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CASE REPORT

Schilder's disease: non-invasive diagnosis?

A case report and review

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Abstract Schilder's disease, or myelinoclastic diffuse sclerosis, is a rare disorder characterised by an inflammatory white matter plaque of demyelination. Clinical signs and symptoms might be atypical for early multiple sclerosis and at imaging the lesion is easily taken for a brain tumour. Regardless of the use of Poser's criteria for clinical diagnosis of Schilder's disease proposed in 1986, diagnostic difficulties are still present, as evidenced by the many reported cases in the English literature revised (Pubmed indexed, period 1998–2008). It clearly emerges that neuroradiological features, observable in additional magnetic resonance sequences are crucial, besides the consideration of Poser's criteria, in differentiating between demyelinating lesions and brain tumours. A 29-year-old female patient is presented, where a careful evaluation of both the clinical and radiological features, which might have been at a first glance misleadingly suggestive for a brain tumour, allowed non-invasive diagnosis of Schilder's disease.

Keywords Schilder's disease · Myelinoclastic diffuse sclerosis · Brain tumour · Magnetic resonance (MR) · MR spectroscopy (MRS) · Non-invasive diagnosis

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Introduction

Schilder's myelinoclastic diffuse sclerosis is a rare acute or subacute demyelinating disorder diagnosed mainly in young patients [1]. Schilder first described the disease in 1912 as diffuse sclerosis [2]. For 80 years after this first report there has been nosological confusion on the use of this eponym. In 1986 Poser et al. [3] established restrictive diagnostic criteria for non-invasive diagnosis of Schilder's disease. These criteria can be resumed as follows: (1) clinical symptoms and signs atypical for an early course of multiple sclerosis (MS)-like bilateral optic nerve involvement, signs of intracranial hypertension, aphasia, psychiatric manifestation, (2) a normal cerebrospinal fluid (CSF) or atypical for MS, (3) one or two symmetrical bilateral plaques measuring at least 3 × 2 cm and involving the centrum semiovale of the cerebral hemispheres on brain scans, (4) no fever, viral or mycoplasmal infection, or vaccination preceding the symptomatology; and (5) a normal serum concentration of very long-chain fatty acids.

Despite the Poser's clinical criteria, the differential diagnosis with brain tumours of these large demyelinating brain lesions is often difficult [4, 5] and invasive procedures are still the gold standard for diagnosis. Unfortunately also biopsy is often unsuccessful: in 19% of the cases described in the revised literature, biopsies were not diagnostic.

Careful analysis of our patient and of other reported cases of Schilder's disease, evidence the helpfulness of some specific neuroradiological considerations when getting through the differential diagnostics. The necessity, but also the feasibility of non-invasive diagnosis is discussed.

Literature review

English literature has been reviewed, published in the last 10 years, between 1998 and 2008. MEDLINE on the PubMed server was searched using the combination of the following terms: "Schilder's disease OR myelinoclastic diffuse sclerosis OR tumefactive demyelination OR monofocal inflammatory demyelination OR pseudotumoral demyelination NOT alpers NOT balo NOT balo's NOT pelizaeus merzbacher NOT canavan NOT alexander's disease NOT alexander NOT cadasil NOT temporal lobe epilepsy NOT leukodystrophy NOT leukoencephalopathy NOT rasmussen NOT mitochondrial NOT muscular dystrophy NOT cerebrovascular disease NOT glial". Of the 79 results, only those case reports were selected (selection was performed by two authors independently) where either the definition "Schilder's disease" or at least 3 of Poser's criteria were mentioned and fulfilled. Following these criteria, 25 papers [6–30] including a total of 33 patients with Schilder's disease, 34 with the present reported case, were analysed for clinical and neuroradiological features, modality of diagnosis and outcome at follow-up.

The clinical and diagnostic aspects of the 34 described cases are summarised in Table 1, while Table 2 shows the described neuroradiological features of the same cases.

Analysis

Age, follow-up and clinical presentation

Amongst the 34 cases described the eponym "Schilder's disease" was not used in eight cases, and the term "tumefactive demyelinating disease" or "monofocal inflammatory demyelination" was used by the authors. In the series analysed the average age of presentation was 23 ± 18 (SD) years, median 18 years and in 62% of the cases the patient was female. Follow-up data is not mentioned in 3 of 34 patients. In the remaining 31 cases, the average time is 24 ± 34 (SD) months, the median 12 months, but in 12 subjects follow-up is shorter than 7 months. In 9% of cases symptoms at presentation were not atypical for MS. However, this non-atypical clinical presentation was not a predictor for the progression of "Schilder's disease" towards MS: in fact in all patients where follow-up documented a progression towards MS (5/34), clinical presentation had been atypical. Nevertheless, follow-up time in many presented cases is too short to document conversion towards MS.

