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Tumefactive demyelinating lesions

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Abstract We studied 21 cases of pathologically confirmed tumefactive demyelinating lesions and reviewed the spectrum of tumefactive demyelinating lesions in the literature. Radiological features and clinical data were reviewed to characterize the lesions as consistent with a known demyelinating disease, most notably multiple sclerosis. Atypical clinical or radiological features (other than tumefaction) were noted. Most lesions were part of a clinical and/or radiological picture consistent with multiple sclerosis. No case strongly suggestive of variants or related diseases, such as Schilder's disease or Balo's concentric sclerosis, were found. There was one case suggestive of acute disseminated encephalomyelitis. Features which help distinguish the lesions from tumour are discussed.

Key words Demyelinating lesions, tumefactive · Multiple sclerosis · Magnetic resonance imaging

Introduction

The spectrum of primary demyelinating disease includes various pathological entities, multiple sclerosis (MS) being the most common [1, 2]. These diseases uncommonly have histological confirmation except where the diagnosis is uncertain, such as when a single or a few large lesions with mass effect simulate glioma or other neoplasms. Large (2 cm or more) demyelinating plaques with mass-like features are well documented in MS [1–13]. Other diseases in which the principal pathological change is primary demyelination can manifest as tumefactive lesions. They include myelinoclastic diffuse sclerosis, also known as Schilder's disease [14–17] and acute disseminated encephalomyelitis (ADEM), also known as postinfectious and postvaccination encephalomyelitis (PPE) [18]. Progressive multifocal leukoencephalopathy (PML) may also present with large lesions, but these have a distinct histopathological appearance, an established viral etiology, and do not usually exhibit mass effect [18]. Balo's concentric sclerosis has a distinct pathological and radiological appearance and is considered an acute variant of MS [19]. The leukodystrophies are inborn errors of metabolism. Central pontine myelinosis has distinct radiological appearance and clinical features and is considered to be a response to electrolyte abnormalities [20]. Kepes [18] has suggested an entity intermediate between MS and ADEM that presents either as a solitary lesion or a few large demyelinating lesions.

We reviewed 21 cases of large demyelinating lesions accumulated over a 15-year period at the Armed Forces Institute of Pathology (AFIP). Radiological features and clinical data were reviewed, attempting to characterize the lesions and to assign the cases to the one of the above-described entities. Atypical clinical or radiological features were also noted.

Table 1 Summary of series. Lesion size is largest diameter (*m* male, *f* female, *CSF* cerebrospinal fluid)

