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Recurrent myelinoclastic diffuse sclerosis: a case report of a child with Schilder's variant of multiple sclerosis

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Abstract Myelinoclastic diffuse sclerosis (MDS, Schilder's disease) is a rare CNS demyelinating disorder affecting mainly children and usually presenting as an intracranial mass lesion. We report the first case of recurrent intracranial MDS where the third episode of demyelination involved the cervical spinal cord. This may represent a subset of the disease, which should be considered as Schilder's variant (childhood form) of multiple sclerosis.

Introduction

Myelinoclastic diffuse sclerosis (MDS, Schilder's disease) is a rare CNS demyelinating disorder affecting mainly children and usually presenting as an intracranial mass lesion [1–4]. In an attempt to restrict the use of the eponym to diseases identical to the original description by Schilder in 1912 [5], Poser [6] in 1985 established restrictive diagnostic criteria for 'true' Schilder's disease. In 1970, Poser had renamed the original disorder described by Schilder as MDS [7].

In more recent years there have been a few papers discussing not only the variable presentation and imaging findings of this disease, but more importantly its management and longer term follow-up and outcome. [1, 3, 4, 8].

We present, we believe, the first reported case of recurrent intracranial MDS (fulfilling Posner's criteria) where the third episode of demyelination involved the cervical spinal cord. This may represent a subset of the disease, which should be considered as Schilder's variant (childhood form) of multiple sclerosis (MS) [1, 9, 10].

Case report

A 6-year-old boy was admitted with a 3-day history of altered gait. His previous medical history was unremarkable; in particular there was no preceding viral illness or recent vaccination. On examination, he was afebrile and had a left hemiplegic gait with circumduction of the left leg, left foot drop and an up-going plantar response. He also showed left arm drift and weakness of left shoulder abduction. Routine blood tests, including ESR, were normal. Lumbar puncture and CSF analysis were normal and no oligoclonal bands were present.

Cranial CT scan revealed a 3-cm partially rim-enhancing mass in the deep white matter of the right fronto-parietal lobes. Mass effect was minimal, but perilesional oedema extended deep into the parieto-occipital region (Fig. 1).

Cranial MRI, performed 2 days later, confirmed a solitary right-sided posterior parietal lesion (Fig. 2a), but revealed more extensive perilesional oedema and white matter changes involving the splenium of the corpus callosum (Fig. 2b), as well as white matter changes in the right frontal, occipital and temporal lobes. (Fig. 2c).

The diagnosis of a tumour was suspected because there was no clinical or laboratory indication of infection. The patient was commenced on dexamethasone 2 mg q.i.d. (for the oedema) by the neurological team prior to biopsy.

Histopathological examination of the stereotactic brain biopsy revealed hypercellularity due to PAS-positive macrophages clustering around blood vessels, aberrant intermixed reactive astrocytes and scattered T-cell lymphocytes with no signs of viral

