Multiple sclerosis at Jordan University Hospital

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ABSTRACT

Objective: A study of multiple sclerosis patients admitted to Jordan University Hospital over a 10-year-period with a comparison with other Western and Middle Eastern series.

Methods: The case notes of 32 patients with multiple sclerosis were reviewed to determine the age and sex distribution, clinical findings and results of investigations, treatment and outcome.

Results: There were 32 patients (24 females, 8 males, 3:1), with mean age at onset of 31.4 years, and range 6-50 years. All patients fulfilled Poser's criteria for multiple sclerosis. The most common clinical manifestation was myelopathy followed by a polysymptomatic onset. Two-thirds of the patients had a relapsing - remitting course. The yield of cerebrospinal fluid oligoclonal banding was low (20%). The sensitivities of visual evoked potential was 62%, magnetic resonance imaging of brain 100%, magnetic resonance imaging of cervical spine was 70% and of dorsal spine 44%. Intravenous methylprednisolone Igr for 3-5 days was efficient in acute relapses for all patients. Beta-interferon was efficient in 2 out of 7 patients. After a mean follow-up of 5 years, two-thirds of the patients had mild to moderate disability (Extended disability status scale = 2 and 3).

Conclusion: The age and sex distribution, clinical and magnetic resonance imaging findings were almost similar to other reports. However the yield of visual evoked potentials was low and that of cerebrospinal fluid oligoclonal banding was very low, the results of treatment with beta-interferon were modest and the outcome at a mean follow-up of 5 years was relatively good.

Keywords: Multiple sclerosis, myelopathy, cerebrospinal fluid oligoclonal banding, beta interferon.

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Multiple sclerosis (MS) is a common disease of the central nervous system affecting approximately one million young adults, mostly women, worldwide.[1] It is characterized by episodic neurologic symptoms that are often followed by fixed neurologic deficits, increasing disability, and medical, socioeconomic, and physical decline over a period of 30 to 40 years.[2] Only a few studies have been carried out in Jordan,[3] therefore, the present retrospective study was undertaken with the purpose of assessing: 1. Age and sex distribution of patients; 2. Clinical presentation at onset and clinical course; 3. Sensitivity of cerebrospinal fluid oligoclonal banding (CSF OCB), visual evoked potentials (VEP) and magnetic resonance imaging (MRI) of brain and spinal cord; 4. Results of treatment modalities and 5. Outcome. The case notes of 32 patients with MS seen at Jordan University Hospital (JUH) over a 10-year-period were reviewed and results compared with those in the Western and Middle Eastern literature.

Methods. The case notes of 32 consecutive patients with MS (age range at onset 6-50 years; 24 females, 8 males, ratio 3:1) seen at JUH over a 10-year period were studied. All the patients fulfilled Poser's criteria for MS[4] and they were put in the following disease categories: 1) clinically definite MS; 2) laboratory supported definite MS; 3)

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clinically probable MS and 4) laboratory supported probable MS. The disease course was categorized according to an international survey[5] in relapsing-remitting, secondary progressive and primary progressive courses. Clinical relapses were defined as clear-cut episodes of functionally significant worsening each lasting 24 hours and separated by at least one month. A secondary progressive course was defined as being preceded or accompanied by relapses and a primary progressive course was defined as a gradual neurological deterioration from the onset. All the patients were admitted to hospital and had MRI brain whereas MRI cervical and dorsal spine were carried out when clinically indicated. All patients had complete blood count, erythrocyte sedimentation rate (ESR), kidney and liver function tests, serum B12 and folate as well as antinuclear antibody (ANA) titers, C-reactive protein (CRP), rheumatoid factor (RF) and serum venereal disease research laboratory (VDRL) to rule out central nervous system (CNS) vasculitis. The majority had lumbar puncture with studies for CSF cells, protein, sugar as well as CSF immunoelectrophoresis using agarose gel to look for OCB. Pattern-shift VEPs were carried out using a Medelec MS 60 machine. According to Kupersmith[6] and Thompson[7] all the patients received pulse steroids (one gr of intravenous (IV) methylprednisolone for 3 to 5 days) during relapses. Beta-interferon (Beta INF) could be used in only 7 ambulatory patients with active relapsing - remitting MS with or without secondary progression (Kurtzke's[8] extended disability status scale, EDSS < 6) according to the recommendations of Polman[9] whose criteria for 1. a clear efficacy was defined as absence of relapses during treatment; 2. moderate efficacy as a decrease of relapses but still the need of one or 2 pulse steroids during treatment and 3. lack of efficacy as the continued progression over 6 months despite treatment or the necessity for 3 courses of pulse steroids during one year while on treatment. Over 7 months we recruited 7 patients with relapsing - remitting MS, not receiving any previous immunomodulatory treatment, to have monthly doses of IV Immunoglobulins (IV Ig) (0.2 gr/kg) according to the method of Fazekas.[10] Immunosuppressants (Azathioprine, Cyclo-phosphamide) were temporarily used in a few refractory cases. The physical disability was assessed according to Kurtzke's scale.[8]

