Peripheral Poly Neuropathy in Iraqi Patients with Behçet's Disease

Sami Salman*, Ph.D
Khalid Ibrahim Ph.D**
Ammar H. Abed*

Summary:

Background: *To determine the prevalence of peripheral nervous system involvement in Iraqi patients with Behçet's disease.*

Patients and methods: *Seventy-five patients (50 males and 25 females) who fulfilled the International study group criteria for B.D were studied, full history was taken and complete clinical examination was done for all patients with special concentration on the presence of peripheral neuropathy. Nerve conduction study was done for all patients and investigations include pathergy test, HLA/B5 &51, general urine examination, renal function tests, liver function tests, random blood sugar, hemoglobin and erythrocyte sedimentation rate were determined.*

Results: *Fifteen of the seventy-five patients (19.98%) had symptoms of peripheral nervous system involvement. One patient only (1.33%) had peripheral poly-neuropathy proven by history and physical examination, and confirmed by electro-neurography (ENG) and nervous conduction study (NCS).*

Conclusion: *Peripheral poly-neuropathy in patients with Behçet's disease is rare manifestation and when present it was not the first manifestation of the disease but developed during the course of the disease.*

Introduction:

Behçet's disease (BD) is a chronic multisystemic and symptomatic recurrent vasculitis affecting all organs of the body concurrently or consecutively (1). Peripheral neuropathy may be diffuse processes affecting all nerves or individual nerve which can be affected by local pathology (trauma, compression and entrapment).It can be caused by numerous causes including: metabolic and endocrine, toxic causes like alcohol, Inflammatory disorders, Genetic hereditary motor and sensory neuropathy, Deficiency states and Malignant disorders (2). Peripheral neuropathy can be divided into two types: axonal lesion and demyelination lesions (3). Peripheral nervous system involvement in patients with BD is rare, and few reports are found in the literatures, some of them are doubtfully due to BD (4).

Aim Of The Study:

To determine the prevalence of peripheral neuropathy in Iraqi patients with Behçet's disease.

* *Dept of Medicine, Rheumatology Unit, Faculty of Medicine, University of Baghdad.*
** *Dept of Medicine, Neurology unit, Faculty of Medicine, University of Baghdad.*

PATIENTS AND METHODS

Seventy-five patients with B.D. 50 were males and 25 were females, attending the B.D. clinic in Baghdad teaching hospital who fulfilled the international study group criteria for B.D were evaluated and included in the study from November 2003 to July 2004.All the patients agreed to participate in the study.

Age of the patient, age at the onset of BD and age at development of peripheral neuropathy were recorded.

Full history was taken and complete clinical examination was performed for all patients with special concentration on the peripheral nervous system.

The performance of the neurological examination and the conformation of the results was done by Senior Neurologist in the Department of Neurology at Baghdad teaching hospital. Electrophysiological study was performed for all patients whether showing neurological signs and symptoms or not.

Patients with diabetes mellitus, history of liver and kidney impairment, alcohol abuse and family history of peripheral nerve disorders were excluded from the study.

Each patient was investigated for bilateral median nerve, ulnar, common peroneal, tibial nerves and sural nerves by the following electrophysiological studies:-

1-Sensory latency (SL)
2-Distal motor latency (DML)

3-Sensory nerve conduction velocity (SNCV)
4-Motor nerve conduction velocity (MNCV).

Using surface or needle electrodes, it is possible to record action potentials from the nerves which lie close to the skin surface, if the recorded potential is smaller than expected this provide evidence of reduction in the number of axons (2) Sensory distal polyneuropathy was diagnosed if sensory conduction velocity is reduced and the sensory latency is delayed(5).

Laboratory investigations including general urine examination, renal function tests, liver function tests, random blood sugar ,hemoglobin and erythrocyte sedimentation rate were determined. Pathergy test* was performed using a standard technique (6), HLA/B5 &51 was performed to all patients (7). The mean, percentage and standard deviation were obtained by using statistical equations.

*This test represents a nonspecific skin hyperreactivity induced by intradermal needle prick. It is performed by using two subcutaneous prick with blunt 20-gauge sterile needle to one arm and two subcutaneous prick with a sharp needle to the other ann simultaneously. All tests are read at 48 hours, and the result is considered positive if a sterile erythematous papule of more than 2mm forms (6).

Results

Seventy-five patients (50 were males with mean age 30.02 years and 25 were females with mean age 32.04 years) with BD were evaluated. The duration of the disease ranged from 1-20 years

Table (1): The demographic characteristics of 75 patients with BD studied.

