Neuropathic manifestations in rheumatoid arthritis: a clinical and electrophysiological assessment in a small sample of Iraqi patients

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Rheumatoid arthritis (RA) is an inflammatory systemic disease mainly affecting joints. Frequent extra-articular manifestations are often recognized too late. Extra-articular manifestations affect the skin, the cardiovascular system, the kidneys, the eyes, the gastrointestinal tract, the liver, the nervous system and the blood. In a retrospective cohort study of 489 RA patients admitted to University Hospital, Malmö, Sweden, during the period 1990-94, it was found that serositis and cutaneous vasculitis were the predominant extra-articular manifestations of rheumatoid arthritis (ExRA), and mortality was greater in the ExRA than in the non-ExRA subgroup, perhaps due to a high frequency of associated heart disease. In another retrospective cohort study of 424 cases of RA, classified by the American College of Rheumatology 1987 criteria for RA in Olmsted County, MN, USA, and diagnosed during the period 1955-1985, the investigators found that the incidence of extra-articular manifestations was 3.67/100 person-years.

In addition, it has been found that survival among rheumatoid patients with extra-articular manifestations was markedly decreased compared to the general population and to patients without extra-articular manifestations. Clinical involvement of the peripheral nervous system is not uncommon in rheumatoid arthritis; the most common disorders are multiple mononeuritis, sensorimotor neuropathy, and entrapment neuropathy.

Rheumatoid patients may have electrophysiologic and histologic findings of peripheral nerve damage, even in the absence of clinical evidence of peripheral nerve involvement. Lanzillo et al reported that 65% of cases exhibited electrophysiologic findings consistent with a sensorimotor neuropathy in rheumatoid patients without clinical symptoms or signs of peripheral nerve involvement. Necrotizing vasculitis is responsible for the different patterns of noncompressive neuropathies in rheumatoid arthritis, including mononeuropathy multiplex and distal symmetric sensory or sensorimotor neuropathy.

In Said’s series of 200 patients with peripheral nerves vasculitis, 21% were due to rheumatoid arthritis. The present study aimed to assess the pattern of neurological manifestations in a small sample size of rheumatoid patients in Baghdad based on neurological examination and electrophysiological studies.

Patients and Methods
Eighty rheumatoid arthritis cases were selected randomly from the consultant clinic of Rheumatology and Rehabilitation at Al-Yarmouk Teaching Hospital, Baghdad, Iraq during the period January-July 2002. Patients who fulfilled the Criteria of the American College of Rheumatology classification 1987 were enrolled in this study. All
patients were on disease modifying antirheumatic drugs (methotrexate and/or chloroquine). A table of random numbers was used in choosing patients. Patients were included in this study only if they gave free verbal informed consent. The Research Committee at the College of Medicine/Al-Mustansiriya University approved the protocol study.

Each patient was assessed clinically (rheumatological and neurological assessment) for neuropathic manifestations in terms of subjective and objective observations. Clinical assessment was supported by electrophysiological studies using the Dantec Counterpoint Clinical EMG system to categorize the neuropathic manifestations of rheumatoid arthritis. This system includes four-channel preamplifiers and two built-in isolated stimulators with separate jacks. A group of controls in the keyboard of the control unit is used for setting the stimulus intensity (1-99 mA), duration (0.05-1 msec), polarity positive, negative and alternate] and frequency of presentation (0.1-100Hz). A group of controls in the keyboard is used to adjust the amplification (sensitivity), sweep spade (time scale) and the various measurements of the displayed signals.

The data are presented as number and percentage. The results, whenever possible, were analyzed by differences between percentages and simple correlation taking \( P<0.05 \) as the limit of significance.

### Results

The eighty rheumatoid patients (48 females and 32 males) ranged from 20 to 75 years of age. The highest percentage of cases (27.5%) were within the age range of 40 to 49 years, but the percentage was not significantly different from other age ranges except for the youngest (20-29 years, 10%) and oldest (70+ years, 2.5%) The female to male ratio was 1.5:1.0. Fifty percent of cases had a history of rheumatoid arthritis of less than 10 years. The number of cases presented with rheumatoid arthritis of 5 to 9 years duration (17.5%) was significantly less than others.