Results. With regard to the age and sex distribution at the onset of the disease, 3 female patients had onset below the age of 20 years; 14 (8 females, 6 males) between 21 and 30 years; 9 (8 females, 1 male) between 31 and 40 years and 6 (5 females, 1 male) above the age of 41 years. Thus the majority (23 out of 32 patients) had the disease onset between 21 and 40 years. The mean age of onset was 31.4 years and the respective mean ages of onset in males and females were 30.5 years and 32.5 years. Two patients were siblings (one male and one female with respective ages of 35 and 28 years).

With regard to the presenting clinical manifestations, myelopathy was noted in 15 patients (47%), optic neuritis in 6 (19%), brainstem signs in 2 (6%) and a polysymptomatic onset (namely myelopathy + optic neuritis + brainstem and cerebellar signs) in 9 (28%). Thus the most frequent was myelopathy followed by a polysymptomatic onset. According to Poser's criteria,[4] 23 patients

Table 1 - Results of treatment with Beta Interferon.

Disease category	Type of INF	Time of use after onset	Duration of treatment	Efficacy	Side effects	Treatment outcome
Secondary Progressive	1 A	4 years	2 years	No	Skin lesions	Stopped
Secondary Progressive	1 B	4 years	2 years	No	None	Stopped
Relapsing Remitting	1 A	1.5 years	2 years	No	None	Stopped
Secondary Progressive	1 A	1 year	2 years	No	None	Stopped
Secondary Progressive	1 A	6 years	2 years	No	None	Stopped
Relapsing Remitting	1 A	1.5 years	1.5 years	Yes	None	Still on treatment
Secondary Progressive	1 A	4 years	1.5 years	±*	None	Still on treatment

* 2 pulses of steroids were used while on treatment, INF - Interferon

Table 2 - Outcome (mean follow-up = 5 years).

Disease category	Disability Scores (EDSS)						
	1	**2**	**3**	**4**	**5**	**6**	**Total**
* Relapsing - Remitting	4	9	6				**19**
* Secondary - Progressive			5	1	1	1	**8**
* Primary progressive			2	3			**5**
Total	**4**	**9**	**13**	**4**	**1**	**1**	**32**

EDSS - Extended disability status scale

(71%) had clinically definite MS (category A1 = 19 and A2 = 4), 5 patients (17%) had laboratory definite MS (Category B1 = 2, B2 = 1 and B3 = 2) and 4 (12%) had clinically probable MS (Category C1 = 1 and C3 = 3). Nineteen out of 32 patients (60%) had a relapsing - remitting course, 25% (8 out of 32 patients) a secondary progressive course and 5 (15%) a primary progressive course. The time between the relapsing remitting and secondary progressive stage ranged from 2 to 10 years (mean = $4^1/_2$ years).

Lumbar puncture (LP) was carried out in 29 patients and, among the 23 patients with clinically definite MS, LP was carried out in 20 and showed CSF positive OCB in only 20% (4 out of 20 patients). Visual evoked potentials were carried out in 24 patients and were abnormal in 15 (62%), 7 unilaterally and 8 bilaterally. Magnetic resonance imaging of brain was carried out in all patients and was abnormal in all of them by showing multiple hyperintense T2 - weighted and hypointense T1 - weighted lesions (with or without enhancement) in one or more of the following locations: Periventricular, centrum semiovale, corpus callosum, brainstem and cerebellum. Magnetic resonance imaging of the cervical spine was abnormal in 17 out of 24 patients (70%) and MRI dorsal spine was abnormal in 4 out of 9 patients (44%).

With regard to treatment, pulse steroids led to improvement in all the patients in whom they were used. The results of treatment with Beta INF are shown in **Table 1**. Conspicuously it was inefficient in 5 out of 7 patients, moderately efficient in one patient and clearly efficient in another. Immunosuppressants were also inefficient. The patients on IV Ig showed no relapses since the beginning of treatment but we are waiting for the results after a follow-up of one and 2 years. After a mean follow-up of 60 months (range 7 months - 140 months), the outcome is shown in **Table 2** which indicates that 69% (22 out of 32 patients) had mild to moderate disability (EDSS 2 and 3).