Disease duration (years)	No. of patients			Mean age (years)		
	male	female	total	male	female	Total
1-4	20	13	33	29.25	27.38	28.51
4-8	6	4	10	35.83	31	33.9
8-12	5	4	9	38.6	40	39.22
12-16	10	2	12	39.1	38	38.91
16-20	9	2	11	42.33	42.5	34.63

The presenting symptom was oral ulcers in(91%) but during the course of the disease all of the patients (100%) had recurrent oral ulceration. Genital ulcers was present in 69 patients (62%), skin lesions in 30 patients (40%), Pathergy test was positive in 73 patients (97%) and HLA/B5 &51 were determined in 63 patients (84%). Ocular manifestations in 25 patients (33.33%), vascular involvement was represented as DVT. in 4 patients (5.33%).CNS involvement presented as stroke in 2 patients (2.66%).Peripheral articular manifestation in 65 patients, 5 of them (6.66%) had arthritis and the other 60 patients (80%) had arthralgia, GIT involvement was in the form of gastric ulcer in 3 patients (4.04%) all of them were males as shown in (table 2).

Table (2): Shows the clinical manifestation for 75 patients with Behcet's disease.

Manifestations		No. of patients			Percentage of total (%)
		Male	female	total	
Mucocutaneous	Mouth ulcer	50	25	75	100
	Genital ulcer	47	22	69	92
	Skin lesion	20	10	30	40
	Pethargy test	49	24	73	97.33
Ocular		17	8	25	33.33
Vascular	DVT.	3	1	4	5.33
	Cardiac	0	0	0	0
	Hepatic	0	0	0	0
	Pulmonary	0	0	0	0
CNS.	Epilepsy	0	0	0	0
	Meningitis	0	0	0	0
	Stroke	1	1	2	2.66
Articular	Peripheral arthritis	3	2	5	6.66
	Arthralgia	40	20	60	80
GIT.		3	0	3	4.04

Fifteen of the seventy-five patients had symptoms of peripheral neuropathy (pain sensation, burning, numbness, pricking and parasthesia) by history as shown in table 3.

Table (3): Shows the symptoms of peripheral neuropathy in patients with Behcet's disease .

Symptoms		No. of patients		
		male	female	total
Pain sensation	UL*	3	5	8
	LL**	3	4	7
Burning sensation	UL	4	3	7
	LL	1	3	4
Numbness	UL	3	5	8
	LL	3	4	7
Pricking sensation	UL	1	3	4
	LL	2	2	4
Tingling	UL	2	2	4
	LL	1	3	4

*UL= upper limb.
**LL= lower limb.

One patient showed peripheral poly neuropathy proven by nerve conduction study. This patient with peripheral poly neuropathy-proven by nerve conduction study had signs of decrease in pin prick sensation, temperature sensation, light touch sensation and Joint position and vibration sensation as shown in table 4

Table (4): Shows the signs of peripheral neuropathy in patient with Behcet's disease and nerve conduction study findings.

Signs			No. of patients			Percentage
			male	female	total	of total(%)
Motor examination	Weakness		0	0	0	0
	Wasting		0	0	0	0
	Tone		0	0	0	0
	Power		0	0	0	0
	Reflexes		0	0	0	0
Sensory examination		RT*(UL)	0	0	0	0
		LT**(UL)	0	0	0	0
	Pain & Temp.*	RT(LL)	1	0	1	1.33
		LT(LL)	1	0	1	1.33
		RT(UL)	0	0	0	0
		LT(UL)	0	0	0	0
	Touch	RT(LL)	1	0	1	1.33
		LT(LL)	1	0	1	1.33
		RT(UL)	0	0	0	0
	Joint position & Vib.#	LT(UL)	0	0	0	0
		RT(LL)	1	0	1	1.33
		LT(LL)	1	0	1	1.33
Nerve conduction Peripheral poly neuropathy			1	0	1	1.33

*RT= right, **LT=left, "temp= temperature, #vib=vibration.

One of the fifteen patients proved by electrophysiological examination to have distal sensory polyneuropathy involving the lower limbs while the other 14 showed symptoms of peripheral neuropathy. The nerve conduction study for the patient with peripheral poly neuropathy is shown in table 5.

Table (5): The nerve conduction study (SL, SNCV) of the right sural nerve, (DML and MNCV) of the right common peroneal nerve in patient with Behcet's disease who has peripheral poly neuropathy .

