NEUROPHTHALMOLOGICAL MANIFESTATIONS IN MULTIPLE SCLEROSIS

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ABSTRACT

Background and Objective: Multiple sclerosis is an autoimmune demyelinating disorder of the nervous systems that is commonly manifested by visual system involvement and that my initially present with ophthalmologic symptoms .Manifestations of MS in the eye include both the afferent and efferent visual pathways. Optic neuritis, the most common neurophthalmological manifestation of MS, may be the initial clinical disease manifestation. Our aim is to assess the proportion of neurophthalmological manifestations in MS patients, with frequency of ocular dysfunction as presenting symptoms.

Patients and Methods: (120) patients with clinically definitive MS criteria, whom attended to center of MS during the period from November2006 and July2007 were included in this study. The study depends on clinical examination (V.A, V.F, color test, papillary reflex, fundoscopy) and patient report.

Results: 120 MS patient had a mean age 29.6 year, 60% were female, 40% were male. Arabic were 55% and Kurdish were 45% of patient. The common type of MS was RRMS in 79.17%,followed by PPMS 14.16% and SPMS in 6.67% of patient. Optic neuritis was found in 16.7% as initial presentation & Diplopia occurs in 1.6% only. RRMS was the commonest type associated with optic neuritis 83.95%. Optic neuritis represented the commonest symptoms of neurophthalmological manifestations, which recorded in 67.5% followed by INO in 7.5%, while 6.67% didn't have any neurophthalmological manifestations. Unilateral ON was observed in 92.59%, abnormal VA 85.19%, central and cecocentral scotoma 70.37%, ocular or periorbital pain was found in 86.42% and optic disk swelling was recorded in 25.93% of MS patients.

Conclusions: More than 93% of Iraqi MS patients had at least more than one type of neurophthalmological manifestations. Neurophthalmological finding was common as presenting symptoms or during the course of MS and optic neuritis represented the commonest manifestation of MS with high relationship with relapsing remitting MS.

Key words: Multiple Sclerosis, neurophthalmological manifestations.

INTRODUCTION:

Multiple sclerosis is characterized clinically by episodes of focal demyelinative disorder of the optic nerves, spinal cord, and brain, which remitted to a varying extent and recurred over a period of many years[1].About 85% of patients initially experienced one or more relapses followed by complete or incomplete recovery; this clinical pattern is referred to as the relapsing–remitting phase. Over 10 years, roughly 50% of these patients will to the secondary progressive phase [2,3] ,which is characterized by gradually worsening disability with or without superimposed relapses. About 10% of patients experience a clinical course that is progressive from onset, primary progressive multiple sclerosis. The remaining 5% of patients experience progressive disability from onset that is later accompanied by one or more superimposed relapses; this pattern is referred to as progressive relapsing multiple sclerosis[4-6].

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Part-1 -The afferent visual system in MS:

1-1-**Optic neuritis** : Is a condition involving primary inflammation of the optic nerve . It may be associated with a variety of systemic autoimmune disorders , but the most common form , acute demyelinating optic neuritis is associated with multiple sclerosis [7–10]. The incidence of acute demyelinating optic neuritis is about three per 100 000 people in the USA ,in low-risk regions such as Japan, the incidence approaches one per 100 000 population per year[10,11].Acute demyelinating optic neuritis is the presenting feature in 15-20% of patients with MS , and it a occurs at some time during the course of the disease in 50% of patients [12-14].Optic neuritis is more frequently bilateral in children than in adults and is more commonly associated with optic disk swelling in children than in adult [15-17].Around 50-60% of patients with optic neuritis will have periventricular white-matter abnormalities consistent with demyelination on an initial MRI scan 18-21.56% of patients with one or more white-matter lesions on their baseline brain MRI scan developed MS, whereas 22% of patients with a normal baseline MRI developed MS at 10 years [22].

1-2- Other afferent neuro-ophtha lmological problems in MS:

In addition to the optic nerve , any part of the visual sensory pathway can be affected , including the chiasm , tracts , radiations , and striate cortex [22]. Any type of field defect may occur , depending on the location of the demyelinating lesions [23,24].Symptomatic homonymous field defects are infrequent in MS , occurring in less than 1% of patients [24].Ocular inflammalion may occasionally be seen in patients with MS , manifestations may include uveitis , periphlebitis , and pars planitis. Uveitis is ten times more common in patients with MS than in the general population. Anterior uveitis as a complication in MS is typically granulomatous in nature , and it may manifest before any other clinical evidence of MS [23,25].

