MRI CHARACTERISTICS OF CNS DEMYELINATING DISEASE IN ETHNIC INDIAN PATIENTS

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Introduction

CNS demyelinating disease is increasingly recognized as a disorder of worldwide prevalence with heterogeneity in clinical presentation that varies according to race and ethnicity (1,2). It has been demonstrated in multiple studies that there are variants of CNS demyelinating disease in non-Caucasian populations, which can include the "classic" or "western" variant; opticospinal MS thought typical of Asian populations, Neuromyelitis Optica (NMO), NMO spectrum disorders and others, as distinct nosologic entities or as pathologies falling within a spectrum (3-9). How this pathology manifests in varying clinical phenotypes according to race has not previously been extensively studied, and available data is often limited by a large Caucasian bias. MS in Asia has been characterized by fewer brain lesions and involves both the optic nerve and spinal cord more frequently with cord lesions spanning greater than three spinal segments compared to MS described in Western populations (8-9). The Asian variant is also associated with more frequent relapses and more severe disability(6-9). Most of the literature on Asian MS comes from studies performed in Japan and only recently have other Asian populations been studied. Only a handful of studies have investigated MS in those of Indian ethnicity, and the results are mixed as to whether Western or Asian MS is more prevalent in the Indian population (10-11).

This study aims to clarify the radiologic phenotype of CNS demyelinating disease in a small cohort of patients of Indian ethnicity specifically by evaluating the imaging characteristics using established Barkhof's criteria for the diagnosis of clinically definite MS (12). The clinical phenotype of this disease in those of Indian ethnic heritage has not previously been studied extensively and remains largely unknown. Findings from this study could help guide future research to determine optimum therapy for an under recognized minority, and in so doing contribute to human welfare.

Methods

All patients referred to our Neuroimmunology clinic who self-identified as ethnic Indians were selected for participation. Patients with a diagnosis of any CNS demyelinating disease were included, however no distinction was made regarding clinical diagnosis of MS, CIS, NMO or NMO spectrum disorder.

Study data was obtained under a protocol approved by the Institutional Review Board at Stanford University. Written informed consent was obtained from all patients participating in this study.

Previously acquired MR images were collected and subsequently reviewed by 3 independent reviewers blinded to clinical characteristics and clinical status of patients. Subjects with imaging features that met 3 out of 4 Barkhof's criteria were considered meeting Western MS radiologic phenotype (12). Asian MS radiologic phenotype defined as features not meeting Barkhof's criteria and the presence of cord lesions greater than 3 spinal levels (8-9). Individual results were then compared and consensus opinion reached following panel discussion.

Results

A total of 24 patients were identified for inclusion in the study, only 16 patients had images available for review. All had MR brain images and 7 had spine images. 81% met 3 of 4 Barkhof's criteria for Western MS radiologic phenotype. None met criteria for Asian MS radiologic phenotype, although of the 3 patients who did not meet Barkhof's criteria, one did not have spinal images to review.

Patient Characteristics			
	Age	Sex	Birthplace
1	39	f	USA
2	32	f	USA
3	28	f	India
4	24	m	USA
5	35	f	India
6	36	m	India
7	32	f	India
8	58	m	Kenya
9	38	m	India
10	43	f	USA
11	39	f	USA
12	21	m	USA
13	53	f	India
14	39	f	USA
15	32	f	Unknown
16	39	f	Ethiopia

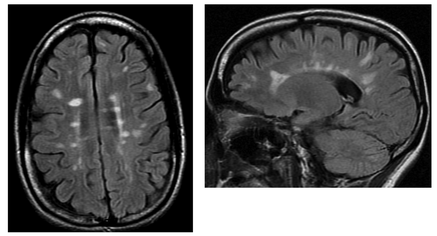

Figure 1: Axial and saggital FLAIR with typical ovoid demylinating lesions. Note periventricular and juxtacortical lesions.

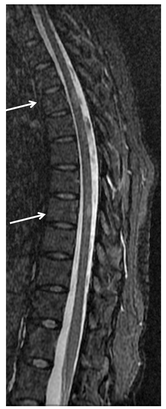

Figure 2: Saggital STIR sequence of spinal lesions in the same patient. 2 lesions present, but only 1 verterbral section in length.

Radiographic Phenotype

subject	>1 gad enhancing lesions or >9 t2 hyperintense brain or cord lesions	>1 infratentorial or cord lesions	>1 juxtacortical lesions	>3 periventricular lesions	c/t spine lesion: equal or greater than 3 vertebral sections	Western vs Asian MS vs none
1	x		x	x	absent	western
2	x		x	x	absent	western
3					absent	none
4	x		x	x	n/a	western
5	x	x	x	x	n/a	western
6					n/a	none
7	x	x	x		n/a	western
8	x		x	x	n/a	western
9	x	x	x	x	n/a	western
10	x		x	x	absent	western
11	x	x	x	x	absent	western
12	x		x	x	n/a	western
13	x	x	x	x	n/a	western
14	x	x	x	x	n/a	western
15		x	x		absent	none
16	x		x	x	absent	western

Conclusions

1) This small cohort suggests that radiographically, CNS demyelinating disease in those of Indian ethnicity is of Western MS phenotype based on Barkhof's criteria.
2) Our study population was balanced in terms of those born in the United States as well as those born in India and whether or not this has any clinical implications remains to be seen.
3) The existing McDonald's criteria and Barkhof's criteria is based on Caucasian populations and therefore its applicability to non-Caucasian populations have been questioned (4-5). The newest revision has been simplified to help address this issue, however further studies will need to determine how useful this criteria is for non-Caucasian populations (2).
4) Limits include small sample size, retrospective review focused on radiologic phenotype and therefore lack of clinical data to correlate with radiologic phenotype, and referral bias to a university setting.
5) It is becoming evident that CNS demyelinating disease differs in terms of diagnosis, clinical features, disease coarse, severity depending on race and ethnicity. This may imply a separate immune mediated mechanism such as a genetic admixture with Caucasian populations versus common environmental risk factors with increased industrialization and travel.
6) Future studies should include epidemiologic studies to understand the true prevalence of CNS demyelinating disease in this Indian and other minority populations, as well as clinical comparisons between treatment response, immunologic differences and biomarkers in these minority populations. Findings could be of benefit in improving recognition, understanding and well-being of minority populations with MS and related diseases.

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