid or caseous necrosis. Perivascular cuffs of small lymphocytes were present with focal infiltration throughout the vessel walls. There was no associated mural necrosis or thrombosis of the vessels. No meningeal proliferation was seen.

Immunocytochemistry revealed a predominant polyclonal B cell population admixed with small CD4⁺ T lymphocytes and a few CD68⁺, S-100⁻ histiocytes. The polyclonal genotype of the B and T cell population was confirmed both by semi-nested PCR selectively amplifying the junctional region of immunoglobulin heavy chains and TCR α respectively (Algara *et al.*, 1994 ; Essop *et al.*, 1997), and by cytogenetic studies of allelic polymorphism.

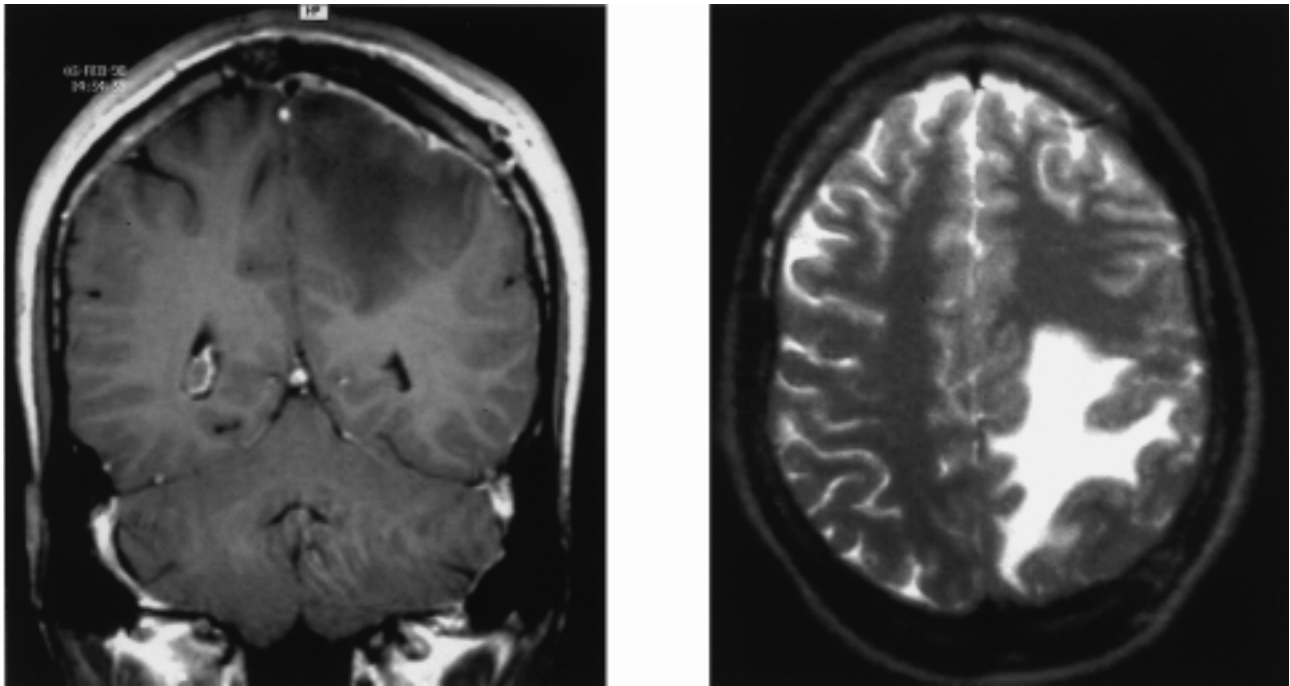


FIG. 2. — Post-operative cranial MRI. Extensive brain parenchymal oedema in the area facing the operative site, without evidence of residual meningeal tumour : a) coronal plane, T1-sequence + Gadolinium, b) axial plane, T2-sequence.

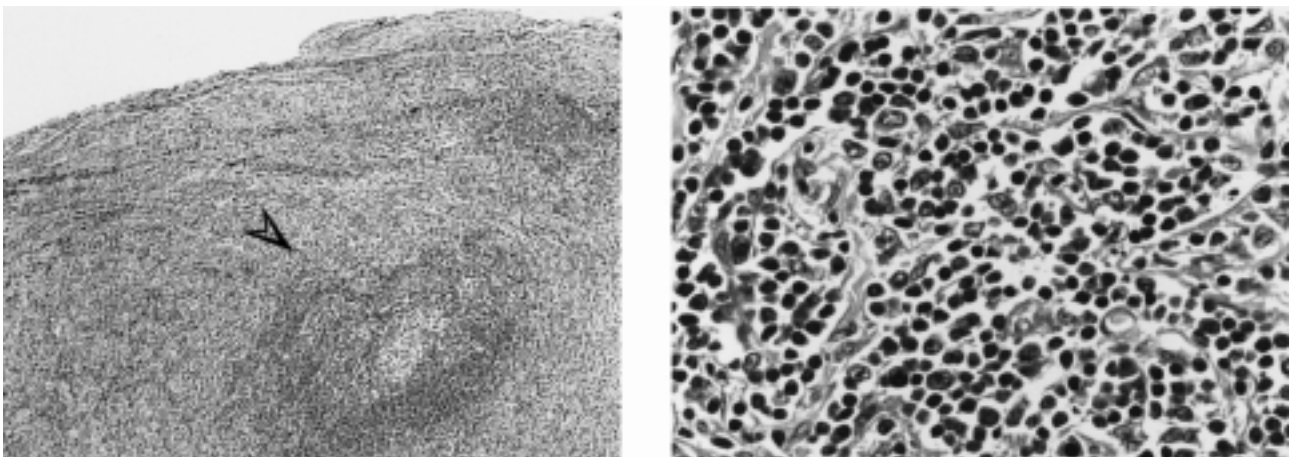


FIG. 3. — Biopsy specimen from meningeal mass : the tumour consists of a dense lymphoid infiltrate with occasional follicles (arrow), including plasma cells, small lymphocytes and numerous blasts with centroblastic or immunoblastic features (H&E, (a) 50 \times , (b) 400 \times).