Patient	Age years/ sex	Principal lesion	Other lesions	Clinical data
1	22f	2 cm round well-defined premotor lesion, minimal mass effect (Fig. 4)	Classic radiological features of MS	Classic waxing and waning symptoms, oligoclonal bands in CSF
2	36m	2 cm lobular well-defined peritrigonal lesion, minimal mass effect	Rim enhancing, cystic left cerebellar lesion	Ataxia and central facial and arm weakness, clonus 1 year ago
3	43m	CT only, 4 cm frontal with poorly defined border, vasogenic edema	Smaller right frontoparietal subcortical lesion	Depression, headache, weight loss
4	40m	CT only: 6 cm lobular well-defined left frontal ring-enhancing lesion with moderate mass effect	Occipital, frontal and middle cerebellar peduncle lesions	Unsteady gait 4 months, acute decreased vision
5	56f	6 cm frontal lobular well-defined mass with vasogenic edema (Fig. 2)	Other lesions consistent with MS	Clinically diagnosed as MS 2 years ago
6	31f	CT only: 11 cm poorly defined area of vasogenic edema frontal and parietal lobes, marked mass effect	Periventricular decreased attenuation	Not available
7	34f	2 cm lobular poorly defined temporal lesion, minimal mass effect (Fig. 3)	None	Decreased vision 1 month prior to imaging
8	33f	7 cm ill-defined peritrigonal lesion extending to corpus callosum, minimal mass effect	Small temporal lesion	2 weeks numbness and weakness with acute exacerbation, aphasia
9	53m	2 cm frontal ring-enhancing lesion with vasogenic edema, moderate mass effect	None	20 year history of "demyelinating disease", acute deterioration arm function
10	n/a	3 cm well-circumscribed peritrigonal cyst/mass	Perioccipital horn signal abnormality	Not available
11	22 m	5 cm poorly defined peritrigonal mass with moderate mass effect, homogeneous enhancement (Fig. 5)	Multiple coalescing lesions, some enhancing, medullary §lesion	2 month history of flu-like symptoms leading to hemiparesis, stupor; improved with steroids
12	41f	5 cm lobular welldefined perifrontal horn rim enhancing cyst/mass	Contralateral frontal lesion, peritrigonal mass lesion, nodular periventricular signal abnormalities, cerebellar lesion	1987 diagnosis of Alexander's disease; Rosenthal fibers not confirmed, chronic visual deficits, chronic seizures
13	39f	2 cm lobular welldefined corona radiata mass	Periventricular and callosal signal abnormalities	2 week history of weakness
14	33f	5 cm lobular welldefined periventricular mass	None	None available
15	41m	CT only: 6 cm lobular well-defined rimenhancing frontoparietal mass, crosses corpus callosum	None	3 weeks of confusion, blurred vision and memory deficits
16	20f	4 cm lobular welldefined perifrontal horn mass/cyst, rim enhancement, T1-weighted bright rim [2]	Corona radiata and occipital lesion	None available
17	40f	3 cm poorly defined frontal lobe mass, vasogenic edema, moderate mass effect	None	None available
18	51m	10 cm ill-defined area of vasogenic edema and rim enhancement frontoparietal white matter, marked mass effect (Fig. 6)	Old occipital infarct	"History of MS" for 20 years, confusion and memory loss for 2 years, recent acute paresthesia and weakness
19	58m	CT only: 4 cm lobular well-defined rim-enhancing lesion around posterior lateral ventricle, minimal mass effect	None	None available
20	10f	5 cm lobular welldefined rim-enhancing frontoparietal lesion, vasogenic edema	None	None available
21	45f	4 cm oval well-defined enhancing lesion along lateral ventricle (Fig. 1)	No	Optic neuritis 1 year previously

Materials and methods

The records of 21 patients with demyelinating lesions in the brain with "mass-like features" accumulated between 1980 and 1995 from various institutions for radiological and pathological consultation were reviewed. Tissue for pathological review was available in all cases. Biopsy was performed most commonly because of atypical clinical or radiographic features (solitary lesion, size or mass effect, discordant symptoms, contrast enhancement, infiltration). "Mass-like features" were defined as a lesion 2 cm or more in diameter, with mass effect or edema of any degree.

Pathological specimens were obtained within 2 weeks of the imaging study in every case and were reviewed by at least one board-certified neuropathologist. All lesions were confirmed to have the characteristic feature of demyelination: myelin loss with relative preservation of axons. Perivascular inflammation, lipid-laden macrophages, gliosis, necrosis, hemorrhage, and calcification were variable findings. Neoplasia was definitely excluded in all cases.

Of the 21 cases, 16 underwent MRI, including at least one proton-density or T2-weighted sequence. T1-weighted sequences before and after gadolinium were available in all but one of these cases, which was limited to a T2-weighted series. Five patients were imaged with CT only (all with images before and after contrast medium).

Radiological features consistent with MS were defined as at least three lesions, with two either abutting the lateral ventricle, in an infratentorial location, or larger than 5 mm [21, 22]; a periventricular lesion was defined as having an interface with the ventricular surface. Contrast enhancement was considered non specific, although multiple lesions, some with varying degrees of enhancement, were considered consistent with MS. Atrophy was considered a compatible concomitant feature of MS. Mass effect was graded as mild (sulcal effacement), moderate (minimal subfalcine or uncal herniation), or marked (more than 1 cm subfalcine or uncal herniation). Edema was categorized as: mild (less than 1 cm from the lesion), moderate (1–3 cm from the lesion), and marked (> 3 cm from the lesion) [2]. Additional features assessed were cyst formation and site.

Clinical features consistent with MS were at least a history of relapsing and remitting symptoms [23]. The clinical data usually included a brief relevant past medical history, pertinent signs and symptoms, and laboratory results. In 7 cases no clinical data was available.

For each patient an attempt was made to classify the case as characteristic or not characteristic of MS, on clinical or radiological grounds.

Results

Table 1 is a summary of the cases.

