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Clinical and MRI Characteristics of Multiple Sclerosis in Iranian Children and Adolescents

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Abstract

Objective

To determine the clinical and MRI characteristics of multiple sclerosis (MS) in the children and adolescents.

Material & Methods

In this cross-sectional study, information of 95 MS patients was obtained from the Iranian MS registry. Disease characteristics and imaging data were collected using medical records.

Results

Ninety-five patients including 64 female and 31 male subjects with mean age of 13.97±2.4 years (range, 8-18) years were enrolled. The most frequent signs and symptoms were ophthalmic symptoms (n=61, 64.2%), brainstem signs (n=44, 46.3%), cerebellar signs (n=32, 33.6%) and pyramidal signs (n=26, 27.3%). Blurred vision (n=21, 34.4%) was the most common ophthalmic symptom and ataxia (n=24, 75%) the most prevalent cerebellar sign. The most common brainstem signs/symptoms were motor symptoms and vertigo (each n=14, 31.8%) and the most common pyramidal sign/symptom was right upper monoparesis (n=14, 23.3%). Active demyelinating lesions were reported in brain MRI of all patients, mostly appeared as periventricular (n=91, 95.8%) and pericallosal (n=55, 57.9%) lesions. Acute demyelinating spinal lesions were presented in 38 patients (51.3%) with a prominent involvement of the cervical spine (n=33, 86.8%).

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Conclusion

In our study, the most frequent signs and symptoms were eye symptoms, brainstem signs, cerebellar signs and pyramidal signs, respectively. Moreover, our results showed that MRI plays a critical role in the diagnostic evaluation of MS in children with presence of brain lesions in all patients and spinal lesion in a considerable portion of patients.

Keywords: Multiple sclerosis; Natural history studies; Epidemiology; Childhood; Adolescence
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Introduction

Multiple sclerosis (MS) is an immune-mediated disease that mainly occurs during adulthood (1). However, about five percent of cases are reported during childhood, mainly in the second decade of life (2-5). There is a female predominance, especially throughout adolescence and early adulthood, with a ratio of up to 4.5:1 (6).

Despite the similarity in the radiologic characteristics between adult-onset and pediatric-onset MS, the clinical features and course of the disease are entirely distinct in pediatric-onset MS. Almost all of these cases present with a relapsing-remitting (RR) course (4). Optic neuritis, brainstem/cerebellar symptoms, and spinal cord manifestations in adults and pediatrics are among the most common presenting symptoms. However, the sensory deficit is initially more prevalent in pediatric-onset MS (1). Moreover, higher relapse rates in pediatric-onset MS have been reported, which can happen for a long time following the initial onset (7, 8).

Epidemiological and clinical features of pediatric-onset MS have previously been studied in Iran (9-13), but its radiologic features have been overlooked (14). This study aims to determine the clinical and MRI characteristics of MS in children and adolescents.

Materials & Methods

This cross-sectional study obtained data from ninety-five children and adolescents with MS from the Iranian MS registry (2015-2020). The Ethics Committee of Shahid Beheshti University of Medical Sciences, Tehran, Iran, approved the study's protocol. The definitive diagnosis of MS was established using the McDonald criteria. Data included age, sex, parents' educational status smoking habit, family history of MS, disease characteristics including ophthalmic, cerebellar, brainstem involvement, cognitive impairment, pyramidal signs, any abnormalities in the brain, and spinal MRI. The double data entry method was used, and all discrepancies were resolved before recording in the database of the IBM SPSS Statistics V21.0. Descriptive analyses were used to describe the study population, including mean, standard deviation, frequency, and percentage.

