

## SHORT REPORT

## Devic's neuromyelitis optica and Schilder's myelinoclastic diffuse sclerosis

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### Abstract

**An adult patient developed both Devic's neuromyelitis optica and Schilder's myelinoclastic diffuse sclerosis, suggesting that these entities represent rare topographical and aggressive variants within the spectrum of multiple sclerosis.**

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Since the original descriptions of neuromyelitis optica by Devic<sup>1</sup> and Schilder's myelinoclastic diffuse sclerosis,<sup>2</sup> there has been controversy as to whether they are separate nosographic entities,<sup>3-5</sup> two topographical variants of one aetiologically undefined demyelinating inflammatory process, or rare variants of multiple sclerosis (MS).<sup>6</sup> Factors to support delineation from MS are the non-disseminated mono- or bifocal distribution of the lesion,<sup>4</sup> a CSF syndrome considered as characteristic,<sup>5</sup> and involvement of the spinal grey matter in neuromyelitis optica.

There is only one detailed description of a case of necropsy proven transitional myelinoclastic diffuse sclerosis and neuromyelitis optica,<sup>7</sup> although such an association has been described previously.<sup>8</sup> We describe a patient who developed features of neuromyelitis optica and myelinoclastic diffuse sclerosis, with full clinical, neuroradiological, biochemical and neuropathological findings.

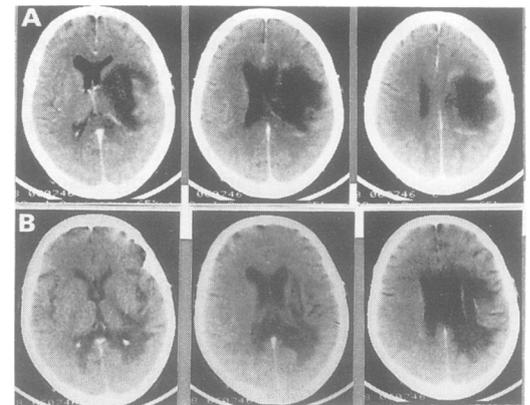
### Case report

A previously healthy 40 year old woman developed paresis of the lower limbs which progressed within two weeks to complete paraplegia with sensory level at T-10 and bladder and bowel dysfunction. Myelography and consecutive CT scan of the thoracic spine were normal. Two days later fever occurred, and the sensory level ascended to T-5. Blood leukocytes were 16,600/ $\mu$ l; the erythrocyte sedimentation rate was 27 mm in the first hour. CSF had 277 predominantly polymorphonuclear cells per  $\mu$ l, its protein was 1.65 g/l, CSF/blood sugar ratio was 2,33/7,77 mmol/l. Intrathecal IgG, IgA and IgM production was found with indices of 0,74; 0,54 and 0,93, respectively. Antibodies against neurotropic viruses, *Borrelia burgdorferi*, *Brucella abortus*, *Legionella*, *Yersinia* and *Toxoplasma gondii* were absent in paired blood and CSF samples. Blood and CSF cultures for bacteria, including

*Mycobacterium tuberculosis*, and for fungi remained sterile. MRI showed a high signal intensity lesion in the cord at T5-8. Because of relapsing fever and persistent leukocytosis, antibiotic therapy with penicillin G, oxacillin, chloramphenicol, and Latamoxef-Dinatrium was started. Within one week, the fever subsided and CSF findings turned to normal. Paraplegia remained unchanged. Transverse myelitis of unknown aetiology was the first diagnosis.

Ten months later, the patient presented with progressive loss of vision on the right eye. Optic neuritis was diagnosed and corticosteroid therapy was initiated. One week later, she developed left sided optic neuritis. Corticosteroid therapy was continued for 3 weeks with partial improvement of visual capacity. Cerebral CT scan and CSF were normal. The patient was put on 50 mg/d azathioprine.

Three months later, progressive weakness of the left upper extremity developed. CSF had a normal cell count but slight intrathecal IgG production. Cerebral CT scan showed a small hypodense lesion in the right basal ganglia. Three weeks later, the CT scan showed enlargement of the hypodense area with slight mass effect and contrast enhancement at the margins of the lesion (fig 1A). A stereotactic needle biopsy of the parietal white matter on the right side was performed. Histopathology



**Figure 1** CT scans after application of contrast medium. (A) Six weeks before death, a right hemispheric hypodense lesion with contrast enhancing margins compresses the right lateral ventricle and causes slight midline shift to the left. (B) One month later, the hypodense lesion involves, with exception of the frontal lobe, almost the whole right hemispheric white matter and the corpus callosum without mass effect. The margins of the lesion still show slight contrast enhancement.