Outcome and prognosis

From the literature, it emerges that the course of the disease is not always benign: 16/31 (52%) patients improved, one patient remained stable, in 8/31 (26%) some neurological symptoms persisted despite the improvement, further, one patient had two exacerbations, one had a rapid progression, in one case new lesions were detected afterwards, and one patient died (3%) because steroid therapy was complicated by sepsis. In five patients (16%), the disease progressed towards MS. The occurrence of seizures is mentioned in 5/31 cases (16%), where follow-up is notified.

Diagnosis I: Poser's criteria

Not all reports exactly specify the fulfilment of each of Poser's criteria for non-invasive diagnosis: atypical onset was present in 31/34 (91%) of patients, CSF analysis is reported for 27/34 (79%) and in one patient oligoclonal bands were detected. Further, the absence of infection is mentioned in 26/34 (76%) cases; one patient harboured TBC. Long fatty acids investigations are mentioned only for 19/56 (63%) of patients. Only in few cases (12%) normal adrenal function is explicitly mentioned, while in 34% normal blood tests are reported. The lesion (demyelinating plaque) was bilateral in 32% of cases, monolateral in the others—two of these patients had two lesions on the same side (detailed description of clinical features of the cases analysed is provided in Table 1).

Diagnosis II: Neuroradiology

Brain CT scans in the described cases of Schilder's disease revealed subcortical, initially hypodense lesions, except for three patients, where the first CT scan was negative. On brain magnetic resonance (MR), lesions appeared hypodense on T1 sequence and hyperintense on T2. The presence of mass effect is usually inconsistent with the lesion size and has been shown or described in 9/34 (26%) patients. Contrast enhancement of the lesion margins is only present during the acute inflammatory stage in white matter inflammatory diseases. According to some authors, the open ring contrast enhancement is highly specific for brain demyelination [31]. In the series analysed, contrast enhancement is mentioned or shown in 30/34 cases. Amongst these, the classic open ring can clearly be recognised in 63%, although it was mentioned only in 20/34 (59%) of the cases. Further, in 5/30 (17%) the enhancement ring was more a patchy one, in 4/30 (13%) there was a patchy lesion. In only two patients (7%) there had

Table 1 Summary of case series reviewed from literature- clinical aspects

References	Use term SD	Age	Sex	Poser et al. diagnostic criteria (1986) for Schilder's disease							Diagnosis				Follow-up (months)	Outcome
				Onset atypical for MS	CSF normal or atypical for MS	No infection	Long fatty acids	Normal adrenal function	Bilateral	Mono-lateral	Biopsy	Surgery	Clinical neuroradiological	Autopsy		
Pretorius et al. [6]	x	11	F	x	x	x	x	nm	x				x		4	Sd
	x	6	F	x	x	x	x	nm	x				x		12	Sd
	x	4	M	x	x	TBC	x	nm		x			*x*		12	I
Garell et al. [7]	x	17	M	x	nm	x	x	NB		2x		x			60	I
	x	11	F	x	nm	x	x	NB		x		x			6	NL, SD, SZ
	x	12	F	x	nm	x	x	NB		x	x				5	Rapid PR, SZ
Leuzzi et al. [8]	x	12	M	x	x	x	x	x		x		x			72	I
	x	4	M	x	x	x	x	x		x			x		168	PR to MS
Fitzgerald and Coleman [9]	x	6	M	x	x	x	x	NB		x	x				40	PR to MS
Iñiguez et al. [10]	x	21	M	x	x	x	x	NB		x		x			30	PR to MS
Afifi et al. [11]	x	7	F		x	x	x	NB	x		x				5	I
Censori et al. [12]	x	41	M	x	x	x	x	nm	x			x			56	I, SZ
Heyman et al. [13]	x	19	F	x	nm	nm	nm	nm		x	x (1.GBM; 2.DM)				12	PR to MS
	x	27	M	x	x	nm	nm	nm		x	2x (1.N 2.DM)				2	Sd
	x	61	F		x	nm	nm	nm		x	x				12	Sd
Kiernan et al. [14]	x	50	F	x	x	x	x	NB	x		x				12	Sd
Gutrecht [15]	no	21	F	x	x	nm	nm	nm		x	x				39	Sd, SZ
Khoshyomn et al. [16]	no	34	F	x	x	x	nm	nm		x	x				nm	nm
Kotil et al. [17]	x	25	M	x	x	x	x	NB		2x		x		x	5	I
Law et al. [18]	no	49	F	x	x	nm	nm	nm		x	x				nm	nm
Nejat et al. [19]	x	9	M	x	nm	x	x	nm	x		x				24	I
Kurul et al. [20]	x	9	F	x	OB	x	nm	nm	x				x		24	optic neuritis, I
Obara et al. [21]	x	6	M	x	x	x	x	x	x		x	x			6	I
Sastre-Garriga et al. [22]	SLO	24	F	x	x	x	nm	nm	x				x		7	PR to MS
Tan et al. [23]	no	30	M	x	x	x	nm	nm		x	2x (1A 2.DM)		x		2	Stab
Anderson et al. [24]	x	12	F	x	nm	nm	nm	nm		x		x	x		6	I, SZ
Akimoto et al. [25]	no	48	F		x	x	nm	NB		x		x	x		18	I
Miyamoto et al. [26]	x	69	F	x	x	x	nm	NB	x				x	x	1	D (sepsis after steroids)
Ragel et al. [27]	x	22	F	x	nm	nm	nm	nm		x		C	x		6	I
Cianfoni et al. [28]	no	50	M	x	x	x	nm	NB		x			x		nm	I
Yilmaz et al. [29]	x	8	F	x	x	x	x	NB		x			x		24	I
	x	9	F	x	x	x	x	NB	x				x		72	I
Riva et al. [30]	no	10	F	x	x	x	nm	nm		x		x (1.GBM;2.DM)			5	Sd
Present casex	x	29	F	x	x	x	x	x		x			x		18	I

