

## A Clinico-Pathological Study in Seronegative Arthropathies

SAMIA M. ABDEL-MONEM, M.D. and  
HANI A. BASSIOUNI, M.D.

*The Departments of Rheumatology & Rehabilitation and  
Orthopedic Surgery, Banha Faculty of Medicine.*

### Abstract

Fifty patients with a seronegative arthropathy were evaluated. Forty of them had no apparent associated primary disease (idiopathic) 5 with Bilharzial arthropathy, 3 with ankylosing spondylitis and 2 with Reiter's syndrome. They were 40 males (60%) with a mean age of 29.4 years and 20 females (40%) with a mean age 29.5 years. The mean duration of the disease was 2.25 years. All the patients were examined clinically and radiologically with a histopathologic study of some enthesopathic specimens. Peripheral arthritis was present in 60% patients, while 40% had arthralgia. The Knee and the sacroillii were the highly affected joints. All the patients had enthesopathic signs, where tenderness at the insertion of the planter aponeurosis and Achillis tendon was highly observed. All the patients shared the same radiological abnormalities of periosteal reaction, marginal irregularity, erosions, calcification, sclerosis and spurs. Radiological calcaneal abnormalities were highly associated with enthesopathic signs. Histopathological enthesopathic changes were comparable in all the patients. Our results indicated that striking similarities existed between different entities of the seronegative arthropathy groups.

### Introduction

LAMPMAN [1], said that the English speaking rheumatologists have attached the term 'enthesopathy' (enthes = insertion) to disorders of the bony insertions of tendons, ligaments and capsules. This word has merit because it calls attention to a group of physical and histopathologic findings characteristic of spondylarthropathies.

Calin [2], emphasized that spondylarthritis is a term used to refer to a group of inter-related syndromes i.e. Ankylosing

Spondylitis (AS), Reiter's Syndrome (RS) and other reactive arthritides following documented salmonella, shigella, yersinia infection or non gonococcal urethritis. Pain resulting from inflammation at the enthesis is a characteristic feature of this form of arthritis.

All these disorders share common clinical properties and it is often difficult to distinguish one from another [3].

Masi [4], reported that muscle histopathology in AS shows frequent changes ear-

ly in disease consistent with neuropathic and myopathic mechanisms of a non-inflammatory nature. He inferred that sex steroid imbalance in persons susceptible to AS target axial and proximal muscle tissues, resulting in relative functional hypertonicity. Such phenomenon, developing in preteen and younger adult ages, may contribute to peripheral and axial manifestations of enthesopathy in this disease by complex and currently unknown mechanisms.

The aim of the work is to study the pattern of seronegative arthropathies clinically, radiologically and histopathologically.

#### Patients and Methods

This study was carried out on 50 adult patients with seronegative arthropathy (SNA). They were selected from the outpatient clinic of the Rheumatology and Rehabilitation department of Banha University Hospitals.

Patients were included into this study when they fulfilled the following 4 criteria as proposed by Rosenberg and Petty [5]:

- 1- The onset of musculoskeletal symptoms at the age of 16 years or older.
- 2- The absence of classical IgM rheumatoid factor.
- 3- The presence of enthesopathic signs.
- 4- The presence of arthralgia with or without objective signs of arthritis.

All the patients were interviewed according to a standard examination scheme as follows:

- 1- General and regional examination of the musculoskeletal system.
- 2- Examination of enthesal regions by discrete localized pressure at the insertion of ligaments, tendons or fasciae.

- 3- Laboratory investigations including: urine and stool analysis, urine culture and latex agglutination test.
- 4- Radiological study: radiographs were obtained only for the clinically affected enthesal regions.
- 5- Histopathological study: Specimens were obtained from the insertions of the Achilles tendon (posterior heel) and planter fascia (inferior heel), by open surgery under general anesthesia.

Sections were prepared by the paraffin technique [6] and stained with haematoxylin and eosin [7].

#### Results

Fifty patients with a seronegative arthropathy (SNA) were evaluated. Forty of them had no apparent associated primary disease (idiopathic), 5 patients were found to have Bilharzial arthropathy diagnosed according to Bassiouni and Kamel [8], 3 patients satisfied the proposed diagnostic criteria for AS [9] and 2 patients presented with the Reiter's triad of arthritis, conjunctivitis and urethritis.

Thirty patients (60%) were males, whose ages ranged between 20-42 years (mean 29.4 years) and 20 patients (40%) were females whose ages ranged between 20-40 years (mean 29.5 years). The disease duration ranged between 1-5 years (mean 2.25 years).