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did not give an unequivocal decision between a low grade glioma and an unusual demyelinating process. Neurological signs and symptoms progressed continuously, leading to left hemiplegia. Within weeks the right extremities also showed spastic paresis. Another CT scan two weeks before death showed extension of the lesion to almost the whole hemispheric white matter on the right and to the corpus callosum (fig 1B). Seventeen months after onset of illness, the patient died in a decerebrate state.

### Necropsy

The internal organs were congested, the lungs were oedematous and the heart was dilated. Formalin fixed brain and spinal cord were examined. Grossly, the white matter of the brain showed a huge zone of diminished consistency, predominantly in the right hemispheric white matter. This lesion involved the periventricular deep white matter of the frontal lobe, the whole corpus callosum and almost the whole white matter of the parietal, occipital and temporal lobes (fig 2B). In the left hemisphere, the lesion was confined to the medial white matter (fig 2A). The whole spinal cord was atrophic, predominantly in the lumbosacral region. Histology of the white matter lesion of the brain revealed a sharply delineated continuous demyelinating process with comparatively well preserved axons, reactive astrogliosis, and perivascular lymphoid cell infiltrates of varying prominence. Subcortical U-fibres were generally spared. In addition to active lesions, burnt out areas of dense fibre gliosis encompassed the whole chiasma opticum (fig 3A) and the spinal cord from the midthoracic to the lumbosacral levels. In the lumbosacral region, there was extensive transverse necrosis with numerous fat laden macrophages and mononuclear cells between fibrovascular septa (fig 3C). At upper thoracic and cervical levels of the spinal cord, the tractus graciles and, to a lesser extent, the pyramidal tracts showed Wallerian degeneration. In the anterolateral funiculi, patchy demyelination and gliotic areas focally exten-

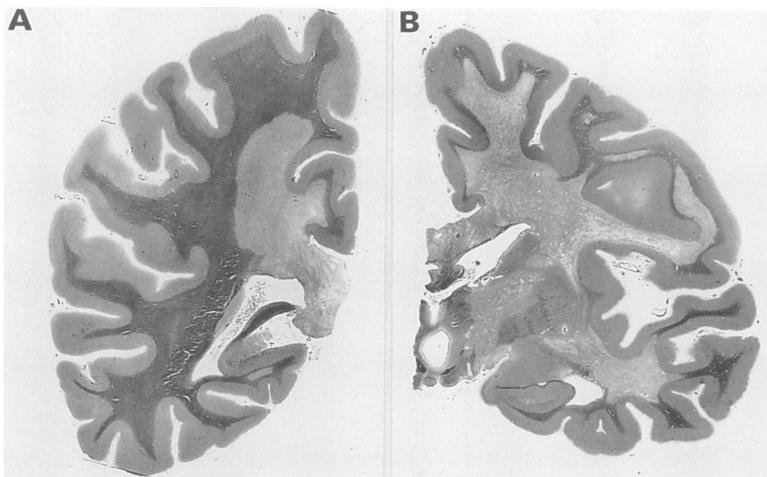


Figure 2 (A) A left parieto-occipital section shows demyelination involving the corpus callosum and the adjacent periventricular white matter. (B) A right hemispheric section shows almost complete demyelination with sparing of the subcortical U-fibres. A, B: Luxol fast blue stain for myelin.