In particular the presence of Poser's criteria is analysed, the modality of diagnosis, follow-up period and outcome

SD (Schilder's disease), *SLO* (Schilder's-like onset), *M* male, *F* female, *nm* not mentioned, *OB* oligoclonal bands, *TBC* tuberulosis, *NB* normal blood values, without extra mentioning adrenal function, *A* astrocytoma, *GBM* glioblastoma, *DM* demyelination, *N* normal tissue, *C* decompressive craniotomy, *I* improved, *Sd* some deficits, *Stab* no progression, *EXH* exhacerbations, *NL* new lesion, *PR* progression, *PR to MS* progression towards multiple sclerosis, *D* dead, *SZ* seizures

Table 2 Summary of case series reviewed from literature-neuroradiological features

References	Radiological features			CT ↓	c. enh.	MR		Imaging in acute phase	MRS		
	Subcortical location	Mass effect	Mentioned open ring enhancement			T1 ↓	T2 ↑	Other imaging modalities (MR or radionuclide)	Cho	NAA	Lac
Pretorius et al. [6]	x	x	x	nm	or	x	x				
	x	x	x	x	or						
	x	x	x	nm	or	x	x				
Garell et al. [7]	x	no	x	x	or	x	x				
	x	no	x	nm	or	x	x				
	x	x	no	x	nm	x	x				
Leuzzi et al. [8]	x	x	no	1.CT normal	nm		x				
	x	x	no	1.CT normal	nm						
Fitzgerald et al. [9]	x	no	x	x	or	x	x	FLAIR: ↑, core (↓), huge extension			
Iñiguez et al. [10]	x	no	x	nm	no	no	x		Cho/Cr ↑	NAA/Cr↓	Lac↑
Afifi et al. [11]	x	no	x	nm	or	x	x				
Censori et al. [12]	x	no	x	x	or	x	x	Proton Density: = / ↑			
Heyman et al. [13]	x	no	no	nm	pr	x	x				
	x	no	no	nm	pp	x	x				
	x	no	x	x	or	x	x				
Kiernan et al. [14]	x	no	no	x	pp			FLAIR: ↑, additional lesions			
Gutrecht et al. [15]	x	no	no	nm	no	nm	nm	FLAIR: ↑			
Khoshyomn et al. [16]	x	no	no	nm	pp	x		DWI: 'negative for ischaemia', GE: no haemorrhagic products, FLAIR: ↑	Cho↑	NAA ↓	
Kotil et al. [17]	x	x	x	nm	or	x	x				
Law et al. [18]	x	no	no	nm	pp		x		Cho↑	NAA (↓)	inverted doublet
Nejat and Eftekhar [19]	x	no	no	x	pr	x	x				
Kurul et al. [20]	x	no	no	x	or	x	x				
Obara et al. [21]	x	no	x	nm	or	x	x	FLAIR: ↑	Cho/Cr ↑	NAA/Cr ↓	Lac/Cr ↑
Sastre-Garriga et al. [22]	x	no	no	1.CT normal	pr	x	x	fast FLAIR: T2 weighted ↑			
Tan et al. [23]	x	no	x	x	pr	x	x		(↑)	NAA ↓	
Anderson et al. [24]	x	x	x	nm	or	x	x	DWI: ADC ring of diffusion restriction GE: no haemorrhagic products	Cho↑	NAA ↓	LacLipC
Akimoto et al. [25]	x	no	x	x	pr	x	x	DWI: core ↓, ring ↑ Thallium 201 SPECT no uptake			
Miyamoto et al. [26]	x	no	no	nm	nm	x	x				