2-1- Internuclear ophthalmoplegia :

INO is characterized by slowing or imitation of the adducting eye with abducted eye nystagmus during horizontal saccades and it is the result of damage to the MLF within the dorsomedial pontine or midbrain egmentum , adjacent to the fourth ventricle and cerebral aqueduct, spectively. Internuclear ophthalmoplegia is one of the neuro-ophthelmologic hallmarks of MS and is presentednj in 17-41 % of patients [26].While a third of all patients with INO were found to have MS in two major recent studies , and an increased risk of MS is associated with bilateral INO [27,28].The duration of INO ranges, but a recent study of 65 affected patients revealed recovery within 3 months in only 23 % [27].

- 2-2- The one-and-a-half syndrome:

A gaze palsy in one direction and INO on the attempted gaze contralaterally is reffered to as the one-and-a-half syndrome [29] . This syndrome is produced by a lesion that damages either the paramedian pontine reticular formation (PPRF) or abducens nucleus (or both) together with the MLF on the same side .

2-3 –Nystagmus: The classification of nystagmus is perhaps best approached by considering the disorders of the gaze holding networks themselves in the brainstem and cerebellum and the inputs to them which can become imbalanced. Pathological nystagmus on eccentric gaze. Gaze evoked nystagmus refers to a "jerk" nystagmus with a slow drift in one direction and a resetting saccade in the other. This commonly indicates failure of the neural integrators[22]. Pendular nystagmus (nystagmus in which there is a back and forth slow- phase oscillation) can also arise from disturbances in the neural integrators, usually involving critical feedback pathways that interconnect brainstem networks and the cerebellum[30,31].

2 -4- Nuclear and fascicular lesions:

Nuclerar and fascicular cranial nerve syndromes have been described in MS. Sixth nerve paresis is the most common [32-34].

Aims of the study:
1-to identify the proportion of neurophthalmological manifestations in MS patients.
2-to identify the frequency of neurophthalmological manifestations as presenting symptoms.
3-to recognize the most common neurophthalmological feature that occurs during the course and types of MS patients.
4-to recognize the relationship between the course of MS and optic neuritis.
5-to show the relationship between optic neuritis and its character.

PATIENTS METHODS:

Design of the study: the current work represents a case series study for (120) MS patients, which is conducted from the period extended from the between first November 2006 and the end of July 2007.
Socio-demographic characteristics: the study is conducted in the department of Neurology at Baghdad Teaching Hospital (Multiple Sclerosis Clinic).
The study groups: a among (120) MS patients –diagnosed according to poser criteria, whom course of the disease is either RRMS,SPMS or PPMS. All the MS patients are included in this study except, those patients with reassessment and evaluation their condition, whom previously recorded in this study .
Questionnaire and data collection: utilizing the available information about MS by a special questionnaire has been prepared by the investigator. For each patient an isolated questionnaire had been filled in by conducting direct interview with patient. Each patient was interviewed and assessed according to a questionnaire paper, and patient report, who recorded in MS clinic because some of them had memory impairment due to cognitive disorders.
Examination: the diagnosis of cases had done by the neurologist then the clinical assessment for every case with MS was examined for the following points:
by :
-Visual acuity
-Visual field.
-Relative afferent papillary defect.
-Fundoscopy.
*Efferent visual pathway which assessed by :
-Extra-ocular eye movement.
-Statistical analysis: the data collected on (120) MS patients, who were included in the study were studied to assess the proportion of ocular manifestations in MS patients. Conventional statistical techniques were applied to the data in this study of distribution by frequency percentage, mean and table representation.

RESULTS:

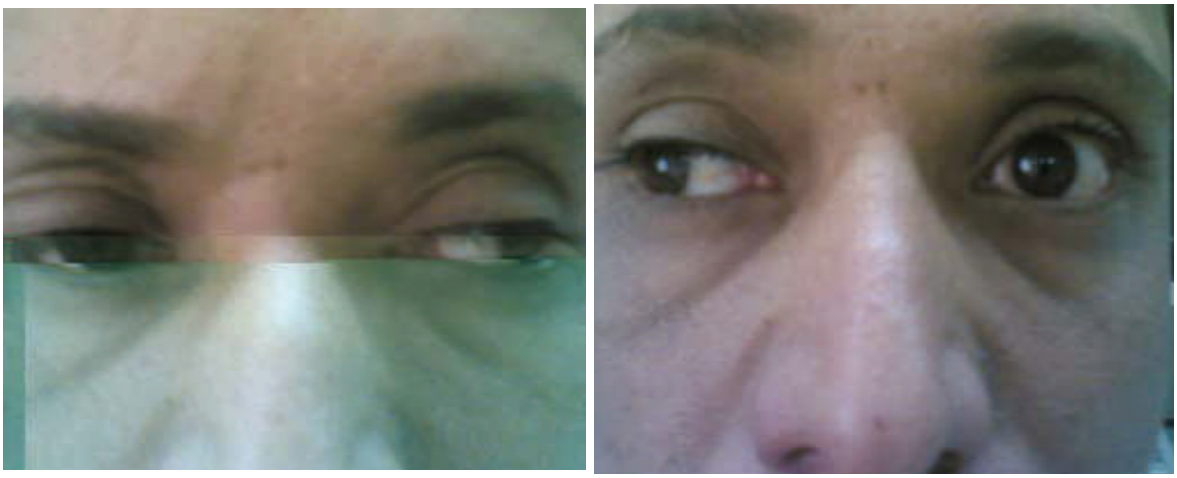
One hundred-twenty patients ,72 female (60%) and 48 male (40%) with a mean age of (29.6 year) , range(32) years were included in this study, analysis of MS patients according to age group shew that four(3.33%) of one hundred-twenty patients were younger than 20 years. According to ethnicity ,66 Arabic (55%) and 54 Kurdish (45%) patients were studied (Table1).
Table1 : The Distribution of The MS Patients According to Gender and