Results

Ninety-five patients were studied, including sixty-four females (67.4%) and thirty-one males (32.6%) with a mean age of 13.97±2.4 years (range: 8-18 years). The patients' familial history of MS was reported in 14.7%. Most of the patients live in an urban area (73.6%) (Table 1). The most frequent signs and symptoms were ophthalmic symptoms (n=61, 64.2%), brainstem signs (n=44, 46.3%), cerebellar signs (n=32, 33.6%), and pyramidal signs (n=26, 27.3%). Blurred vision (n=21, 34.4%) and ataxia (n=24, 75%) were the most common ophthalmic symptoms and cerebellar signs, respectively. The most common brainstem signs/symptoms were motor symptoms (n=14, 31.8%) and vertigo (n=14, 31.8%), and the most common pyramidal signs/symptoms were right upper monoparesis (n=14, 23.3%) and left monoparesis (n=8, 13.3%) (Table 2). Active demyelinating lesions were seen in brain MRI of all patients, mainly appearing as periventricular (n=91, 95.8%) and pericallosal (n=55, 57.9%) lesions (Table 3). Acute demyelinating spinal lesions were seen in thirty-eight patients (51.3%) with prominent cervical spine involvement (n=33, 86.8%). The primary diagnosis was not MS in ten patients (10.5%), including isolated syndrome in four cases, acute disseminated encephalomyelitis, chorea, brain edema, vascular changes, neuritis, neuromyelitis, and optica, each in one case. MS manifested with a relapsing-remitting course in ninety-one patients (95.7%), and the remaining had a secondary-progressive course.

The ophthalmologic evaluation was performed on ten patients, revealing six cases of optic neuritis (three bilateral). VEP evaluations were abnormal in 68% of patients (n=34). Moreover, positive CSF, OCB, and MOG ab beside elevated IgG index were reported in 76.6%, 0%, and 46.4%, respectively. NMO ab levels were measured in 20 patients, showing no abnormal evidence.

Table 1. Patients' characteristics

	Mean±SD	Frequency	Percent
Age at the diagnosis	10.39±0.8		
Current age	13.97±2.4		
Sex			
Male		31	32.6
Female		64	67.4
Living location			
Rural area		25	26.4
Urban area		70	73.6

Table 2. Clinical findings of our participants

	Frequency	Percent
Eye Symptoms	61/95	64.2
Diplopia	18	31.1
Blurred vision	21	34.4
Blindness	5	8.2
Ophthalmoplegia	1	1.6
Diplopia and blurred vision	15	24.6
Cerebellar signs	32/95	33.6
Ataxia	24	75
Dysarthria	2	6.3
Nystagmus	4	12.5
Ataxia and dysarthria	2	6.3
Cognitive impairment	0	0
Brainstem signs	44/95	46.3
Bladder dysfunction	2	4.5
Cranial nerve palsy	4	9.1
Sensory symptoms	6	13.6
Motor symptoms	14	31.8
Vertigo	14	31.8
Intestinal dysfunction	1	2.3
Urination & defecation dysfunction	1	2.3
Sensorimotor dysfunction	2	4.5
Pyramidal signs	26/95	27.3
Right hemiparesis	5	8.3
Right monoparesis	14	23.3
Right hemiparesthesia	7	11.6
Left hemiparesis	6	10
Left monoparesis	8	13.3
Left hemiparesthesia	5	8.3
Lower paraparesis	6	10

	Frequency	Percent
Upper paraparesis	3	5
Upper bilateral paresthesia	4	6.6
Lower bilateral paresthesia	2	3.7

Table 3. MRI findings of our participants

	Frequency	Percent
Brain lesions	95	100
Periventricular	91	95.8
Pericallosal	4	4.2
Juxtacortical	40	42.1
Brainstem	55	57.9
Infratentorial	34	35.8
Spinal cord lesions	38	51.3
Cervical	33	86.8
Thoracic	5	13.2
Lumbo-sacral	0	0