Table 2 continued

References	Radiological features			CT ↓	c. enh.	MR		Imaging in acute phase	MRS		
	Subcortical location	Mass effect	Mentioned open ring enhancement			T1 ↓	T2 ↑	Other imaging modalities (MR or radionuclide)	Cho	NAA	Lac
Ragel et al. [27]	x	x	x	x	or	x					
Cianfoni et al. [28]	x	no	no	nm	or	x	x	at MRS: β, γ-Glx ↑	Cho ↑		Lac ↑ Lipids ↑
Yilmaz et al. [29]	x	no	x	nm	or	x		SE: T1 weighted ↓			
	x	no	x	nm	or	x		SE: T1 weighted ↓			
Riva et al. [30]	x	no	x	nm	or	x	no				
Present case	x	no	x	x	or	x	x	DWI: cystic portion ↓, solid portion and ring ↑, ADC: cystic portion ↑↑, solid portion and ring ↑, PWI: cystic portion ↓↓, solid portion and ring ↓, DTI: anisotropy↓, DTT: no means of reconstructing fibres within the lesion FLAIR: core↓, ring ↑, DE: T2 core (↓), ring↑ T1 core slightly ↑, ring ↑ MRS: β, γ-Glx ↑	Cho ↑ Cho/Cr ↑	NAA (↓)	Lac↑ no Lipids

Site of the lesion, presence of mass effect, mentioning of open ring sign by the authors, CT density, contrast enhancement (either by CT or by MR), T1 and T2 MR appearance, other imaging characteristics shown or discussed by the authors and classical MRS evaluation (Cho, Cr, NAA, Lac, Lipids)

nm not mentioned, *c. enh.* contrast enhancement, *or* open ring, *pr* patchy ring, *pp* patchy parenchyma, ↑ increased signal, ↓ decreased signal, (↓) slightly decreased signal, *MRS* MR spectroscopy, β, γ-Glx glutammate/glutammine, *Cho* choline, *Cr* creatinine, *NAA N*-acetylaspartic acid, *Lac* lactate, *LacLipC* lactate/lipid complex

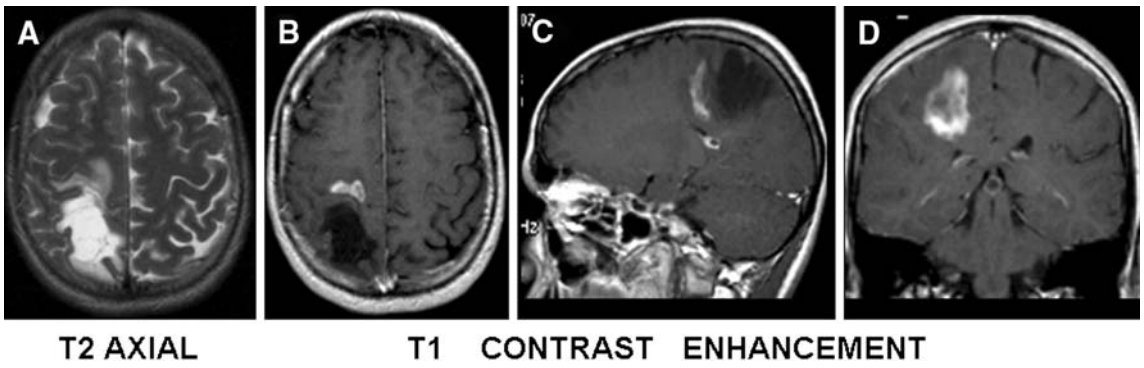

Fig. 1 MRI study in the acute phase: T2-weighted axial view (**a**), T1 contrast-enhanced, axial (**b**), sagittal (**c**) and coronal (**d**) views. The MRI study shows an intracranial subcortical lesion in the right parietal lobe, hypointense in T1, hyperintense in T2, associated with a relatively small amount of oedema

