Neurol Sci (2004) 25:S386–S388
DOI 10.1007/s10072-004-0349-6

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Monofocal acute large demyelinating lesion mimicking brain glioma

Abstract We report the case of a 34-year-old woman with clinical, neuroradiological and intraoperative histological findings, suggesting a low-grade astrocytic tumour. The demyelinating nature of the lesion was established through biopsy only after neurosurgery. The lesion size, in fact, greatly exceeded that of the perivenous demyelination seen in typical multiple sclerosis (MS) and tended to present as a space-occupying mass. This case underlines the importance of considering demyelinating isolated lesions in the differential diagnosis of a brain mass. Since misdiagnosis can result in unwarranted and aggressive therapy, it is critical for the neurologist to be aware of this serious diagnostic pitfall.

Key words Monofocal acute demyelinating lesions • Brain neoplasm

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Introduction

The demyelinating diseases of the central nervous system (CNS) include several clinical entities, MS being the most common and best known. Whereas the neuroradiological picture of MS is characterised by multiple demyelinating lesions separated from each other in space and time, acute, large, isolated white matter demyelinated lesions are encountered in a less defined group of diseases, usually affecting the cerebral hemispheres, and with radiological appearance and clinical course resembling a brain tumour [1]. The differential diagnosis, in addition to neoplasm, includes Schilder's disease, acute demyelinating encephalomyelitis, Balo's concentric sclerosis, Marburg's variant of MS, and brain infectious processes. Moreover, adrenoleukodystrophy, post-infection and post-vaccination encephalomyelitis and progressive multifocal leukoencephalopathy may rarely present as a mass lesion, while the concurrence of MS and brain tumour is exceptional [2].

Since misdiagnosis can result in unwarranted procedures [3], it is critical for the neurologist to be aware of this diagnostic pitfall.

Case report

A 34-year-old healthy woman began to perceive rotation of the surroundings, with loss of postural control, and tendency to list towards the left. At examination, left deviation during the Unterberger test was observed, and a torsional nystagmus during Semont manoeuvre appeared in the II left position. Benign paroxysmal positioning vertigo was diagnosed and the patient was treated with particle repositioning. Because of the persistence of unsteadiness, the patient was submitted to neuroradiological investigations revealing a 20 mm cystic, space-occupying lesion, with surrounding edema, and located in the subcortical white matter of the right frontal lobe. The lesion was hypodense on CT scan, hypointense on T1 (Fig. 1a), and hyperintense on T2 and proton density MRI (Fig.

