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CLINICAL PRACTICE ARTICLE

Systemic Aspects of Soft Tissue Rheumatic Disorders (STRDs)

Mohammad Bagher Owlia[1] and Golbarg Mehrpoor[2]

Abstract

Objective: To determine the markers of systemic inflammation in soft tissue rheumatic disorders (STRDs).
Study Design: Case series.
Place and Duration of Study: Rheumatology Clinic, Yazd, Iran, from November 2010 to December 2011.
Methodology: Patients aged 20 years or above with known diagnosis of STRD according to clinical criteria and/ or paraclinical investigations for at least 3 weeks duration were longitudinally followed. Patients with diagnosis of rheumatoid arthritis, hypothyroidism, or any other known systemic conditions (other than diabetes mellitus) were excluded. After careful and detailed history taking, laboratory tests indicating systemic inflammation including erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and routine screening rheumatologic tests were assessed.
Results: Of the 90 patients, 75% were female and 25% were male and 28 (31.1%) of patients had diabetes mellitus. Fifty six (62%) and 49 (54%) of all studies cases had some degrees of morning stiffness and remarkable fatigue respectively. Twenty two (24%) had elevated CRP and 5 (5.5%) had abnormal ESR. Rheumatoid factor (RF) and anti-CCP was positive in 5 (5.5%) and 12 (13.3%) of patients accordingly. Three (3.3%) patients suffered from anemia of chronic disease. Mean ESR was 48 ± 7.34 (hl) and mean CRP was 10.06 ± 1.96 mg/dl. Mean RF was 10.8 ± 1.64 U/ml and mean anti-CCP was 18.5 ± 2.71 U/ml. Mean hemoglobin was between 10.4 ± 1.01 g/dl.
Conclusion: Features of subtle systemic inflammation are positive in some cases of soft tissue rheumatism.

Key Words: *Soft tissue rheumatic disorders. Inflammation. Fibromyalgia. Non-articular rheumatism. Systemic aspect.*

INTRODUCTION

Soft tissue rheumatic disorders (STRDs) are a group of non-articular disorders which are generally considered as non-systemic conditions.[1] It is believed that inflammatory signs and systemic manifestations is usually lacking in these conditions.[2,3] Overuse, nerve entrapment, structural abnormalities, autonomic dysfunction and psychologic factors are among the most common reported mechanisms. Neuroendocrine dysfunction is more obvious in case of fibromyalgia syndrome (FMS).[4]

Systemic features necessitating systemic management are not negligible in these diseases and some of them can evolve to a frank rheumatisms over time.[5]

The rationale of the study was to highlight the possible role of systemic aspects and more clearly the role of systemic inflammation in some of so-called local soft tissue rheumatic diseases, by determining the markers of systemic inflammation in soft tissue rheumatic disorders.

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The aim of the study was to determine the markers of systemic inflammation in soft tissue rheumatic disorders (STRDs).

METHODOLOGY

In this cross-sectional study, 90 patients with diagnosis of STRDs were longitudinally followed from November 2010 to December 2011 who referred to a rheumatology clinic in Yazd central Iran. All patients with age 20 years or above who were suffering from any type of STRD according to clinical criteria and/ or paraclinical investigations for at least 3 weeks duration were included in the study. Patients with diagnosis of rheumatoid arthritis, hypothyroidism, or any other systemic condition (other than diabetes mellitus) or recent history of direct trauma were excluded from the study.

Age, gender, duration of disease, co-morbid disorders, clinical and laboratory findings were recorded. The indices of subtle systemic features were marked fatigue, any degrees of morning stiffness, nocturnal accentuation of symptoms, anemia of chronic disease (hemoglobin < 14 g/dl in men and < 12 g/dl in women with normal MCV and MCH), positive laboratory tests such as C - reactive protein (CRP) > 6 mg/dl, erythrocyte sedimentation rate (ESR) > 25 (h1), rheumatoid factor (RF) > 6 units/ml, anti-nuclear antibody (ANA) > 2 units/ml or anti-cyclic citrullinated peptide (anti-CCP) > 18 units/ml. Data were analyzed by Statistical Package for Social Sciences (SPSS) software version 17 and laboratory data were shown as mean ± standard deviation of the mean.

Table I: Important signs and symptoms among the studied patients that may indicate subtle inflammatory or systemic nature of STRDs.