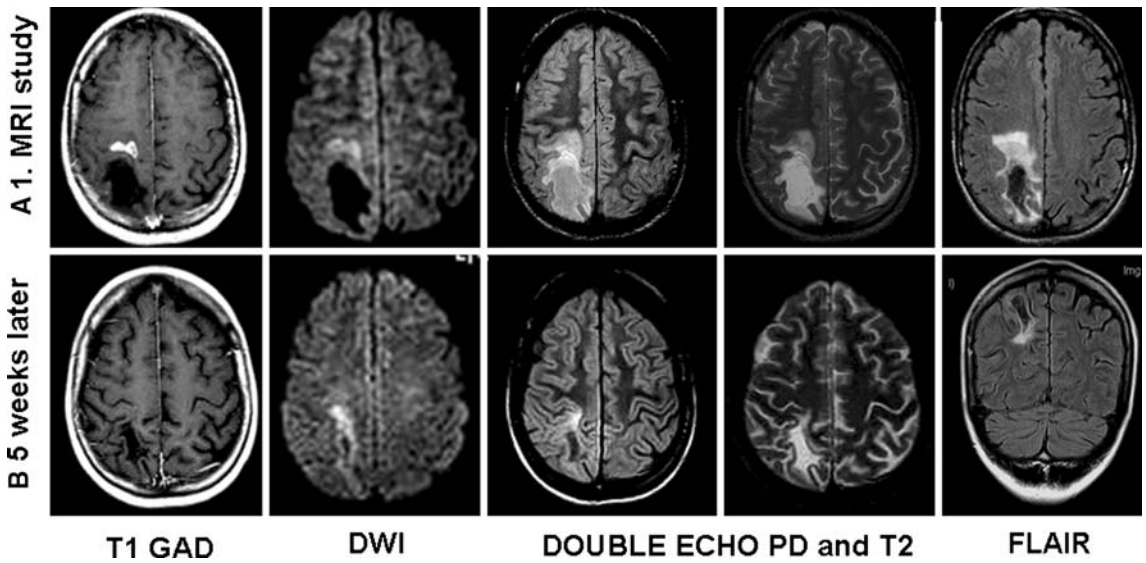

Fig. 2 Comparison between the first (**a**) and the second MRI examination (**b**) taken 5 weeks later. Axial T1 contrast-enhanced, *DWI* double echo (PD and T2-weighted and FLAIR sequences (the FLAIR control scan was available only in the coronal view). The progressive reduction of the cystic portion of the lesion is detectable in the second examination

been no enhancement and this might depend on the time point where imaging was performed.

In the revised literature seven cases of Schilder's disease studied with magnetic resonance spectroscopy (MRS) are described in addition to ours [10, 16, 18, 21, 23, 24, 28]. The *N*-acetylaspartate (NAA) peak on MRS is always decreased or slightly decreased but present, as is the *N*-acetylaspartate/creatine (NAA/Cr) ratio, choline (Cho) and choline/creatine (Cho/Cr) ratio are always increased, lactate (Lac) is described as increased, and some lactate–lipid (Lac-Lip) complexes are mentioned.

Other described neuroradiological features are: increased signal on fluid attenuated inversion recovery (FLAIR) sequence, increased apparent diffusion coefficient (ADC), no thallium 201 uptake at SPECT and abnormal elevation of the glutamate/glutamine peaks at short-echo time MRS (detailed description of neuroradiological features of the cases analyses is provided in Table 2).

Diagnosis III: Neuropathology

Because Schilder's disease is very rare and its neuroradiological features frequently mimic a brain tumour, diagnosis might become critical and relies on neuropathological analysis. In the revised literature, 65% of cases were in fact diagnosed by means of an invasive approach. Amongst these, 13 patients underwent biopsy; in two the procedure had to be repeated (the first diagnosis was of normal brain tissue in one case and of astrocytoma in the other case), in a further case the histology sections were revised recognising a demyelinating inflammatory disease after a first interpretation of glioblastoma, and even the