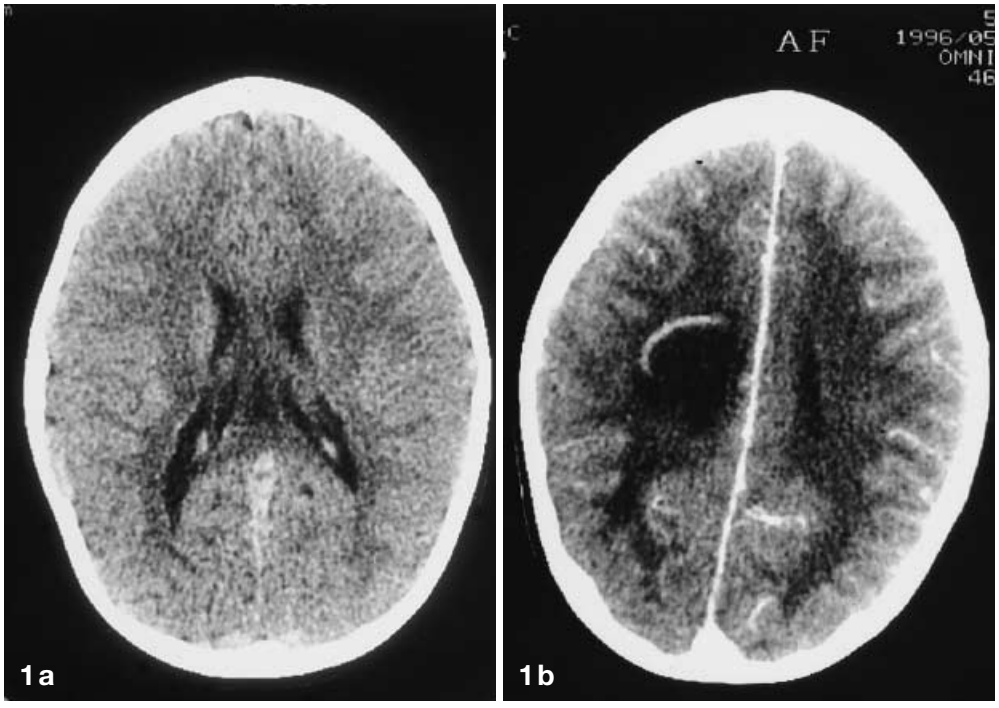
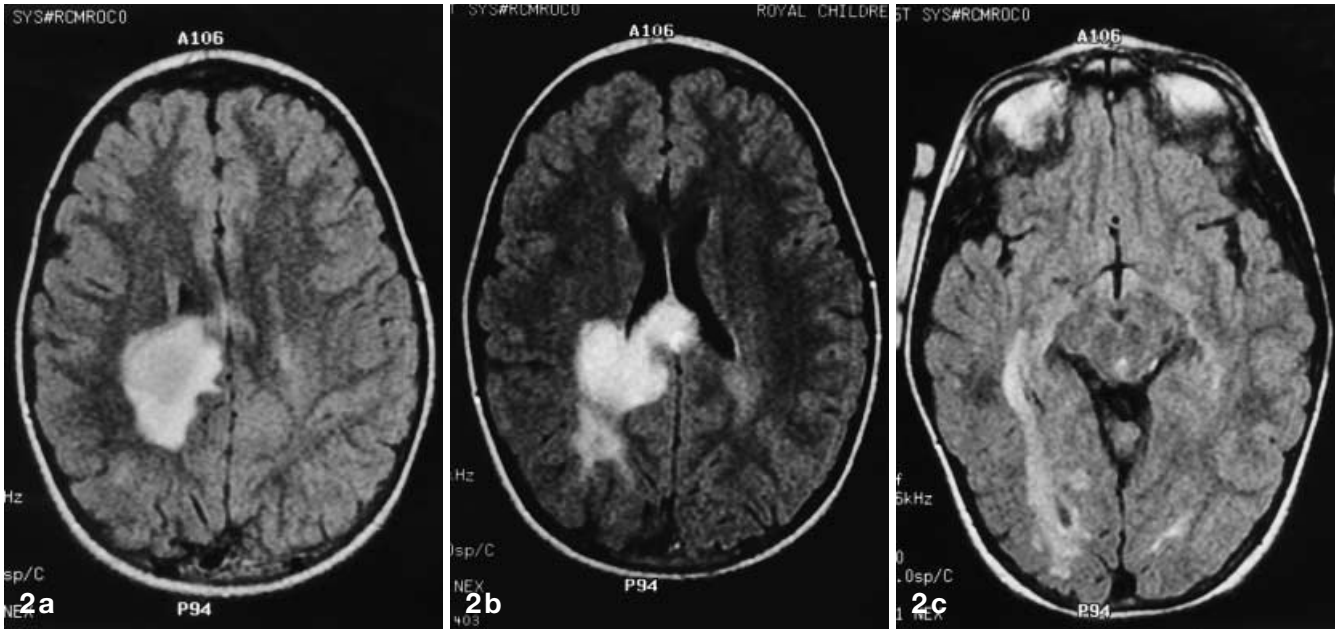