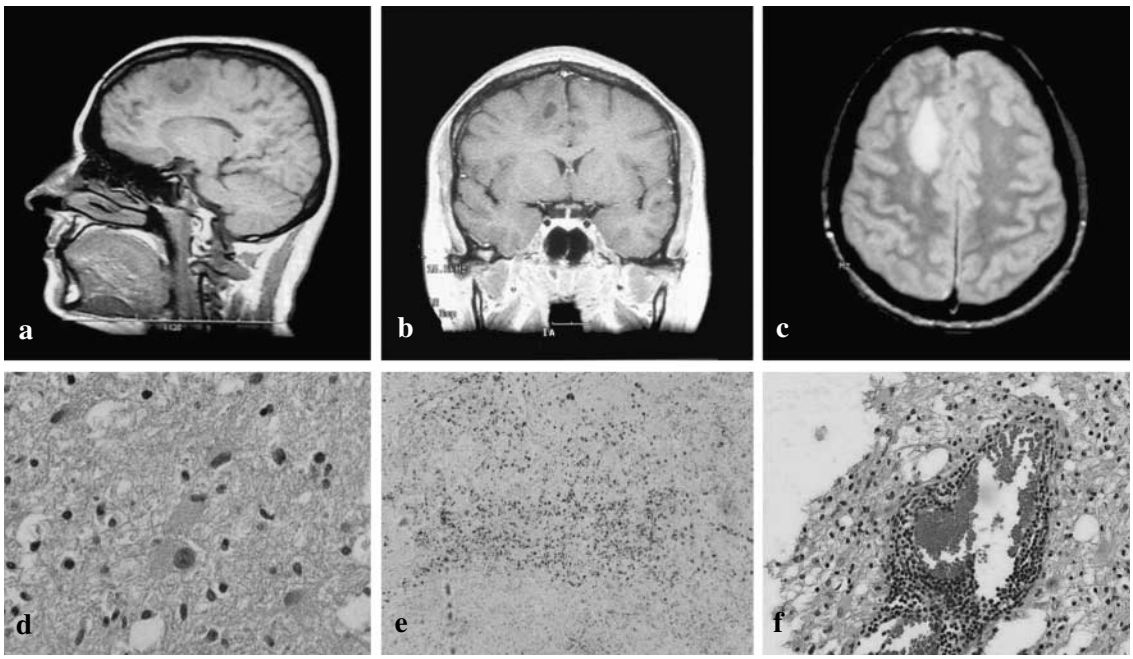

Fig. 1a Sagittal T1-weighted MRI; **b** Coronal post-Gadolinium T1-weighted MRI; **c** Axial proton density MRI, showing a not enhancing cystic space-occupying lesion, located in the subcortical white matter in the right frontal lobe, with perilesional edema, mimicking a low grade glioma. **d** Hematoxylin-eosin staining of biopsy specimen showing foamy macrophages and moderate gliosis (original magnification x 400); **e** Macrophages are identified by immunostaining for CD68; **f** perivascular infiltration of lymphocytes, lipid-laden macrophages and some reactive astrocytes, cuffing around some of the venules (hematoxylin-eosin, original magnification x200)

1c), without contrast enhancement (Fig. 1b). Neurosurgery was performed under the presumptive diagnosis of glial neoplasm. At macroscopic examination the lesion presented as a subcortical, greyish, not well-defined solid mass with a cystic area inside. Intraoperative frozen sections showed marked hypercellularity with a prominent astrocytic component, having pleomorphic, slightly irregular nuclei, suggesting a low-grade glioma. The lesion was completely removed, and the patient was discharged with full recovery. However, a subsequent histological examination revealed a diffuse infiltration of inflammatory cells in the white matter, mainly reactive astrocytes and lipid-laden macrophages (Fig. 1d), and perivascular cuffing by T-lymphocytes and macrophages (Fig. 1f). Myelin staining showed demyelination foci with relative axons sparing in areas of myelin loss. Immunostaining with CD68 (Fig. 1e), CD3, CD79, GFAP, and antineurophilaments antibodies showed abundant infiltrating and reactive macrophages. No atypical astroglial nuclei, necrosis, or vascular proliferation were observed. The histological picture was consistent with a unique demyelinating lesion.

Lumbar puncture was then performed, and CSF standard analysis was normal, blood-brain barrier (BBB) damage, IgG intrathecal synthesis, and oligoclonal IgG bands were absent. Serum and CSF antibodies to Borrelia Burgdorferi and Treponema Pallidum, CSF culture for bacteria and fungi, and CSF and blood n-PCR for a large panel of viral agents were negative. Evoked potentials (EP), routine laboratory values, thyroid function, B12 vitamin and folic acid were normal. Autoimmune diseases were excluded by appropriate tests. After a two-year follow-up, the patient was relapse-free and no evidence of further lesions was found at control brain and cervical MRI.

Discussion

Solitary, tumour-like demyelinating lesions (TLDL) of the brain are rare. A few papers describe series of such cases, the largest ones including 31 and 14 patients [1, 3]. These lesions are estimated as 1–2/1000 cases of MS or chronic CNS inflammatory disorders [4]. The onset may occur at any age, and women seem to be more interested than men. TLDL are mainly localised in the subcortical hemispheric white matter, without preference for periventricular areas [1]. Their nature is uncertain. It has been suggested that they may represent a transition to MS, a variant of MS [4], or a unique form of isolated demyelinating diseases between MS and postinfectious/postvaccination encephalitis [1]. Clinical manifestations include single episodes without relapses, or with one or two relapses in the short term but no recurrence over many years, and, despite the extensive demyelination, the course is rather benign. TLDL may rarely evolve to MS, but this is unpredictable [1]. In our patient the absence of CSF and EP abnormalities, the lack of clinical relapses, and of MRI worsening after two years, make MS unlikely.

The unspecific features of TLDL represent a diagnostic challenge. MRI is the method of choice showing different patterns of enhancement (homogeneous/patchy and ring/nodular), correlated with active demyelination and BBB breakdown in the acute stage [5]. A smooth contrast-enhancing rim with little surrounding edema, the "open ring" sign [6], MRI diffusion and perfusion sequences, and MR spectroscopy profile [7], may guide toward the demyelinating nature of the lesion. However, neuroimaging may not be helpful in the case of TLDL resembling low grade astrocytomas, as reported here, and, if the physicians do not consider this possible diagnosis, only histology following invasive procedures reveals a demyelinating lesion.

The key distinguishing histological features are the presence, in the white matter, of foamy macrophages uniformly distributed along the axons, and of atypical gemistocytic astrocytes adequately distanced from each other and with well-formed processes [8]. Perivascular infiltration of macrophages and T lymphocytes, sharply limited myelin loss with axons preservation, and effective immune-staining for histiocytes, also support this difficult diagnosis.

In conclusion, the present case illustrates the importance of considering a demyelinating isolated lesion in the differential diagnosis of brain mass lesions, before performing inappropriate and aggressive treatments.

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