#### Discussion

Enthesopathy is a clinical term for a number of pathological painful changes in the insertion of tendons [10].

Rosenberg and Petty [5], described the clinical picture of 39 patients with a syndrome of seronegative enthesopathy and arthropathy (SEA). The clinical findings of

Table (1): Incidence of Joint Affection in the 50 Patients with SNA.

Affected joints	No. of patients	%
knees	27	54
Sacroilii	27	54
Ankles	20	40
Shoulders	18	36
Lumber and sacral spines	13	26
Tarsals	11	22
Wrists	9	18
Elbows	5	10

Table (2): Incidence of Tenderness in the Various Enteseal Regions of Upper and Lower Limb in the 50 Patients with SNA.

Enteseal region	Unilateral		Bilateral		Total no. of pts with tenderness	Total %
	No. of pts.	%	No. of pts.	%		
Lateral epicondyle of humerus	15	30	3	6	18	36
Humeral head	12	24	4	8	16	32
Medial epicondyle of humerus	12	24	1	2	13	26
Olecranon processes	5	10			5	10
Inferior heel	21	42	20	40	41	82
Posterior heel	22	44	18	36	40	80
Sacro iliac joints	12	24	15	30	27	54
Symphysis pubis					15	28
Greater trochanter of the femur	11	22	3	6	14	30
Iliac crest	8	16	6	12	14	28
Ischial tuberosity	4	8	8	16	12	24
Tibial tuberosity	6	12	3	6	9	18
Anterior superior iliac spine	5	10	3	6	8	16

Table (3): Radiological Findings in Various Enthesal Regions of the Upper and Lower Limb.

Enthesal region	No. of pts. with tenderness	No. with spur	No. with erosions	No. with periosteal reaction	No. with calcification	No. with sclerosis	No. with marginal irregularity
Lateral epicondyle of humerus	18 (36%)			2 (4%)	2 (4%)		
Humeral head	16 (32%)		5 (10%)	3 (6%)	2 (4%)		
Medial epicondyle of humerus	13 (26%)			3 (6%)	4 (8%)		
Olecranon processes	5 (10%)						
Posterior heel	40 (80%)	40 (80%)	1 (2%)	8 (16%)	4 (8%)		
Inferior heel	41 (80%)	41 (82%)	1 (2%)	4 (8%)			
Tibial tuberosity	9 (18%)		3 (6%)				
Iliac crest	14 (28%)			6 (12%)	3 (6%)		
Symphysis pubis	15 (30%)		4 (8%)	2 (4%)	2 (4%)	36%	4 (8%)
Ischial tuberosity	12 (24%)		7 (14%)	4 (8%)	3 (6%)		6 (12%)
Greater trochanter of the femur	14 (28%)			3 (6%)			
Anterior superior iliac spine	8 (16%)				3 (6%)		

N. B: One or more of these findings were observed in the same patient.

Table (4): Incidence of Radiological Changes Clinically Affected Enteseal Regions of the Upper and Lower Limb (Expressed as %).

Enteseal region	No. of regions examined	Radiological changes (%)
Humeral head	20	60
Olecranon processes	5	60
Medial epicondyle of humerus	14	50
Lateral epicondyle of Humerus	21	19
Posterior aspect of the calcaneum	58	100
Inferior aspect of the calcaneum	61	100
Iliac crest	20	70
Ischial tuberosity	20	70
Symphysis pubis	15	53.3
Sacro iliac joints	42	52.4
Anterior superior iliac spine	11	45.5
Greater trochanter of the femur	17	35.3
Tibial tuberosity	12	25



Fig. (2): Radiograph of the pelvis: P.A. view, demonstrates:  
 - Erosions of the ischial tuberosity (bilateral)  
 - Sclerosis of the symphysis pubis.  
 - Calcification of the iliolumbar ligament at its attachment to the iliac crest (bilateral).

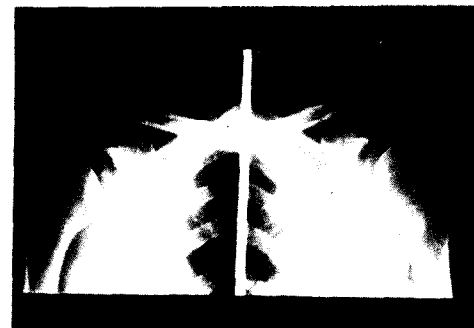


Fig. (3): Radiographs of both shoulders: P.A. view, demonstrates bilateral erosions of the humeral heads (enteseal lesions).