Fig. 1 a, b Axial contrast-enhanced CT. **a** Through the bodies of the lateral ventricles and splenium of the corpus callosum. There is no abnormality. **b** Through the centrum semiovale. There is a large, low-attenuation, partially ring-enhancing mass in the right frontoparietal white matter

Fig. 2 a–c Axial FLAIR MRI. **a** The mass shows as an extensive area of variable high signal. **b** There is much more extensive white matter oedema and mass effect, including involvement of the splenium of the corpus callosum than in the CT image at the same level (Fig. 1 a). **c** There is involvement of the right temporal lobe white matter



infection. Findings were compatible with sharply demarcated acute demyelination. Lysosomal enzyme studies and plasma very long chain fatty acids (VLCFA) were normal.

The patient was commenced on i.v. methylprednisolone with gradual improvement in symptoms and was discharged on a tapering dose of prednisolone, which was discontinued. Review at 6 months showed good functional recovery with only very mild left hemiplegia and residual up-going left plantar response.

The patient was re-admitted 25 months after his original presentation with a right hemiparesis. Examination revealed right leg weakness, gait ataxia and impaired proprioception on the right. There was no change in the residual up-going left plantar response or very mild left hemiplegia.

CT and MRI showed a new, 3-cm, left-sided, parietal white-matter lesion with imaging characteristics similar to the original right-sided area of tumefactive demyelination, again showing partial peripheral enhancement (Fig. 3). Residual white-matter signal change remained in the right parietal lobe (Fig. 3 b), but was less when compared to the original imaging. No other lesions were identified.

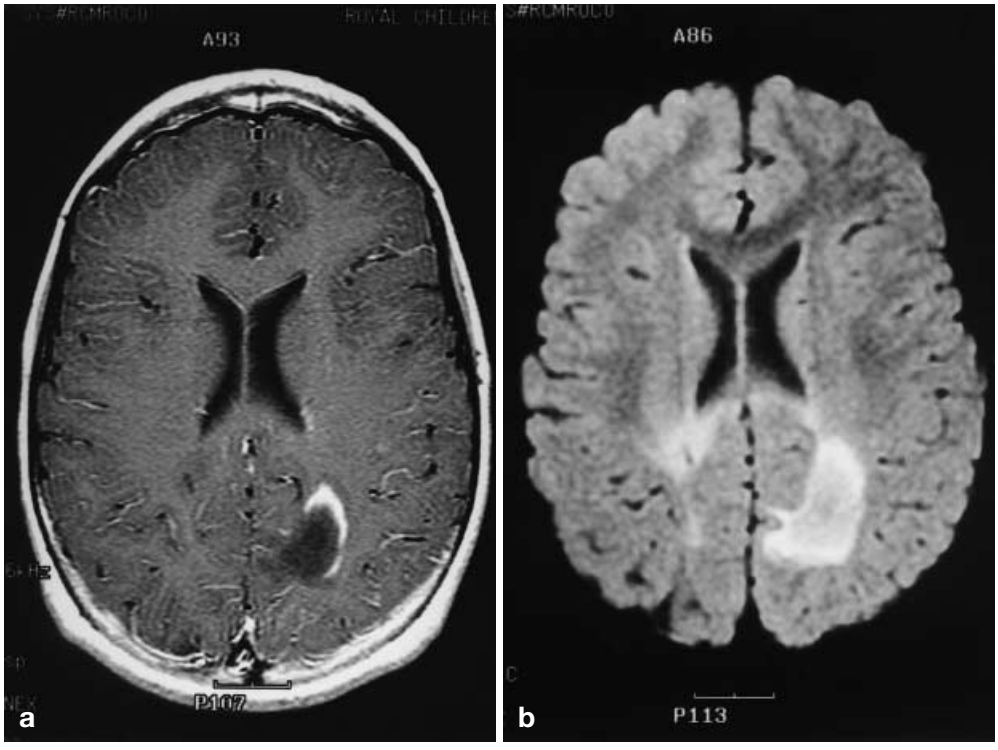


Fig. 3 a, b MRI 25 months after the original presentation. **a** T1-W post-gadolinium image, showing a large hypointense partially ring-enhancing lesion in the left parietal region. **b** EPI FLAIR image showing the new hyperintense lesion with more extensive oedema and the residual white matter changes in the right periventricular white matter and splenium