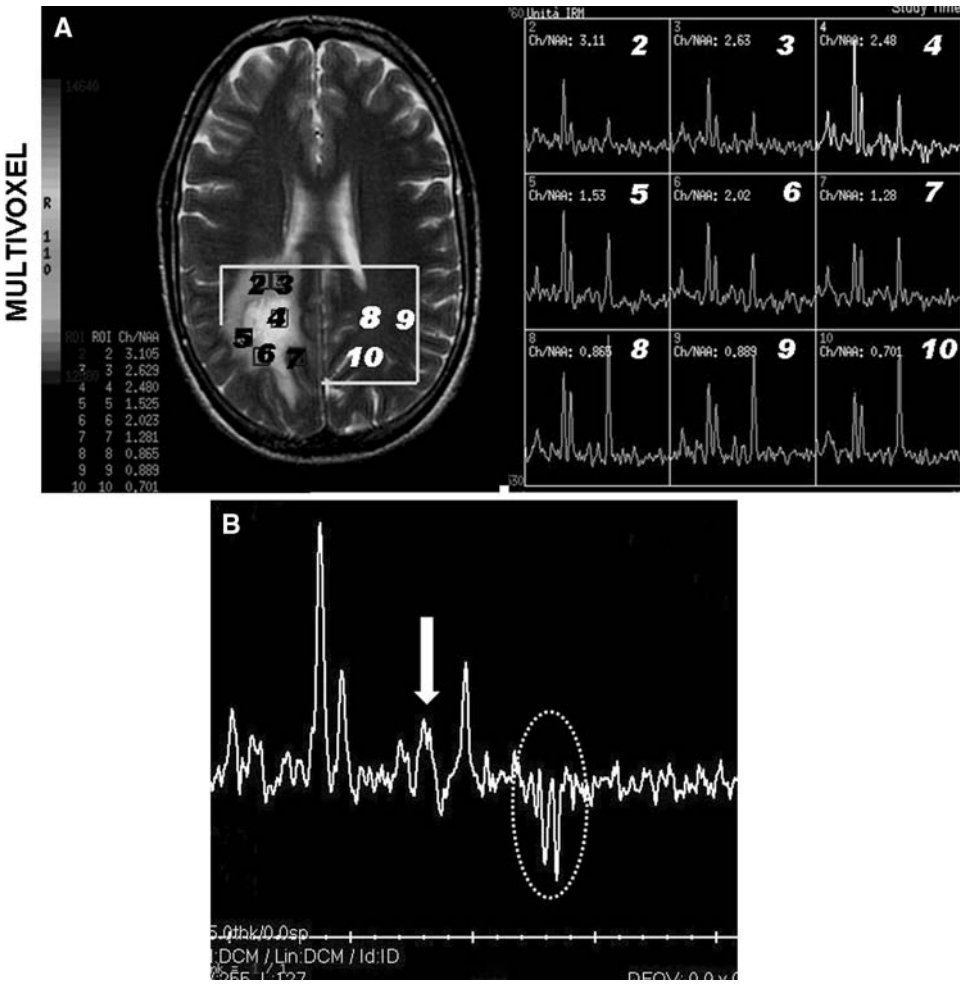

Fig. 3 **a** Multivoxel proton magnetic resonance spectrometry (H-MRS). The lesion is characterised by an increase in choline to creatine ratio (Cho–Cr) and choline to *N*-acetylaspartate ratio (Cho-NAA). The Cho-NAA ratio is higher in portion of the lesion with signs of BBB breakdown. A reduction of *N*-acetylaspartate (NAA) peak is also detectable. **b** In the cystic portion of the lesion, a lactate peak is better seen with single voxel MRS (*dotted circle*). A peak in the glutamate/glutamine spectral region seems to be detectable (*arrow*) despite the MRS had been performed with a long echo time

initiation of chemotherapy. However, even a surgical specimen had been initially misinterpreted as glioblastoma. Out of 11 patients that underwent craniotomy, mass effect seemed to be present only in four. One patient underwent both biopsy and craniotomy.

Illustrative case

We here report the case of 29-year-old woman where non-invasive diagnosis of Schilder's disease has been feasible by the neuroradiological analyisis. The patient had been admitted to an emergency ward for hypoesthesia, paresthesia and movement impairment, initially involving the lower left limb and successively also the upper left limb, the trunk and the left half of the face. These symptoms had evolved progressively during the 10 previous days. Clinical history was relevant for psoriasis and for an uncomplicated delivery a few months before. In the emergency ward, the brain CT evidenced an intraparenchymal right parietal hypodense lesion, with maximum diameters of $4.5 \times 4 \times 3$ cm^3 further characterised by hyperdense spots at the margins, little mass effect on the brain sulci, and signs of perilesional oedema towards the trigonal homolateral area. Successive CSF chemical-, physical-, microbiological analyses, oligoclonal bands and tumour cell search were all negative. Blood examination including very long fatty acid plasma concentration and adrenal function were normal. Further, an MRI was performed, using T1, T2, FLAIR sequences, DWI, MRS and T1 sequences after contrast administration (Figs. 1, 2a). In all sequences, an altered signal in the anterior and inferior portions of the lesion was detected. In the same region, a contrast enhancement (open ring sign) was evident after gadolinium administration. In the core of the lesion, ADC appeared increased. On multivoxel MRS (Fig. 3a) the lesion was throughout characterised by an increased Cho peak and by the absence of Lip. Cho and Cho/Cr ratio were particularly increased in the anterior, contrast-enhancing portion of the lesion; the NAA peak was reduced with an increase and inversion of the Cho/NAA ratio. In the spectrum obtained with single volume technique a Lac peak was evident (Fig. 3b). On the basis of these images, the neuroradiologist ruled out an abscess, an ischaemic