Gender	No. of cases	Percentage
Male	48	40
Female	72	60
Total	120	% 100
Ethnicity	-	-
Arabic	66	55
Kurdish	54	45
Total	120	% 100

Regarding initial presentation , the most frequent symptom was pyramidal weakness, in 52 patients (43.3%) ,followed by sensory loss (numbness) ,with 32 patients (26.7%) .An optic neuritis was pathway disorders , the most frequent was unilateral internuclear ophthalmoplegia (INO), in 9 patients (7.5%) ,the second common symptoms of neurophthalmo logical manifestations was horizontal

Table 2: The Presenting Symptoms of MS Patients.

presenting symptoms	NO. of cases	Percentage
-optic neuritis	20	16.7
- pyramidal weakness.	52	43.3
- sensory loss.	32	26.7
-Cerebellar.	14	11.7
-horizontal. Diplopia.	2	1.6
Total	120	%100



Impaired Adduction Ataxic Nystagmus Right INO

Ataxic Nystagmus Impaired Adduction Left INO

Figure 1: Bilateral Internuclear Ophthalmoplegia

in 20 patients (16.7%) , while cerebellar symptoms was found in 14 patients (11.7%) . Other uncommon presentation was horizontal diplopia that occured in two patients (1.6%) only .(Table 2).

According to prevalence of neurophthalmological manifestations, optic neuritis represented the most common features , in 81 patients (67.5%) of MS . Another afferent visual pathway disorder was optic atrophy (OA) present in two patients (1.66 %). Regarding the Nystagmus which found in 8 patients (6.67%) while vertical nystagmus was uncommon occured in two patients (1.67%). Sixth cranial never paresis was the most common extraocular nerve involvement that found in eight patients (6.67%) while two patients (1.67%) presented with horizontal diplopia as presenting symptoms and in sixth patients (5.00 %) during the course of the disease . Other rare presentation was one-and a half -syndrome in two patients (1.67%).

Whereas none of patients had 3rd , 4th and gaze palsy in this study. Eight cases of MSpatients didn't have any ocular manifestation (Table 3)The most common type of MS patients was relapsing remitting multiple sclerosis (RRMS) that presented in 95 case (79.17%) of patients, that most frequently associated with optic neuritis which found in 68 patient (83.95%), primary progressive multiple sclerosis (PPMS), in 17 case (14.16%) of patients which correlated with optic neuritis that occured in 8 cases (9.88%) ,and the last type was the secondary progressive multiple sclerosis (SPMS) ,in 8 cases (6.67%) of patients which associated with optic neuritis that presented in 5 cases (6.17%). (Table 4).

Table (3) The Distribution of Neurophthalmological & non-Neurophthalmological Manifestations in MS Patients .

Manifestations	NO. of cases	percentage
-Optic neuritis.	**81**	**67.5**
-Optic atrophy.	**2**	**1.66**
-Sixth C.N . paresis .	**8**	**6.67**
-Third C.N paresis .	**- -**	**- -**
-Fourth C.N .paresis .	**- -**	**- -**
-Internuclear ophthalmoplegia.	**9**	**7.5**
-One- and a half syndrome.	**2**	**1.66**
-Gaze palsy.	**- -**	**- -**
-Nystagmus: a– horizontal. b– Vertical.	 **8** **2**	 **6.67** **1.67**
-Non- neurophthalmological.	**8**	**6.67**
Total	**120**	**100%**

Table (4) The Distribution & Correlation of MS With Optic Neuritis.