Neurological assessment of cases revealed that subjective findings of neuropathy were present in 10% to 37.5% of cases vs 12.5% to 25% of cases with positive objective findings (Table 1). Parasthesia was the most common subjective finding which tended to be significantly \( (P<0.001) \) different from that of burning pain. While decreased grip power was the most common objective finding, it was insignificantly different from other objective findings (Table 1). The electrophysiological studies revealed several forms of neuropathies in 35 patients, which accounted for 43.8% of neuropathic manifestations (Table 2). Polyneuropathy and carpal tunnel syndrome were the relatively most common type of nerve involvement in rheumatoid arthritis, accounting for 22.8% of cases (8 of 35 cases) each. Further analysis of the data revealed that the association of polyneuropathy with rheumatoid arthritis occurred in 10% of cases (98 out of total 80 case).

There was no relationship between the duration of illness and the occurrence of neuropathy \((r=-0.209, P>0.050)\) (Table 3, Figure 1). In fact, rheumatoid patients with a history of illness less than 5 years are more likely to be complicated by neuropathy.

| Manifestations                  | No | % |
|--------------------------------|----|----|
| **Subjective findings**        |    |    |
| Paresthesia                    | 30 | 37.5|
| Numbness in fingers and toes (or) decreased sensation or anesthesia | 26 | 32.5|
| Burning pain in the fingers and toes | 8  | 10  |
| **Objective findings**         |    |    |
| Decreased grip power           | 20 | 25  |
| Decreased pain prick sensation distally in gloves and stocks distribution | 18 | 22.5|
| Symmetrical decreased or absent reflexes | 16 | 20  |
| Impaired position and vibration sense | 11 | 13.8|
| Asymmetrically decreased or absent reflexes | 10 | 12.5|
| Mononeuropathy (sciatica and carpal tunnel syndrome) | 10 | 12.5|

Table 1. Neuropathic manifestations in 80 rheumatoid arthritis patients.

| Diagnosis                    | No | % (n=35) |
|------------------------------|----|----------|
| Carpal tunnel syndrome       | 8  | 22.8     |
| Polyneuropathy               | 8  | 22.8     |
| Mononeuritis multiplex       | 6  | 17.2     |
| Sciatic neuritis             | 6  | 17.2     |
| Ulnar neuritis               | 3  | 8.6      |
| Tarsal tunnel syndrome       | 3  | 8.6      |
| Radial neuritis              | 1  | 2.8      |
| **Total**                    | 35 | 100      |

Table 2. Abnormal electrophysiological findings in rheumatoid arthritis patients by diagnosis.
Discussion

Neurological manifestations associated with rheumatoid arthritis have been extensively studied. These complications are not always evident clinically, and their eliciton during clinical neurological examination creates much pain and suffering to the patient, especially during the active stage of the disease.

The data reported in this study revealed that subjective and objective clinical findings were inconsistent with the abnormal electrophysiological findings. Electrophysiological studies showed mononeuropathies in 27 patients whereas clinically they were detected in only 10 cases. Warner et al reached the conclusion that abnormal nerve conduction studies in asymptomatic individuals were not predictive of future symptomatic complaints (mononeuropathy) and if used for preplacement screening, they should be done with caution. However, it is essential to take into consideration that arthritic symptoms, including pain and tenderness, may be responsible for the decrease in grip power and impaired tendon reflexes in addition to the involvement of nerves in arthritic process. Korshunov et al studied the hands of 45 rheumatoid patients clinically, by dopplerography and by electroneuromyography and found that only one third of his cases showed electrophysiological changes of polineuropathy while 74% of cases had some elements of defective regional blood flow. Therefore, parallel affections of vascular, neurological and functional origin contribute to deficient functional performance in RA patients. The percent of nerve involvement in rheumatoid arthritis in this study (35 of 80 cases) is higher than other reports. The explanation may be the higher number represents cases that attended the clinic of rheumatology and rehabilitation, a number of whom take chloroquine or methotrexate therapy, which may add a further cause for neuropathy.

Our finding that the neurological complications related to rheumatoid arthritis are unrelated to the duration of disease suggests more than one etiology in the pathogenesis of this illness. This observation is in agreement with others who found that disease duration is not correlated with functional disabilities. In conclusion, abnormal electrophysiological findings existed in more than 40% in rheumatoid arthritis and were independent of disease duration. According to this finding, we suggest that patients be investigated electrophysiologically despite the associated discomfort of testing.

Table 3. The relation between the duration of illness and the occurrence of neuropathic complications.

| Duration       | No | % of neuropathic cases (n=35) |
|----------------|----|-----------------------------|
| 1-4 years      | 14 | 40                          |
| 5-9 years      | 4  | 11.4                        |
| 10-19 years    | 8  | 22.9                        |
| 20 and more    | 9  | 25.7                        |

![Figure 1. Showed in significant correlation between the duration of rheumatoid arthritis and the occurrence of neuropathy (r=-0.209, P<0.05)](image)

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