Ultrastructural examination failed to show any meningotheial proliferation or viral inclusions. No immunostaining for EBV was seen in the meningeal lymphoid infiltrate.

Discussion

Meningeal inflammatory masses constitute a heterogeneous group of uncertain aetiology and have been variously reported as hyalinizing plasmacytic granulomatosis (Nazek *et al.*, 1988), inflammatory pseudo-tumour (Eimoto *et al.*, 1978), or plasma cell granulomas (PCG) (Llena *et al.*, 1975 ; Eimoto *et al.*, 1978, West *et al.*, 1980 ;

Castell *et al.*, 1983 ; Mirra *et al.*, 1983 ; Maeda *et al.*, 1984 ; Canella *et al.*, 1988 ; Figarella-Branger *et al.*, 1990). These various denominations reflect a wide spectrum of histological findings dominated by abundant numbers of lymphoid cells infiltrating both the dura mater and subarachnoid spaces. A variable meningotheial component is often mixed with lymphoid cells, representing either nests of hyperplastic meningotheial cells trapped in an inflammatory pseudotumour or islands of meningioma in a lymphoplasmocytic rich meningioma (Horton *et al.*, 1979 ; Kleihues *et al.*, 1993 ; Yamaki *et al.*, 1997).

A subset of tumours consisting almost exclusively of reactive polyclonal plasma cells have been

termed plasma cell granulomas, with reference to histologically similar lesions occurring outside the neuraxis. Russell bodies, rare histiocytes, varying degrees of fibrosis and cellularity, and a few eosinophils have been described admixed to plasma cell infiltrates (Figarella-Branger *et al.*, 1990 ; Le Marchadour *et al.*, 1994). Although a dural origin or attachment is present in the majority of intracranial PCGs, there are at least 9 cases which were intraparenchymal and one that was intraventricular (Maeda *et al.*, 1984).

Another nosological quandary concerns the classification of rare cases of idiopathic hypertrophic pachymeningitis presenting as solitary or multiple nodules (Michel *et al.*, 1969 ; Ghilain *et al.*, 1988 ; Deprez *et al.*, 1997). Various histological patterns and clinical settings have been described in these lesions but characteristically, inflammation is almost exclusively restricted to the dura mater.

The diagnosis of inflammatory pseudotumour is made at the time of histological examination and is considered after exclusion of infectious, neoplastic, or dysimmune causes. In this case, cultures of serum, CSF and on the surgical specimen were negative, notably for *Mycobacterium tuberculosis* (Michel *et al.*, 1969 ; Callebaut *et al.*, 1990), *Treponema pallidum* (Feringa *et al.*, 1975 ; Moore *et al.*, 1985), *Candida albicans* (Gorell *et al.*, 1979), *Petriellidum boydii* (Schiess *et al.*, 1984), and *Aspergillus flavus* (Mural *et al.*, 1992) all previously described in association with hypertrophic cranial pachymeningitis. However, it is not possible to formally exclude a hitherto unidentified or fastidious organism, particularly given the patient's travel history.

No meningotheial proliferation was observed after thorough sampling of the surgical specimen, followed by immunocytochemistry and electron microscopy, thus ruling out an LPR meningioma.

The reactive nature of the lymphoid infiltrate was demonstrated by immunocytochemistry and genotyping both showing a polyclonal B and T cell population. At 3 years of follow-up, the patient is in good health, with no further medical treatment, militating against a possible lymphoma or an atypical lymphoproliferative disorder.

Complete history, physical examination, and appropriate serological tests failed to show any evidence for an associated systemic disease such as rheumatoid arthritis (Spurlock *et al.*, 1983 ; Kepes *et al.*, 1986 ; Weinstein *et al.*, 1987), polyarteritis nodosa (Aström *et al.*, 1963), sarcoidosis (Ranoux *et al.*, 1992), or Wegener's granulomatosis (Nishino *et al.*, 1995). Interestingly, the long prior history of headache in this patient, the presence of two initial lesions on CT scan and the atypical post-operative oedema might nevertheless be indicative of a slow and multifocal meningeal process with more diffuse involvement than was appreciated intraoperatively.

Previous reports have emphasised the good prognosis of these idiopathic meningeal inflammatory masses and their stabilisation or regression under immunosuppressive regimens (Nishio *et al.*, 1995 ; Tanaka *et al.*, 1996 ; Deprez *et al.*, 1997). In our patient, surgical resection and a three week course of corticotherapy proved curative. Given the difficulties in classification, diagnosis and management of meningeal inflammatory masses, we believe that further case reports will be of interest in order to clarify the pathology and aetiology of these uncommon lesions.

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