Serological investigations remained normal. On this occasion no brain biopsy was performed. A diagnosis of recurrent MDS (Schilder's disease) was made and the patient again treated with i. v. methylprednisolone. His acute symptoms almost resolved during his 2-month admission, but had resolved at his 1-month post-discharge review when he was on oral prednisolone 50 mg twice daily. The residual very mild left hemiplegia persisted as a sequela of the first episode of demyelination.

Over the ensuing 12 months his oral prednisolone was tapered to 10 mg on alternate days with the aim of ceasing medication. However, he represented 40 months after the initial episode and 15 months after the second episode with pins and needles and tingling in both fingers, mild ataxia, nystagmus, new bilateral up-going plantar reflexes and hyperreflexia of the lower limbs.

Repeat MRI of the brain showed new and increased signal in the splenium and posterior body of corpus callosum (Fig 4 a) and stable residual signal changes in the right parietal lobe with mild leukomalacic changes in the area of biopsy. There was complete resolution of the left parietal lobe demyelination. MRI of the cervical spine was performed because of the upper limb signs and showed an area of upper cervical cord (C1–2) signal abnormality with mild cord expansion compatible with tumefactive demyelination (Fig. 4 b). A further course of i. v. methylprednisolone was started with resolution of his new signs and symptoms. He was discharged on oral prednisolone and is currently being considered for beta interferon therapy. At discharge, it was felt the cervical demyelination put him at greater risk of 'Schilder's variant of MS'.

Discussion

This case represents, we believe, the first reported example of recurrent intracranial MDS (Schilder's disease, fulfilling Posner's criteria [6]) with a third episode of demyelination involving the cervical spinal cord 40 months after initial presentation. We postulate that this case should be considered as 'Schilder's variant of MS' [1, 10, 11].

As discussed by Garell et al. [1], it is possible that there are at least two subsets of Schilder's disease, the first being a self-limiting monophasic type and the second a progressive type which may be either recurrent/relapsing intracranial disease or progressive non-relapsing intracranial disease that culminates in death [1, 10]. We suggest our case represents a third subset of remitting/relapsing intracranial Schilder's disease with a further relapse involving the spinal cord. This then becomes 'Schilder's variant of childhood MS'. No abnormal blood or CSF workup has ever been demonstrated so, as discussed in the other papers [1, 4, 8], there is no way of predicting which group each child will fall into until the disease manifests itself.

Given our child's initial presentation and the imaging findings of a large solitary white-matter lesion located in the frontoparietal white matter with oedema, mass effect and incomplete rim enhancement, a glial tumour was thought to be the most likely diagnosis [12]. An abscess was thought unlikely because of the clinical presentation, normal blood workup and because the rim enhancement was limited to only one side of the lesion. Complete ring enhancement is more typical for an abscess [12]. MDS was considered, but felt less likely be-

