

Multiple Sclerosis and Related Demyelinating Disorders in India

Demyelinating disorders of the central nervous system have assumed significance in recent years in India, coinciding with the availability of magnetic resonance imaging facilities (MRI) in teaching and private hospitals in the metropolitan cities of India. Neurologists are in agreement that they see more cases of multiple sclerosis (MS) recently than they did a decade ago. However it is not yet certain whether this is apparent, as a consequence of better diagnostic facilities and greater awareness among specialists, or real. On the other hand post infectious demyelinating disorders or acute disseminated encephalomyelitis (ADEM) are likely to be more common in view of prevailing conditions.

The study of demyelinating disorders of the nervous system in India has been limited by many factors. Neurologists in the past have been significantly influenced by Kurtzke's¹ epidemiological studies which clearly showed India among other tropical countries to have a low prevalence for MS. The diagnosis of MS in India has relied heavily on clinical criteria. Lack of facilities and or financial constraints have prevented the use of radiological and other paraclinical tests on a wide scale in diagnosis. Evaluation of optic neuritis in a tropical setting is beset with problems. Toxic, nutritional and infectious causes of optic neuritis are under-diagnosed. Most patients presenting with acute visual loss are evaluated by ophthalmologists and evaluation of the central nervous system by imaging and lumbar puncture are seldom considered. Record keeping and long term follow up of patients have seen serious limitations in all but the teaching hospitals and continue to hinder data collection and analysis of diseases in India, including demyelinating disorders. One of the direct fall outs for this problem is that there are no longitudinal studies on clinically isolated syndromes (CIS) suggestive of demyelination in India.

In this article a brief overview of demyelinating disorders seen in India is discussed, particularly the prevalence of MS, the contentious issues of optico-spinal MS and neuromyelitis optica, and the available data on immunogenetics of MS. There are many mimics for CNS demyelinating disorders in a tropical set up which are also highlighted.

Multiple Sclerosis

There are no large scale epidemiological studies from India on the incidence and prevalence of Multiple sclerosis. Based on hospital statistics a prevalence of approximately 1.33/100,000 was reported by Singhal et al² in the mid eighties from the west coast of India. An indication to suggest that more cases are being diagnosed in recent times comes from data published from the northwest of India.^{3,4} The incidence of hospitalised MS patients seen at a premier teaching hospital, nearly doubled within a span

of 15 years. In the Parsi population of India, Wadia⁵ observed a prevalence of 26/100,000. Parsis are a closely knit community which migrated to and settled predominantly in the west coast of India, between the 7th and 8th century and more recently in the 19th century, from the Pars province of Iran. Recently a high prevalence of MS was detected in Isfahan, a province that adjoins Pars in Iran, supporting the notion of genetic susceptibility in this community.⁶

Is MS seen in India different from that in the west? Results of some of the recent Indian studies^{7,8} done in the MRI era have found relatively few differences from the west, lending support to the theory that the differences between MS in the West and Indian population are more apparent than real. However what cannot be ignored is the report of high frequency of optic and spinal cord involvement in several Indian studies.⁹ In a recent prospective and longitudinal study of CNS demyelinating disorders which included 51 patients, Pandit et al¹⁰ found 47% of their MS cases to have clinical attacks confined to the optic nerve and spinal cord. The MRI of brain and spinal cord was indistinguishable from conventional MS in all. A larger prospective study with careful documentation of clinical events supported by MRI imaging of brain and spinal cord is important to settle the issue of optico-spinal phenotype of MS and its prominence in Indian MS. The results of one such study, which will be completed by 2010, are awaited. Immunogenetics of MS in India have not been studied in detail. Class II HLA association studies were done for the first time recently in 23 MS patients of non Parsi origin in whom the commonly reported association was with DRB1*1501 (50%) similar to western studies.¹¹

Neuromyelitis optica

In earlier studies neuromyelitis optica was diagnosed as a monophasic illness with involvement of both optic nerve and spinal cord and an interval not exceeding a month between involvement of both sites.^{9,12} Most studies have collectively shown an incidence of 20% or fewer cases of neuromyelitis optica defined by these criteria. A paper by Jain et al¹³ has been widely quoted in western literature as evidence for high prevalence of NMO in India. A careful review of their data of 354 cases of MS collected from nine centres reveal that 33 cases (10.1%) were neuromyelitis optica, defined according to the above mentioned criteria. Prospective studies¹⁰ using the newer diagnostic criteria of Wingerchuck have shown an incidence of 9.5% of NMO. Recurrent myelitis, which is probably a variant of NMO has been reported from the India.¹⁴ Whilst it is probable that NMO is seen more commonly than in western countries, it is certainly not seen in the magnitude reported from other Asian countries, especially Japan.