Type of MS	Distribution		Correlation with optic neuritis	
	No. of cases	percentage	No. of cases	percentage
RRMS	95	79.17	68	83.5
PPMS	17	14.16	8	9.88
SPMS	8	6.67	5	6.17
TOTAL	120	100%	81	100%

The type of optic neuritis was unilateral in 75 patients (92.59 %), and bilateral in 6 patients (7.41%). Regarding visual acuity , the severity of visual loss was varied from mild to moderate, which recorded in this study as abnormal visual acuity in 69 patients (85.19%) while normal visual acuity presented in 12 patients (14.81%). A wide variety of visual field defects were observed including central and cecocentral scotoma in 57 patients (70.37%), normal visual field in 22 patients (27.16%) and altitudinal visual defect in two patients (2.47%). Periorbital or ocular pain might either precede or occur concomitantly with vision loss was common , occurring in 70 patients (86.42%), and 11 patients (13.58%) without pain. Generally the pain lasts for several days and was not correlated with either severity of vision loss or potential for visual recovery .Color vision was desaturated in 64 patients (79.01%), and 17 patients (20.99%) presented with normal color vision. A relative afferent pupillary defect (Marcus Gunn pupil) was observed in 16 patients (19.75%) , and 65 patients (80.25%) present with normal pupillary response .Finally ophthalmoscopic finding was normal, in 60 patients (74.07%), and 21of patients (25.93%) had optic disk swelling.

DISCUSSION:

There are extensive studies on MS in the literatures, dealing with different aspect of the disease. Neurophthalmological findings may be initial manifestation of MS or as occurring in the course of the disease**.** This is the first study carries out in Iraq to evaluated and assessed the incidence of neurophthalmological manifestation in 120 Iraqi MS patients.In this study 60% were female and 40% were male, with a mean age of 29.6 years and range 32 years, which were compatible with others studies that performed in a worldwide centers of MS, except for 3.33% of patients were younger than 20 years, when comparable with [M Ruggieri et al,MS in children, 2004] this is probably because small number of children involved in our study .This study shows that the initial presentation of optic neuritis was documented in 16.7% of patients with MS, which was agreed with other studies in the worldwide of MS center and ONTT, for example the incidence was approximately similar to Slovakin study was 18.2% [M Ruggieri et al,MS in children, 2004[35] study were 5% younger than 16 years, this is probably because small number of children involved in our study .This study shows that the initial presentation of optic neuritis was documented in 16.7% of patients with MS, which was agreed with other studies in the worldwide of MS center and ONTT, for example the incidence was approximately similar to Slovakin study was 18.2% This study showed the correlation between optic neuritis and relapsing remitting course of Ms was found in 83.95% of patients, which approximately compatible with Slovakin stusy was 73%, while when compares the secondary progressive MS 6.17% and primary progressive MS 9.88 % there are a difference with the same study [27%, and zero respectively[36] .Regarding peri-orbital or ocular pain occurring in 86.42% of patients with MS, while 13.58% of MS patients without pain such finding was reported in Harvard medical school study was 92.2% of cases [J.F. Rizzo et al, 1991] [40] and USA study [Ocular manifestation of MS, 2005] [39] .According to abnormal visual acuity were reported in 85.19% and normal visual acuity found in 14.81% of MS patients, while visual field defect represent central cecocentral scotoma 70.37% normal visual field in 27.16% and altitudinal defect in 2.47%.These findings were agreed with ONTT study [Frohman et al, 2005][22] except this study did not concentrated on subdivided of visual field defect. The ophthalmoscopic findings in our study were presented as optic disc swelling in 25.93% while normal finding was 74.07%, which was compatible with Nillson study was 29% [P. Nillson et al, 2005] [41] with relatively similar findings was

the Harvard medical school study 35.3%of disk swelling and 64.7%was normal [Rizzo et al, 1991] [40] , but with significant difference when compared with Tiiwan study was 44.4% with disk swelling [Bee Ys, et al, 2003] [42].

CONCLUSIONS:

Neurophthalmological manifestations assessed by clinical examination and ophthalmoscopic finding were common a among Iraqi MS patients, it is were common as initial presenting symptoms or during the course of disease in MS patients. Optic neuritis was the most neurophthalmological presenting symptoms and its highly correlated with relapsing remitting multiple sclerosis. The percentage of unilateral optic neuritis associated with pain, disk swelling and color desaturation are very high. The percentage of MS in female is greater than in male patients.

RECOMMENTDITIONS:

Proper attention to the assessment and management of ocular function in MS may help to improved the life of those patients, as those disturbances were disabled (may lead to blindness). Simple measure might be taken to overcome such impairment. thus the practicing clinician should be encouraged to look carefully for the neurophthalmological manifestations when they assess their MS patients. Every patient(especially young) presented with a certain neurophthalmological syndrome such as optic neuritis or INO should be interviewed and assessed for MS. Patient with typical of acute monosymptomatic demyelinating optic neuritis should undergo evaluation with gadolinium enhanced MRI of the brain to determine the of development of MS.Cooperative way should be correlated between ophthalmologist and neurologist in certain syndromes , retinal periphlebitis , pars planitis and panuveitis because these syndromes most common associated with MS.

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