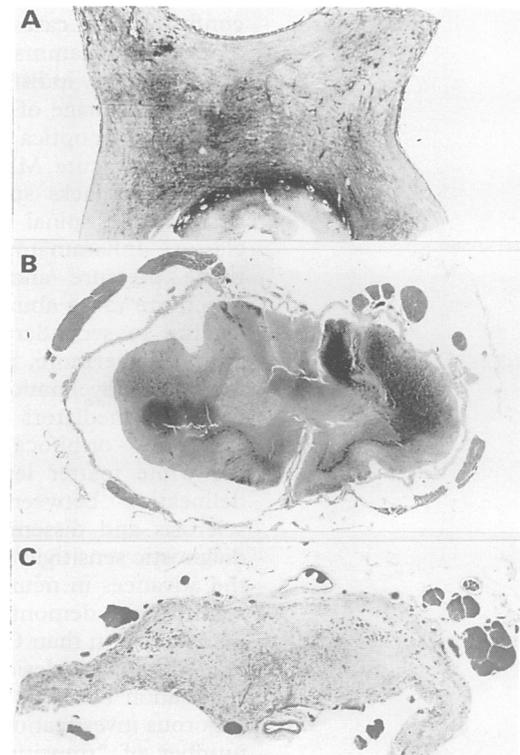


Figure 3 (A) The optic chiasm shows complete demyelination with patchy dense fibre gliosis. (B) At the lower cervical level, extensive demyelination involves the gracile tracts and subpial white matter. The grey matter shows patches of necrosis. (C) The lower thoracic spinal cord shows replacement of normal nervous tissue by fibroglial scar tissue; nerve roots are preserved. A: Kanzler stain for glial fibres, original magnification:  $\times 4$ . B, C: Luxol fast blue stain for myelin, original magnifications:  $\times 11$  (B),  $\times 12$  (C).

ded to the adjacent grey matter (fig 3B).

Thin layer chromatography of extracted lipids of formalin fixed white matter (Drs B Molzer and H Bernheimer, Neurological Institute, Vienna) did not reveal accumulation of very long chain fatty acids.

### Discussion

Classification of most inflammatory demyelinating processes is based on the clinical symptom manifestations and pathological findings. Like all non-aetiological classifications, it is unreliable. Various inflammatory demyelinating lesions of different histopathological character may, in individual cases, present as monomorphic clinical syndromes if they are similar in topography and amount of tissue damage. The clinical complex of DNO occurs in acute multiple sclerosis, acute disseminated encephalomyelitis, and haemorrhagic leukoencephalomyelitis.<sup>6,8</sup> Delineating a CSF syndrome indicative of neuromyelitis optica<sup>5</sup> is difficult because of such heterogeneity. Similarly, myelinoclastic diffuse sclerosis is not a distinct symptom complex and was introduced as a topographically extensive demyelinating white matter lesion of the brain,<sup>3</sup> the features of which caused terminological confusion.<sup>4</sup> Some cases of "Schilder's disease" represent adrenoleukodystrophy; this diagnosis was ruled out in our patient by biochemical analysis. Reviews of the neuropathological literature

confirm most cases of so called Schilder's disease as inflammatory demyelination<sup>4</sup> with histopathology indistinguishable from MS.<sup>4</sup> In contrast, damage of the spinal grey matter in neuromyelitis optica argues against the demyelination of acute MS.<sup>3</sup> Unlike the brain, the spinal cord lacks sufficient space to expand because the spinal pia mater is rather unelastic.<sup>9</sup> Inflammatory oedema may increase tissue pressure and compress microvessels which are more abundant in the grey matter, leading to secondary microcirculatory damage.<sup>9</sup> Furthermore, necroses in acute inflammatory demyelination may be due to focal release of mediators of inflammation.<sup>10</sup>

A mono- or bifocal topographical pattern of the white matter lesion as required for the delineation between myelinoclastic diffuse sclerosis and disseminated MS<sup>4</sup> depends on diagnostic sensitivity which has increased with the advances in neuroradiology. MRI is more sensitive in demonstrating multiple foci of demyelination than CT and may have demonstrated multiple lesions in brains where dissemination has been ruled out only by CT.<sup>11</sup> Rigorous investigation might thus increase the number of "transitional" cases<sup>6</sup> of myelinoclastic diffuse sclerosis (MDS) and further blur the distinction between MDS and MS.<sup>11</sup> At necropsy our patient had lesions at three different sites and of different stages; the burnt out necrotising myelopathy, the old demyelination of the optic chiasm, and the huge cerebral

demyelination with old and more recent lesion stages.

Our case demonstrates by detailed clinical, neuroradiological and neuropathological examination that neuromyelitis optica and MDS may subsequently occur in a patient leading to the suggestion that these entities represent rare topographical and aggressive variants within the spectrum of MS.

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