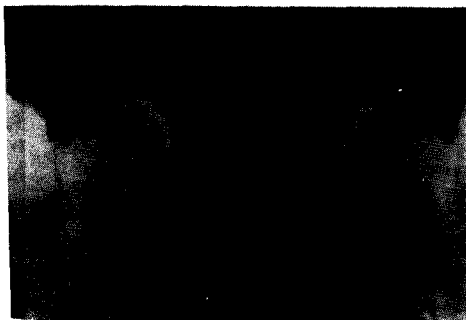


Fig. (1): X-ray of both heels: lateral view shows spurs at the insertion of the both Achilles tendons and plantar aponeurosis bilaterally. Fracture spur is seen at the insertion of the right Achilles tendon.

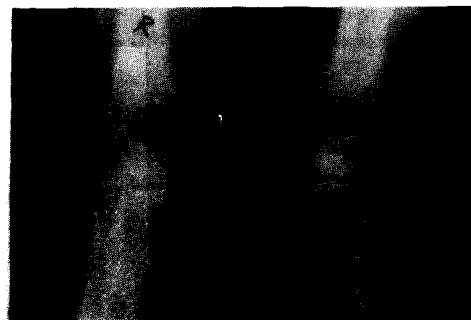


Fig. (4): Radiograph of both elbow joints demonstrates:  
 - Calcification of Rt medial epicondyle.  
 - Periosteal reaction of Rt. lateral epicondyle  
 - Periosteal reaction of both left epicondyles.



Fig. (5): Enthesal biopsy obtained from site of insertion of Achilles tendon showing prominent vascularity and perivascular chronic inflammatory cellular infiltrate. (H & E. x 100).

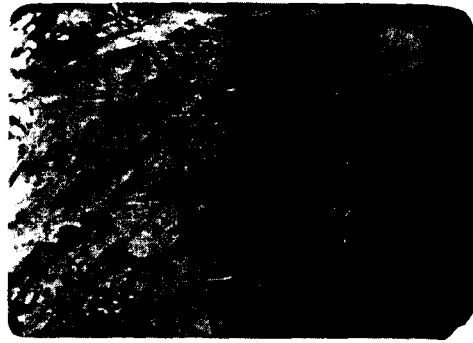


Fig. (6): Histology of enthesis obtained from the site of insertion of the planter aponeurosis showing fibrocartilage / fibroelastic fatty tissue with increased vascularity and perivascular inflammatory cellular infiltrate (H & E x 100).

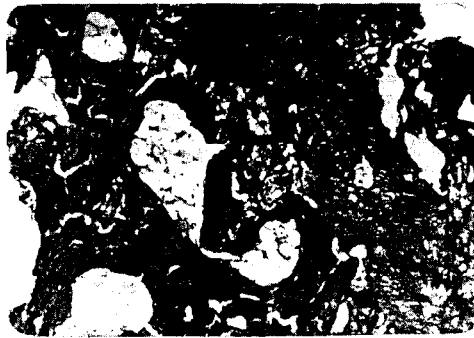


Fig. (7): Biopsy from one of spurs showing bone trabeculae containing yellow marrow and merging with vascularized fibrous tissue (H & E. x 100).

this study were more less coincident with our results, where peripheral arthritis was found in 74.4% of their patients in contrast with 60% of ours. Arthralgia was present in 25.6% of their studied group while it was present in 40% of our cases. Furthermore, enthesopathic signs at the patella and medial malleolus were not detected in our study.

In a study made by Tuncer et al. [11],

asymmetrical oligoarticular arthritis was reported in 66.6% of patients with RS, while enthesopathy was found in 45% of them. Radiological sacroiliitis and enthesopathy was found in 50% and 45.6% of patients respectively.

The clinical finding of our patients with AS fits with the clinical studies of Ball [12] and Niepel and Sitaj [13].

Enthesopathies of a small or medium extent were found in almost all the patients with AS reported by Urbanova et al. [14].

In our study, all the patients shared the same radiological features which were compatible with findings of Bassiouni and Kamel [8], Fritz et al. [15] and Tuncer et al. [11].

Horn et al. [16], found that the insertion of collagen fibers in cartilage or bone in the regions overloaded by tensile forces is identical to that found in epicondylitis in other locations. Histopathological studies in our work were comparable with the findings reported by Resnick and Niwayama [17], Nishikai et al. [18] and Vanlin-

thoudt et al. [19], in spite of difference in sites of elective biopsies.