There were 12 female patients, 8 male, and in one the sex was unknown. The average age was 37 years, range 10–58. Where clinical information was available (14 patients), the average duration of symptoms was 24 months; they included limb weakness (6), decreased vision (5), altered mental status (4), ataxia (3), facial weakness (2), paresthesiae (2), aphasia (2), memory loss (2), seizures (1) and headaches (1). In 8 cases neurological episodes prior to the symptoms that led to the admission for biopsy were recorded 4 months to some years previously. In the remaining 6 patients with clinical data, symptoms were acute, with no prior episode; in these cases the average duration of symptoms was 3.5 weeks.

Some general radiological characteristics were noted (Table 1). The appearances of the lesions were relatively low density on CT or high signal on proton-density or T2-weighted and relatively low signal on T1-weighted MRI, unless otherwise indicated. Enhancement did not occur where not explicitly stated. In all cases, the largest lesion was purely in white matter. The average largest diameter of the 21 tumefactive lesions was 4.6 cm (range 2–11 cm). Of the 20 lesions, 10 enhanced, 9 showing rim enhancement; 7 of the enhancing lesions had well-defined borders on unenhanced images. There was some associated vasogenic edema around 8 of the 20 lesions; none had a concentric pattern to suggest Balo's sclerosis. Mass effect was minimal in 14, moderate in 5, and marked in 2. Four lesions showed "cysts". The lesions were frontal (8), frontoparietal (8), occipital (4), and temporal (1). Tumefactive and periventricular demyelinating lesions are shown in Figs. 1–3, lesions without a ventricular interface in Fig. 4, multiple and confluent deep white matter and periventricular lesions in Fig. 5 and one large, infiltrating lesion in Fig. 6.

Of the 8 patients with prior neurological episodes, 6 had contrast enhancement, two with vasogenic edema around the tumefactive lesion and rim enhancement. In 7 of these cases there were other lesions present on MRI or CT, at least one having a ventricular interface.

In 6 with a monophasic history, 3 had isolated lesions, 4 enhanced, 1 had vasogenic edema, and 2 did not have periventricular lesions. One patient with a monophasic history had a clinical picture suggestive of ADEM (case 11), with a flu-like prodrome and significant improvement with steroids.

Overall, 11 of the 21 patients had at most two lesions; of these 11, only 2, both of whom had periventricular lesions; had a definite relapsing neurological history consistent with MS. Three had an acute presentation, 4 no clinical data, and 2 (cases 9 and 18) had a questionable chronic history with a definite acute presentation.

Lesions with borders flush with the ventricular surface were seen in 17 cases. The other 4 all had vasogenic edema and all enhanced. One (case 3) had one additional lesion and an atypical clinical history, with an acute presentation of depression, headache, and weight loss. Case 9 had an isolated lesion with vasogenic edema and a "questionable" history of MS. The last two cases (17 and 20) had no history.

Discussion

Most cases in our series with a clinical picture of MS also had the appropriate radiological picture. MS plaques are commonly sharply demarcated, frequently occur-