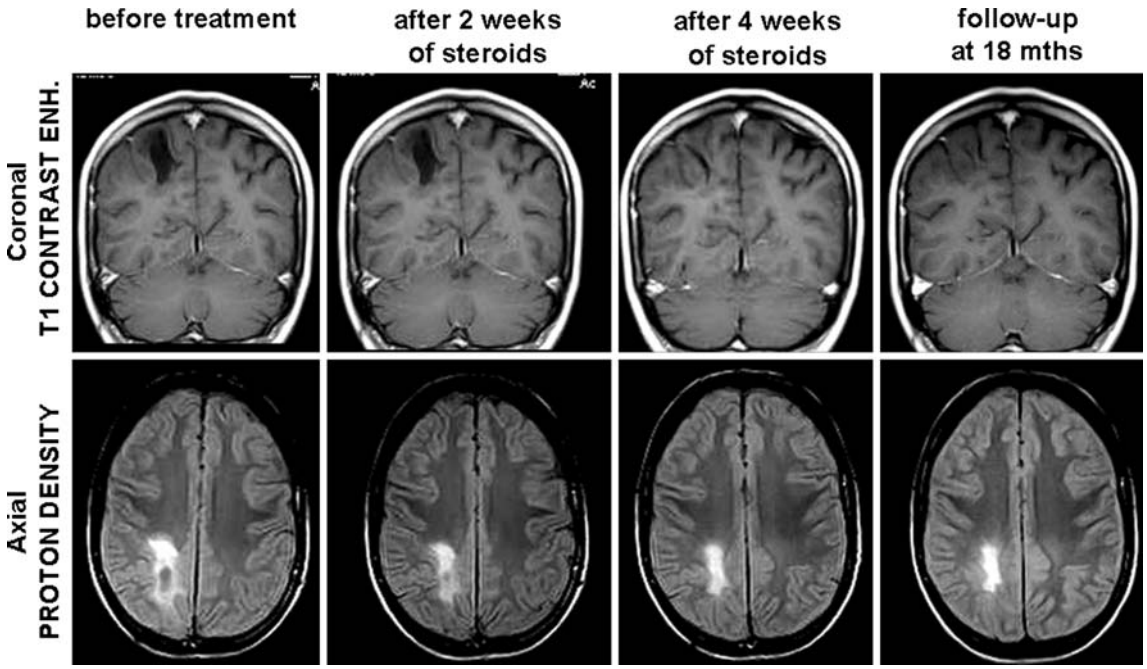

Fig. 4 MRI follow-up: coronal T1 contrast-enhanced (**a**), and axial proton density (**b**), at different time points: before treatment, at 2 weeks of steroids, at 4 weeks of steroids and at follow-up after 18 months

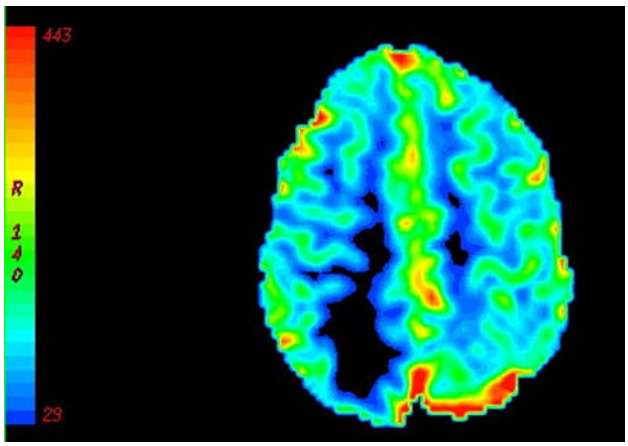

Fig. 5 At perfusion-weighted imaging (PWI), the lesion was markedly hypoperfused, compared with the contralateral unaffected white matter

lesion, and a metastatic tumour and the patient was treated with steroids. Owing to the suspicion of a brain tumour, a neurosurgical consult request was forwarded. After 2 weeks, while re-evaluating the patient prior to surgery, a brain MR was repeated (Fig. 2b) which showed the shrinkage of the cystic portion of the lesion and the almost complete fading of the ring enhancement.