Discussion. Several points emerge from this retrospective study of 32 patients with MS observed over a 10-year period at JUH. With regard to age of onset, the majority of our patients were between 21 and 40 years of age, which is in accordance with Western[11-15] and Middle Eastern Studies.[16-19] With respect to sex distribution, there was a female predominance (F/M ratio = 3/1) which is in agreement with all Western[11-14,20] and Middle Eastern Studies.[16,18,19] The most frequent initial clinical presentation was myelopathy (47%) which is in agreement with other series.[12,13,17,18] Only 19% had optic neuritis at disease onset which approaches the figure of 25% noted by Marsden.[13] A polysymptomatic onset was encountered in 9 out of 32 patients (28%:15% M and 13% F) which approximates the figures noted by Paty[21] (14.5% in females and 11.9% in males). Two thirds of the cases had a relapsing - remitting course which concurs with the study of Gilroy[12] who noted that 70% of MS patients experience a relapsing remitting course initially, and with that of Weinshenker[22] who found 66% of relapsing - remitting cases among a cohort of 1100 patients, as well as with other reports.[11,13,14,16,18] Among the 19 patients with relapsing - remitting course, 13 had the disease onset in the 2nd and 3rd decades with a female predominance of 10/3 [F/M ratio = 3.3], which is in agreement with Noseworthy.[14] A secondary progressive course was found in 25% of our patients after a mean follow-up of 4.5 years (range 2 - 10 years) which is in agreement with Gangopadhyay[18] and Weinshenker,[23] the latter having noticed that 30 to 40% of patients will have a secondary progressive course after a disease duration of 6 to 10 years. A primary progressive course was found in 15% of our patients which approximates the figures of 10% reported by Marsden,[13] Polman[15] and Bohlega[16] and that of 20% reported by Noseworthy[14] but is much less than the figure of 33% found by Weinshenker.[23]

The results of positive CSF OCB (20%) is much less than that found by Daif[17] (98.5%) and by other reported series[2,11,12,18,24] who noted a positive CSF OCB in 90 - 95% of clinically definite MS. This finding is still unexplained but may be due to the variability of technique and interpretation in various laboratories. The VEP was abnormal in 62% of patients which is less than in other reports[11,12] where abnormality was noted in 80 - 85% of definite MS. Magnetic resonance imaging of brain was abnormal in 100% of our patients which is in agreement with Daif[17] (98.5%), Marsden[13] (>95%) and Gilroy[12] (95%) in clinically definite MS. The sensitivity of MRI cervical spinal cord was higher than that of thoracic spinal cord (70% versus 44%) which is in accordance with Kidd[25] who noted lesions in 59 out of 80 patients (74%) and who found more lesions in cervical than thoracic spinal cord. Concerning treatment, IV pulse steroids were efficient for acute relapses in all our patients which is similar to other reported series.[2,6,15,26]

In addition, other studies[7] concluded that high dose IV solumedrol, compared to oral steroids, has a more rapid onset of action, produces more consistent benefits and has fewer side effects. Nevertheless Barnes[27] did not notice a significant difference in any outcome measure at any time point between IV methylprednisolone or low-dose oral prednisolone, and in various studies, all of them small, quite different dosage regimes of oral steroids have been applied.[28] Beta INF was used in only a few patients because of its high cost and unavailability in Jordan a few years ago. Its failure in most of the patients (5 out of 7) may be partially explained by the following: 1. most of the cases were relapsing - remitting secondary progressive MS using Beta INF 1 A (Rebif) whereas some reports[15,29] showed efficacy of Beta INF 1 B in such cases; 2. the delay in using treatment (mean of 3.5 years after onset) thus allowing secondary progression and 3. the possibility of neutralizing antibodies which however are less frequent with Beta INF 1 A than 1 B. However our patients' number is too small to make a definite conclusion concerning the efficiency of Beta INF. With respect to outcome, after a mean follow-up of 5 years, the majority (22 out of 32 patients) had mild to moderate disability (EDSS 2 and 3), mainly due to ataxia or paraparesis which is in contradistinction with Yaqub[30] where the main disability in 16 MS patients was due to visual loss. However our follow-up is not long enough because longer follow-ups[31] have shown more severe evolution where EDSS of 6 was reached in 50% of patients within 16 years of onset and 65% at 25 years.

In conclusion our study shows, 1. Nothing remarkable regarding age and sex distribution; 2. Same initial clinical presentation and clinical course as in other reported series; 3. A low yield of CSF OCB and a high yield of MRI brain and cervical spinal cord; 4. A modest efficacy of Beta INF and 5. A mild to moderate disability at a mean follow-up of 5 years.

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