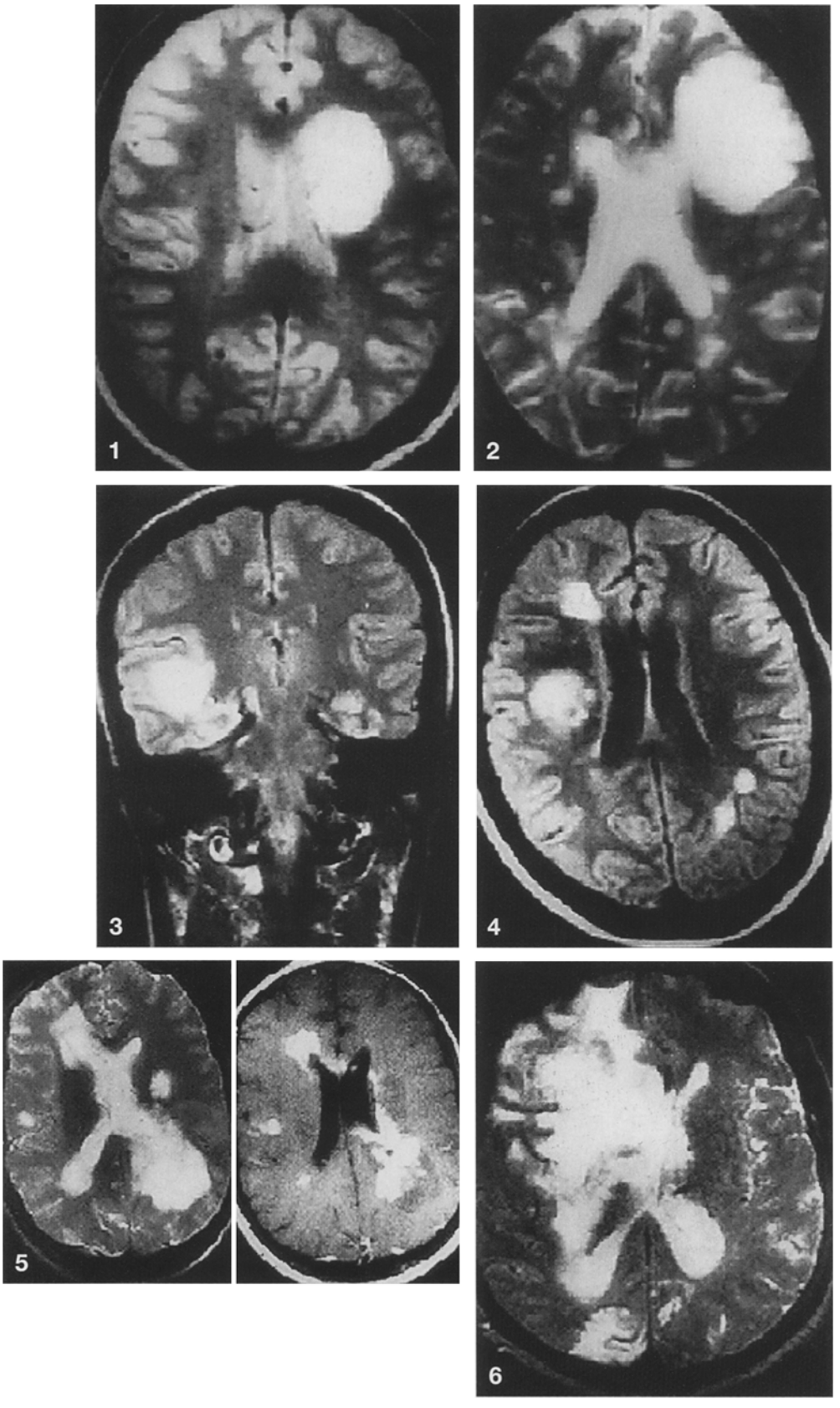

Fig. 1 Case 21, a 45-year-old woman. Proton density-weighted MRI showing a single large demyelinating plaque adjacent to the lateral ventricle

Fig. 2 Case 5, a 56-year-old woman. T2-weighted image showing a large demyelinating lesion with a small ventricular interface. Other smaller deep white matter and periventricular lesions are present

Fig. 3 Case 7, a 34-year-old woman. Proton density-weighted coronal image showing a large demyelinating lesion in the right temporal lobe, along the temporal horn

Fig. 4 Case 1, a 21-year-old. Proton density-weighted image showing a large deep white matter lesion and other subcortical demyelinating lesions, one with a ventricular interface

Fig. 5 Case 11, a 22-year-old man. T2-weighted *(left)* and contrast-enhanced T1-weighted (right) images showing large confluent periventricular areas of signal abnormality with enhancement

Fig. 6 Case 18, a 51-year-old man. T2-weighted image revealing a large infiltrating frontal lesion involving gray and white matter with marked mass effect. The occipital lesion was thought to be an old infarct

ring at the angles of ventricles [20]. The axons are preserved; plaques begin around venules, expanding as an area of oligodendrocyte loss, reactive astrocytosis, and lipid-laden macrophages. Mononuclear inflammatory infiltrates dominate the rim of the lesion [20, 24], diminishing as the lesion becomes more chronic. In a less common subtype the border of the plaque is ill-defined as the inflammatory infiltrate progressively diminishes rather than abruptly ends [20]; this may have been represented in our own series by those cases with "vasogenic edema". One problem is the variable clinical presentation and even pathological findings during various stages of the disease. This has resulted in various eponyms for entities that may actually be variants of a single disease. For example, Balo's concentric sclerosis is now considered a variant of MS [25–27]. We found no lesion with radiological or pathological characteristics of Balo's sclerosis.