Considering the fulfilment of Poser's clinical criteria and imaging characteristics strongly suggestive for a large demyelinating plaque, Schilder's disease was diagnosed and the patient was continued on corticosteroid therapy. After two or more weeks of treatment, the patient improved clinically (Fig. 4). Brain MR showed a reduction of contrast enhancement and the absence of mass effect. After 4 weeks, the cystic component was reduced and the lesion showed no contrast enhancement on brain MR (Figs. 2b, 4). During that time, the patient was asymptomatic. Steroids were maintained for a further month. At 18 months of follow-up, MR scans (Figs.2b, 4) showed the stability of the lesion and the clinical examination was negative for neurological findings. The good clinical and neuroradiological response to steroids at follow-up confirmed further the diagnosis of Schilder's disease, however, histological analyses were not performed, and even in our case, diagnosis occurred not at the first MRI study, but at the second.

Discussion

Despite the Poser's [3] well-established criteria for non-invasive diagnosis of Schilder's disease, diverse clinical cases have been reported afterwards, where diagnosis was only possible through neuropathological examination of brain biopsies. In fact, clinical and neuroradiological features of myelinoclastic diffuse sclerosis can be often misinterpreted leading to diagnose a brain tumour. A critical point is in fact that Poser's diagnostic criteria for non-invasive diagnosis address to suspect Schilder's disease, however, they cannot help to rule out a brain tumour. Therefore, a thorough analysis of neuroradiological features is of crucial support.

Considering the risks associated with craniotomy and the smaller but still existing risks associated with biopsy (3.5% symptomatic haemorrhage [32]) together with the possibility of a misleading diagnosis at biopsy (three cases in our review), it is worth to closer consider the potential of non-invasive diagnosis on the mere basis of clinical and neuroradiological features.

We suggest the following neuroradiological analysis for possibly avoiding invasive diagnostic manoeuvres in Schilder's disease diagnostics. An increased ADC in the core of the lesion can help to rule out the presence of an abscess, because pus would give a reduced ADC signal and appear as hyperintensity on DWI [33] and the same is true for ischaemic lesions [34]. On MRS, the increased Cho peak is a sign of augmented cell density or turnover. The reduced NAA peak is attributable to a reduction in the number of normally functioning neurons and axons due to injury or substitution through infiltration. Despite evidence of injury on morphologic studies, a peak of NAA, even if reduced, is in favour of the non-metastatic nature of the cyst-like lesion, because non-encephalic tissue would not express NAA. Lac is a product of anaerobic glycolysis, and since an abscess could be ruled out as described above, this increase in Lac might be due to active macrophages attracted within a site of inflammation. At this point ischaemia, abscess and metastasis can be ruled out. The dilemma between primary brain tumour and demyelinating plaque remains, since, as discussed by other authors [18, 28, 35], MRS based on the Cho, Cr, NAA, Lac and Lipids seems not to be reliable to this purpose, given the overlap in increased Cho/Cr ratio, decreased NAA/Cr ratio and the non-specific presence of Lac and Lip both in both cases. Two further imaging techniques might support the process of differential diagnostics. As reminded by Tsui et al. [36] since, according to some authors [37] blood vessels in demyelination are normal, while neovascularisation phenomena are typically present in brain tumours, perfusion discriminates between these two entities: on perfusion-weighted imaging there is no increase in relative cerebral blood volume (rCBV) in demyelination. This was also the case in our patient, as we noticed by retrospectively reviewing MR studies (perfusion shown in Fig. 5). A further interesting imaging tool for this final differential diagnostics has been recently presented by Cianfoni et al. [28]: tumefactive lesions present in contrast to neoplasms an abnormal elevation of the glutamate/glutamine peak using short-echo time proton MRS. In our case, despite MRS had been performed with a long echo time, it may be retrospectively possible to identify a peak in the spectral region of glutamate/glutamine (Fig. 3b). This peak has never been described in patients with lymphoma so far.

On the basis of these revised literature cases, we would like to propose non-invasive diagnosis for a demyelinating tumour-like plaque when following conditions are fulfilled: no signs of intracranial hypertension, presence of one or two subcortical cyst-like lesions with eventually open ring sign at CT/MR, exclusion of ischaemia, abscess and metastasis by classical neuroradiological means and further of primary neoplasm by means of perfusion MR and consideration of abnormal glutamate/glutamine elevation on short-echo time MRS. Schilder's disease can be defined at this point if Poser's diagnostic criteria are fulfilled.

Because cases of Schilder's disease are rare, we would like to coordinate a multicentric case collection by inviting you to send following data on your patients to the corresponding author's address: all items mentioned in Tables 1 and 2 should be addressed, further the following images in jpeg might be enclosed: T1 with and without contrast, T2, FLAIR, DWI, perfusion and MRS, possibly indicating the glutamate/glutamine peak, and finally the follow-up a month after steroids and at 18 months. Histopathological consult, where diagnosis occurred invasively might also be included.

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