Dr Lekha Pandit, MD, DM Neurology is the Professor and head of department of Neurology at KS Hegde Medical Academy, Mangalore, Karnataka, in south India. Her areas of interest include Multiple Sclerosis and post infectious demyelinating disorders of the nervous system. Currently she is funded by the government of India for longitudinal and observational studies, epidemiology and immunogenetics of demyelinating disorders seen in India.

Correspondence to:

Dr Lekha Pandit,
Professor of Neurology,
KS Hegde Medical Academy,
Deralakatte,
Mangalore - 575018
Tel. 91 824 2204471 - Ext 2216
Fax. 91 824 2203747
Email. panditmng@gmail.com

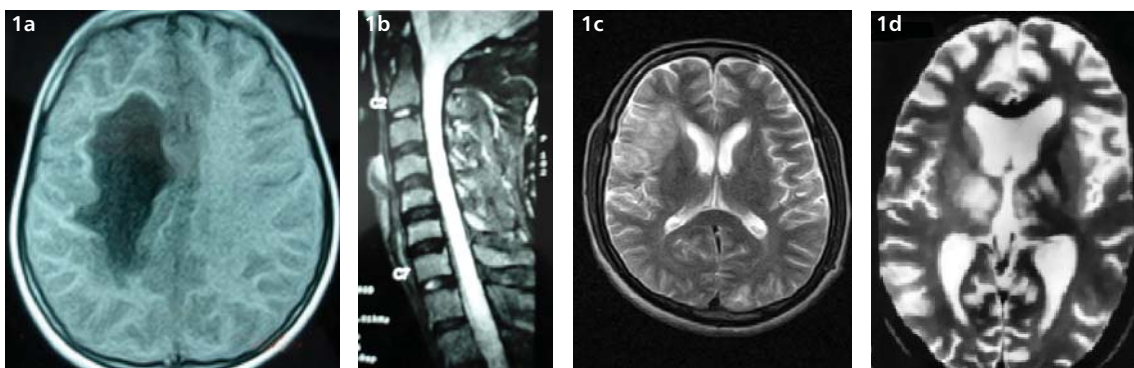
Differential diagnosis of white matter diseases in the tropics

From left – Figure 1a: A case of biopsy proven ADEM, MRI brain with contrast showing incomplete ring enhancing lesion with mass effect.

Figure 1b: A case of Neuromyelitis optica, with MRI spine showing longitudinally extensive transverse myelitis.

Figure 1c: An asymmetric white matter lesion on brain MRI of an HIV positive patient with progressive multifocal leucoencephalopathy.

Figure 1d: A case of Japanese B encephalitis with bilateral thalamic lesions.



Acute disseminated encephalomyelitis (ADEM)

ADEM is a commonly made diagnosis in tropical countries like India where infections abound and vaccinations, especially anti-rabies vaccination (Semple's vaccine) are still freely in use. ADEM as an entity has no definite diagnostic criteria and has a heterogeneous clinical presentation. Most importantly it is a diagnosis of exclusion. Infections, especially HIV, neurosyphilis, Arboviral encephalitides, especially Japanese B encephalitis, which target the basal ganglia and thalamus, tuberculosis of the CNS presenting as isolated parenchymal white matter disease, neurosyphilis and cystic infective brain lesions such as neurocysticercosis can mimic ADEM. Osmotic demyelinating syndrome, especially of the extrapontine type, vitamin B12 deficiency and occasionally mitochondrial disorders which flare up in the background of systemic infections can cause diagnostic confusion.

Conclusion

One of the priorities for specialists working in demyelinating disorders in India is to collect data using uniform criteria, especially when defining conditions such as opticospinal MS and neuromyelitis optica. Clinical descriptions have to be correlated with MRI data of both the cord and brain. This is particularly important in the context of choosing the appropriate disease modifying agents and while recruiting patients for clinical trials for drugs with potentially disease modifying effect. While it is true that only a fraction of diagnosed patients in India are able to afford beta interferon or glatiramer acetate, alternate therapies such as mitoxantrone¹⁵ are being tried with varying degree of short term success. The MS society has 4000 registered patients and it is estimated that there are approximately 40,000 more in the community. Epidemiological studies are urgently warranted to establish the burden of disease in the country. In India, issues regarding health insurance for MS patients (which is not currently available), subsidies for disease modifying agents, disease awareness and rehabilitation of affected patients are concerns which have to be addressed jointly by health professionals, MS societies, the pharmaceutical industry and governmental agencies. The Multiple Sclerosis Society of India, having over ten branches in Indian cities, is very active in arranging social and financial help for the patients and acts as an effective interface between the doctors and the patients.