Nerve conduction	Patient	Normal* Mean ± SD
SL(m/sec)	4.5	3.49 ± 0.25
SNCV(m/sec)	40.25	53.04 ± 3.77
DML(msec/cm)	9.5	5.3 - 8.8
MNCV(m/sec)	40	42.6 ± 4.6

* (8), SD= standard deviation.

The laboratory findings are shown in table 6

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Table (6): Shows the laboratory findings for 75 patients with BD.

Lab. Manifestations	The values (mean ± SD)		
	male	female	total
HLA *B5, 51	43 +ve	20 +ve	63 +ve
R.B.S**(mg/dl)	130.09 ± 7.5	120 ± 3.2	126.66 ± 5.3
SGOT# (U/L)	10 ± 3	13 ± 4	11 ± 3.5
SGPT## (U/L)	12 ± 2	15 ± 3	13 ± 2.4
Bl. Urea (mg/dl)	21 ± 6.2	25 ± 3.1	22.33 ± 4.5
S. creatinine(mg/dl)	0.9 ± 0.2	1.2 ± 0.3	1.1 ± 0.15
Hb (g/dl)	13 ± 3	11.5 ± 2.5	12.5 ± 3
GUE."	Was normal in all patients.		
ESR(min/hr)	Was elevated in 40 patients (30 males & 10 females)		

* HLA= human leukocyte antigen
**RBS= random blood sugar
#SGOT= serum glutamate oxaloacetate transferase
##SGPT= serum glutamate pyruvate transaminase
"GUE= general urine examination.

In this study during the time of evaluation 40 patients were on colchicine (lmg daily), 20 patients were on dapsone (l00mg daily), 3 patients were on therapeutic trail, 7 patients were on Corticosteroids (20mg daily) and 5 patients were on irregular treatment.

DISCUSSION

Iraq is among the countries were Behçet's disease is relatively highly reported, the initial manifestations of the disease and the major clinical features are similar to description of the disease from other parts of the world (9, 10, 11).

Peripheral neuropathy is one of the rare manifestations of Behçet's disease, this manifestation has so far been neglected, and the prevalance of this minor feature seemed to be relatively variable in few reports.

Many reports from different countries about neuro-Behçet's disease showed either absence or very rare finding of peripheral neuropathy among their patients and there was lacking of studies which specifically deal with peripheral neuropathy as isolated feature of Behçet's disease (12, 13).

In our study 15 of the seventy-five patients with B.D showed features suggesting peripheral neuropathy (by history and examination) ranging from impairment of pin prick sensation, decrease superficial sensation, vibration at variable degree, but only one of these patients had electrophysiologicaly proved peripheral neuropathy. However 15 of our patients give history of abnormal sensations, all of them gave history of pain sensation and numbness, 11 patients had burning sensation, 8 patients had pricking sensation and 8 patients had parasthesia of the upper limbs and the lower limbs during the course of their illness (table 3).

The most common probable cause of peripheral nervous system involvement in patients with Behçet's disease is systemic vasculitis. It may involve the small and medium sized arteries and may involve the vasa nervorum of the nerves, which may lead to ischemia and the nerves are highly sensitive to this change(14, 15).

Behçet's disease is a form of vasculitis, so it may lead to peripheral neuropathy of axonal degeneration type (16). The differentiation between axonal degeneration and demeylination lesions is difficult because some patients can have a combination of both lesions, in case of damage to the myelin sheath axonal degeneration can occur and in primary axonal lesions there might be a features of demeylination lesions if regeneration take place (3). The other probable cause of this combination of the lesions in patients with vasculitis is corticosteroids (CS) treatment as CS can produce disease of the peripheral nerves. Administration of high dose of prednisolone in rabbits has been reported to produce demeylination lesions in peripheral nerves.

There are many drugs which can induce disease of the peripheral nerves, for example CS, vincristin, dapsone, nitrofurantoin, thalidomide, chloramphenicol, hydralyzine and isoniazide. Dapsone can lead to axonal disease (5).

Colchicine is one of the common drugs used for treatment of mucocutaneous manifestations of BD. Long-term use of small daily doses of colchicine appears to be relatively safe. However neuromascular syndromes can occur exclusively in patients with chronic renal insufficiency (16).

The most important drugs which can lead to peripheral neuropathy and used for treatment of BD in Iraqi patients are CS, colchicine and dapsone. In conclusion, Peripheral neuropathy is one of the infrequent manifestations of BD among Iraqi patients.

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