Fritz et al. [15], stated that enthesopathies is a condition of reactive low turnover sclerosis. Ossifying enthesopathies have been reported by Scutellari et al. [20]. Enthesopathies have an established radiological as well as histological analysis as stated by Van-linthoudt et al. [19], who emphasized better knowledge of this pathology to prevent unnecessary excision.

From our study it is concluded that musculoskeletal disorders presenting with seronegative arthropathy, either associated with a primary or an idiopathic etiology shared the same clinical, radiological and histopathological abnormalities. Definite criteria for differentiation between these entities were not observed.

#### References

- 1- LAMPMAN J.H.: Origin of enthesopathy J. Rheumatol., 12 (5): 1030-31, 1985.
- 2- CALIN A.: Ankylosing Spondylitis, In Textbook of Rheumatology, 3rd. ed., W.B. Saunders Co., Philadelphia, 1989.
- 3- DOUGADO M., VAN DER LINDEN S., JUHLIN R. and HUITFELDT B.: The European Spondylarthropathy study Group preliminary criteria for the classification of spondylarthropathy. Arthritis. Rheum., 34 (10): 1218-27, 1991.
- 4- MASI A.T.: Do sex hormones play a role in ankylosing spondylitis? Rheum. Dis. Clin. North Am., 8 (1): 153-76, 1992.
- 5- ROSENBERG A.M. and PETTY R.E.: A syndrome of seronegative enthesopathy and arthropathy. Arthritis Rheum., 25: 1041-47, 1982.
- 6- BAKER J.R.: Cytological technique 1 st. ed Methuen, London, 1966.
- 7- HENRY T.: Principles and techniques of histochemistry. 1 st edition. Little, Brown and Company, Boston, 1966.
- 8- BASSIOUNI M.H. and KAMEL M.A.: Bilharzial arthropathy. Ann. Rheum. Dis., 43: 806-9, 1984.
- 9- BENNET P.H. and BIRCH T.A.: New York symposium on population studies in rheumatic diseases: New diagnostic criteria. Bull. Rheum. Dis., 17: 453-58, 1967.
- 10- MANDER M., SIMPSON J., MCLELLAN A., WALKER D. and DICK W.: Studies with an enthesis index as a method of clinical assessment in ankylosing spondylitis. Ann. Rheum. Dis., 46: 197-202, 1987.
- 11- TUNCER T., AMAN M.I., AKYOKUS A., BUTUN B. and UNAL S.: HLA B27 and clinical features in Reiter's syndrome. Clin. Rheumatol. 11 (2): 239-42, 1992.
- 12- BALL J.: The enthesopathy of ankylosing spondylitis. Br. J. Rheum., 22 (2): 25-28, 1983.
- 13- NIEPEL G. and SITAJ S.: Enthesopathy. Clin. Rheum. Dis., 5: 857-72, 1979.
- 14- URBANOVA Z., GATTEROVA J. VAVRIK P. and PAVELKA K. ZR: Replacement of hip joints with total endoprostheses in patients with ankylosing spondylitis. Cas. lek. Cesk., 9, 131 (9): 600-3, 1992.
- 15- FRITZ P., BAIDAUF G., WIKE H.J. and REITTER I.: Sternocostoclavicular hyperostosis: Its progression and radiological features. Ann. Rheum. Dis., 51 (5): 658-64, 1992.
- 16- HORN V., VLACH O. and MESSNER P.: Enthesopathy in the vertebral disc region. Arch. Orthop. Trauma. Surg., 110 (4): 187-9, 1991.

- 17- RESNICK D. and NIWAYAMA G.: Entheses and enthesopathy. *Radiology*, 146: 1-9, 1983.
- 18- NISGIKAI M., SUGIMOTO M., SATO A. and TAKEUCHI H.: Idiopathic peripheral enthesopathy without spondylarthritis. *Ann. Rheum. Dis.*, 45: 774-75, 1986.
- 19- VAN-LINTHOUDT D., VERNET D., PAZ-ERA A. and OTT H.: Enthesopathy of the tuberosities radii. A diagnostic problem. *Acta Orhop. Belg.*, 57 (1): 71-5, 1991.
- 20- SCUTELLARI P. N., ORZINCOLO C., PRINCIVALLE M. and FRANCESCHINI F.: Diffuse idiopathic skeletal hyperostosis. *Radiol. Med. Torino.*, 83 (6): 729-36, 1992.