The distinct nature of Schilder's disease has been questioned [20]. In our series there were no definite case, but the youngest patient, a 10-year-old girl (20 case), may have been a case of Schilder's disease. Although the Poser criteria list bilaterality [14], an exception to this has been reported [16].

ADEM is a monophasic immune reaction triggered within days of a viral infection or a vaccination [20]. Neurological disturbances include headaches, neck stiffness, lethargy, paralysis, and coma; death may occur [20]. ADEM has been experimentally modeled by experimental allergic encephalitis [18, 20]. Perivenular and scattered inflammatory foci within demyelinating plaques are characteristic. We had one case suggestive of ADEM (case 11).

Imaging features suggestive of tumefactive demyelination are important in avoiding biopsy and preventing dangerous treatment when biopsy results are equivocal. Our series suggests that enhancement in these lesions is relatively more common (over 50 %) than in the standard MS plaque [1]. MS lesions tend to be well defined and rounded on MRI or CT and this tends to be true of these tumefactive lesions. A very helpful feature is the presence of other lesions, giving an overall picture consistent with MS. Another is a relative lack of mass effect and sometimes also of vasogenic edema given the size of the lesion.

Although limited in number, this series demonstrates a subgroup in which the diagnosis is uncertain, yet the patients have histological findings identical to those of MS. Atypical features of this ill-defined subgroup include atypical symptoms, the presence of few or isolated lesions, prominent edema or mass effect, and atypical location (not periventricular or infratentorial).

Kepes [18] described a possible immunologically mediated entity somewhere between MS and ADEM, citing cases of tumefactive demyelinating lesion with atypical features and histories not consistent with MS. It is possible that the less well defined subgroup in our series may be this entity; however, our numbers are small and clinical data limited.

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ANNOUNCEMENTS

5th International MRI Course
27–30 October 1996, Riyadh, Saudi Arabia
Information: Department of Postgraduate and Academic Affairs, Riyadh Armed Forces Hospital, P. O. Box 7897, Riyadh 11159, Saudi Arabia, Tel. 00966-1-477 7714 Ext: 4933/4937, Fax 00966-1-476 0853

Ostseesymposium '96
Interdisciplinary Radiologic-Neuroradiologic Symposium
8/9 November 1996, Lübeck, Germany
Information: Dr. H. Twilfer/Frau M. Bischof, Institut für Radiologie, Medizinische Universität zu Lübeck, Ratzeburger Allee 160, D-23538 Lübeck, Germany, Tel. 0451-500-2128/2129/6447, Fax: 0451-500-6497

The British Cervical Spine Society Meeting
8/9 November 1996, Newcastle upon Tyne, UK
Information: Mr N Todd, Newcastle General Hospital, Westgate Road, Newcastle upon Tyne NE4 6BE, UK, Tel. 0191 273 811, Ext: 22472, Fax: 0191 272 2641

MRI Update 1997
Brain, Spine, Head, Neck and Pediatrics
New Techniques: MR Spectroscopy and Functional Imaging
23–28 February 1997, Medical College of Wisconsin, Tucson, Arizona, USA
Information: Marti Carter, CME, Inc., 11011 W. North Avenue, Milwaukee, WI 53226, Phone and Fax: (414) 771-9520, E-Mail: cmemilw@aol.com

7th Pan-Arab Union of Neurological Sciences Conference
2–5 March 1997, Riyadh, Saudi Arabia
Information: Department of Postgraduate and Academic Affairs, Riyadh Armed Forces Hospital, P. O. Box 7897, Riyadh 11159, Saudi Arabia, Tel. 00966-1-477 7714 Ext: 4933/4937, Fax 00966-1-476 0853

Consensus Conference:
Complex Hydrocephalus and Hydrocephalus Complications
April 1997, Assisi, Italy
Information: C. Di Rocco/F. Velardi, Section of Pediatric Neurosurgery, Catholic University Medical School, Policlinico Gemelli, Largo Gemelli, 8, I-00168 Rome, Italy, Tel. +39-6-3015-4495, Fax +39-6-305-13-43

XXVè Congrès de la Société Française de Neuroradiologie
10–11 April 1997, Strasbourg
Information: Prof. J. L. Dietemann, Service de Radiologie 2, CHU de Hautepierre, F-67098 Strasbourg Cedex, France, Tel. 88127889, Fax 88127118