Discussion

This registry-based study was among the most extensive studies on pediatric MS patients in Iran. Most of our patients (67.4%) were female, most of whom were diagnosed in the second decade of their lives with a mean age of 13.97±2.4 years. These findings were consistent with the results of previous studies in Iran (9-12, 14). A study by Etemadifar et al. (2007) in Esfahan, Iran, showed that early-onset MS was primarily diagnosed in females and the mean age of onset was 14.1 years (12). Two hundred twenty-one patients with early-onset MS were assessed in another study by Etemadifar et al. (2016), and the results showed that the mean age of patients was 14.7±1.8 and 183 (82.8%) were females (10). In their most recent study, Etemadifar et al. (2021) reported the epidemiological and clinical features of pediatric-onset MS in 509 individuals younger than 18. Their results showed that 79.4% of the patients were girls, and the mean age at the onset of the disease was 15.8 ± 2.5 years (11). Omrani et al. (2018) reported 300 patients with early-onset MS clinical data in Tehran, Iran. They showed that 78% were female, and the mean age of disease onset was 15.6±2.6 years (9). In two landmark studies by Nasehi et al. (2017 and 2021) in Iran, similar results were reported that more than 75% of patients in each study were female, and most were in the second decade of their lives (13, 14). These findings were also confirmed in other populations (1, 15), although female dominance is more significant in some populations, such as African-American black patients (16).

In the current study, most of the patients (95.7%) had

a relapsing-remitting course with the most frequent presentation as follows: ophthalmic symptoms (n=61, 64.2%), brainstem signs (n=44, 46.3%), cerebellar signs (n=32, 33.6%) and pyramidal signs (n=26, 27.3%). Blurred vision (n=21, 34.4%) and ataxia (n=24, 75%) were the most common ophthalmic symptoms and cerebellar signs, respectively. The most common brainstem signs/symptoms were motor symptoms (n=14, 31.8%) and vertigo (n=14, 31.8%), and the most common pyramidal signs/symptoms were right (n=14, 23.3%) and left-side upper monoparesis (n=8, 13.3%). In a review of clinical and demographic features of eighty-two patients with early-onset MS by Etemadifar et al., sixty-two patients (78%) presented a relapsing-remitting course (12). In their following study on 221 patients with early-onset MS, ninety-six patients (88.6%) also had a relapsing-remitting course (10). Consistent with the results of the current study, the most common initial presentation was ophthalmic symptoms and cerebellar signs in their study (10). Their recent study reported optic neuritis and brainstem-cerebellar disorders as the two most frequent symptoms in children with MS (11). Similarly, Omrani et al. reported the relapsing-remitting course as the most common clinical course of the disease and the ocular problem as the most frequently reported symptom (9). In the previous study (2017), diplopia and visual problems were among the most commonly reported symptoms (14).

The relapsing-remitting pattern was reported in all retrospective and prospective cohorts. In a study by Derle et al. on seventy-four Turkish patients with MS during childhood and adolescence, 97.3% of patients had a relapsing-remitting course (17). Similar results were reported by Langille et al. in pediatric Hispanic-American patients (18). Moreover, Alroughani et al. reported that 100 out of 111 Kuwaiti patients with pediatric-onset MS had a relapsing-remitting course (19).

In the present study, all patients had active demyelinating lesions in brain MRI, which mostly appeared as periventricular (n=91, 95.8%) and pericallosal (n=55, 57.9%), and thirty-eight patients (51.3%) had acute demyelinating spinal lesions with prominent involvement of the cervical spine (n=33, 86.8%). Similarly, in the previous study on pediatric-onset MS patients, 91.5% had periventricular lesions, and 53.1% had spinal cord lesions in the preliminary MRI results (14). Yamamoto et al. reported similar results, including brain lesions in all patients and spinal involvements in up to 40% of patients (20).

In Conclusion

Pediatric-onset MS mainly affects females, and most cases are diagnosed in the second decade of life. Moreover, the most frequent signs and symptoms are ophthalmic symptoms, brainstem signs, cerebellar signs, and pyramidal signs, respectively. MRI plays a critical role in the diagnosis of pediatric MS.

Acknowledgement

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Author's contribution

A.N. and M.M.N. supervised the research and contributed to the final version of the manuscript. S.R. contributed to the interpretation of the results and took the lead in writing the manuscript. M.H. collected the data. All authors discussed the results and commented on the manuscript.

Conflict of interest

None declare

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