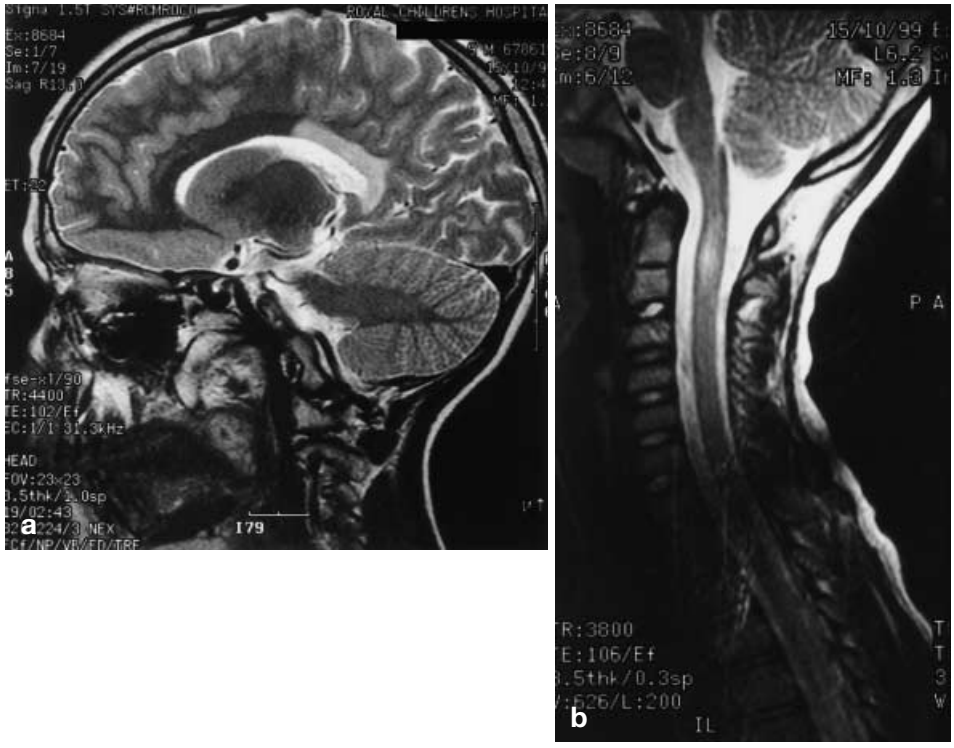


Fig. 4 a, b Sagittal T2-W MRI 40 months after the initial presentation and 15 months after the second presentation. **a** The image through the brain shows the new oedema in the corpus callosum. **b** The image of the cervical cord shows oedema and swelling of the upper cord

cause of the degree of mass effect, oedema and its being a solitary lesion. Lesions of MDS are typically located in the centrum semiovale, often bilateral, with minimal oedema, mass effect and enhancement limited to one side of the lesion [1, 5–7, 9]. More recent reports have now shown that mass effect and oedema may be present, and the lesions may be solitary or multiple, but confined to one hemisphere [1, 3, 4]. Tumefactive MS also has similar imaging findings [8, 10–13].

Acute disseminated encephalomyelitis (ADEM) was not considered because of the lack of history of a recent viral illness ([12, 13], A. Kornberg, personal communication) and the imaging findings in ADEM are often subcortical, less confluent, less likely to have mass effect and in 50–60 % of cases there is associated deep grey matter involvement. Adrenoleucodystrophy (ALD), which has MRI features similar to MDS, is usually bilateral, symmetrical and mainly occipital in distribution, was felt less likely and was excluded biochemically (normal VLCFA).

Histopathological examination of the biopsy specimen described the initial lesion as compatible with acute well-demarcated demyelination, and the diagnosis of MDS was therefore made in conjunction with the imaging findings. However, histopathologically, MS is indistinguishable.

Management involved treatment with high-dose intravenous and then a short course of oral steroids. The second episode of demyelination was managed with a longer course of high-dose steroids, which were being gradually decreased over the subsequent year. However, when on 10 mg prednisolone on alternate days, the third cervical relapse occurred. Although this responded to high-dose steroid treatment, beta interferon is now being contemplated, as this child considered 'at risk' for MS. Others have used intravenous immunoglobulin, with questionable effect [1].

In conclusion, we suggest that our case represents another part of the complex spectrum of childhood demyelination of which ADEM and transverse myelitis could be considered at one end with Schilder's disease and childhood MS at the other ([1, 3–13], A. Kornberg, personal communication). Some authors believe that Schilder's disease is, in fact, a form of MS [9, 12], whereas others see it as a separate disorder. Both have the same histopathology. In the absence of a biological marker, the distinction between ADEM, MDS and MS remains difficult. They have characteristic but non-specific clinical, pathological and neuroradiological features. Currently, clinical history, evidence of viral infection, lesion load, absence or presence of oligoclonal bands, whether the disease is monophasic, progressive, relapsing or remitting, associated with neuroradiological findings are all important in trying to establish a definitive diagnosis.

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