References

1. Kurtzke JF. *Epidemiology of multiple sclerosis*. In: Koetsier JC, editor. *Handbook of clinical neurology*. Vol.3 Demyelinating diseases. Amsterdam: Elsevier Science 1985;259-87.
2. Singhal BS. *Multiple Sclerosis-Indian experience*. *Ann Acad med Singapore* 1985;14:32-6.
3. Chopra JS, Radhakrishnan K, Sawhney BB et al. *Multiple sclerosis in North-west India*. *Acta Neurol Scand* 1980;62:312-21.
4. Syal P, Prabhakar S, Thussu A, Sehgal S, Khandelwal N. *Clinical profile of multiple sclerosis in north-west India*. *Neurol India* 1999;47:12-7.
5. Wadia N, Bhatia K. *Multiple sclerosis is prevalent in the Zoroastrians (Parsis) of India*. *Annals of Neurol* 1990;28:177-9.
6. Etemadifar M, Janghorbani M, Shaygannejad V, Ashtari F. *Prevalence of Multiple Sclerosis in Isfahan, Iran*. *Neuroepidemiol* 2006;27:39-44.
7. Bansil S, Singhal BS, Ahuja GK et al. *Comparison between multiple sclerosis in India and the United States: A case control study*. *Neurology* 1996;46:385-7.
8. Bhatia M, Behari M, Ahuja GK. *Multiple sclerosis in India: AIIMS experience*. *J Assoc Physicians India* 1996;44:765-7.
9. Singhal BS, Wadia NH. *Profile of multiple sclerosis in the Bombay region - on the basis of critical clinical appraisal*. *J Neurol Sci* 1975;26:259-70.
10. Pandit L, Shetty R, Bhat IG, Misri Z, Hegde S. *Spectrum of Multiple Sclerosis and related demyelinating disorders in India in the background of revised diagnostic criteria*. *Ann Ind Acad Neurol* 2007;10:(S2)44-5.
11. Kankonkar S, Jeyanti G, Singhal BS, Shankarkumar U. *Evidence for novel DRB1*15 allele association among clinically definite multiple sclerosis patients from Mumbai, India*. *Hum Immunol* 2003;64:478-82.
12. Pandit L, Subramanya R and Rao SN. *Multiple sclerosis in coastal Karnataka*. *Neurol India* 1993;41:143-6.
13. Jain S, Maheshwari MC. *Multiple Sclerosis: Indian Experience in the last thirty years*. *Neuroepidemiol* 1985;4:96-107.
14. Pandit L, Rao SN. *Recurrent Myelitis*. *J Neurol Neurosurg Psychiatry* 1996;60:336-8.
15. Mehndiratta MM, Phul P, Garg S. *Mitoxantrone a disease modifying agent in multiple sclerosis. GB Pant experience*. *Ann Ind Acad Neurol* 2007;10:(S2)53.



UCL

INSTITUTE OF NEUROLOGY

in association with the

National Hospital for Neurology
and Neurosurgery,
Queen Square, London WC1

Short Courses

12th-23rd May 2008

Sleep	(12 May)
Neuro-ophthalmology	(13 May)
Movement Disorders	(14 May)
FULL *Statistical Parametric Mapping	(15, 16 & 17 May)
Neurosurgery	(19 May)
Neuroanatomy of the Basal Forebrain	(20 May)
Dementia	(21 May)
Stroke	(22 May)
Neuro-oncology	(23 May)

* another SPM course will run in October 2008

Course fee £175 per day

(£125 for 5 or more days;

£150 per day for clinical trainees;

£125 per day student rate).

£600 for the three-day SPM course.

(to include morning and afternoon refreshments,
but not lunch)

For further details please contact:

The Education Unit

Institute of Neurology

National Hospital for Neurology and Neurosurgery

Queen Square, London WC1N 3BG

Tel: 020 7692 2346 Fax: 020 7692 2345

Email: J.Reynolds@ion.ucl.ac.uk

www.ion.ucl.ac.uk

*The Institute of Neurology promotes teaching
and research of the highest quality in
neurology and the neurosciences*