Condition	Number	Morning stiffness	Fatigue	Nocturnal aggravation	Multifocal pain	Diabetes mellitus
Shoulder periarthritis	12	10 (83%)	2 (16.6%)	4 (33.3%)	2 (16.6%)	2 (16.6%)
Adhesive capsulitis	16	16 (100%)	12 (75%)	16 (100%)	4 (25%)	15 (93.7%)
Tennis elbow	11	1 (9.09%)	2(18.18%)	-	3 (27.27%)	-
Fibromyalgia	4	3 (75%)	4 (100%)	4 (100%)	4 (100%)	-
Carpal tunnel syndrome	21	18 (85.7%)	17 (80.9%)	20 (95.2%)	19 (90.4%)	3 (14.2%)
RSDS	2	2 (100%)	2 (100%)	2 (100%)	2 (100%)	-
Trigger finger	8	3 (37.5%)	5 (62.5%)	-	6 (75%)	8 (100%)
De Qeurvian tenosynovitis	8	2 (25%)	2 (25%)	7 (87.5%)	6 (75%)	-
Ganglion	4	-	-	-	1 (25%)	-
Plantar fascitis	4	1 (25%)	3 (75%)	-	3 (75%)	-
Total (percent)	90 (100)	56 (62)	49 (54)	53 (58)	50 (55)	28 (31)

Table II: Laboratory findings (indices of inflammatory state) among the studied patients.

Condition	Number	Raised CRP	Positive RF	Raised ESR	Positive anti-CCP	Anemia of chronic disease
Shoulder periarthritis	12	1 (8.3%)	1 (8.3%)	2 (16.7%)	-	-
Adhesive capsulitis	16	11 (68.7%)	1 (6.25%)	2 (12.5%)	2 (12.5%)	-
Tennis elbow	11	-	-	-	-	-
Fibromyalgia	4	1 (25%)	-	-	1 (25%)	-
Carpal tunnel syndrome	21	5 (23.8%)	3 (14.3%)	1 (4.8%)	5 (23.8%)	2 (9.5%)
RSDS	2	2 (100%)	-	-	1 (50%)	-
Trigger finger	8	-	-	-	-	-
De Qeurvian tenosynovitis	8	2 (25%)	-	-	3 (37.5%)	1 (12.5%)
Ganglion	4	-	-	-	-	-
Plantar fascitis	4	-	-	-	-	-
Total (percent)	90	22 (24)	5 (5.5)	5 (5.5)	12 (13.3)	3 (3.3)

Erythrocyte sedimentation rate (ESR); C-reactive protein (CRP); Rheumatoid factor (RF); Anti- cyclic citrullinated peptide (anti-CCP); Multifocal pain (MP); Anemia of chronic disease (ACD); Diabetes mellitus (DM).

RESULTS

Sixty eight (75%) were females and 22 (25%) were males with mean age of 40.01 ± 9.25 years; age ranged from 24 to 72 years. Duration of symptoms varied from 3 weeks to 8 years with mean of 1.25 ± 1.57 years. Distribution of symptoms is described in Table I.

Mean of ESR was 48 ± 7.34 (h1) and mean CRP was 10.06 ± 1.96 mg/dl (Table II). Mean RF was 10.8 ± 1.64 units/ml and mean anti-CCP was 18.5 ± 2.71 units/ml. Mean hemoglobin between anemic patients was 10.4 ± 1.01 mg/dl. None of them had positive ANA (ELISA) test.

DISCUSSION

Soft tissue rheumatic disorders (STRDs) are a heterogeneous group of clinical disorders which affect periarticular structures and presents most probably with pain, numbness and limited range of motion. They hardly cause severe morbidity but may potentially impact usual daily vocational and avocational activities and can be associated with some degrees of disability.[6] While some constitutional symptoms of fever and fatigue may be the first manifestation of a systemic disease, then some non-articular rheumatism may also do this role as well.

Less clinical studies are devoted to the systemic aspects of STRDs so far. A review article described increased level of some inflammatory markers in complex regional pain syndrome.[7] As many systemic rheumatic diseases may start with rather non-specific clinical features and months or even years are needed to evolve to full picture classic rheumatologic syndromes, it seems that early clinical feature of some systemic conditions like rheumatoid arthritis may be as local as non-articular rheumatisms. The frequent observations during more than 10 years of working experience, convinced us to start this pilot study. It seems that some STRDs like carpal tunnel syndrome, fibromyalgia and adhesive capsulitis had more systemic background than the others; nevertheless, none of them had fulfilled criteria for any specific systemic rheumatic disease at their initial presentation. In one study by Gumina *et al.* it was indicated that there was correlation between ESR and CRP with prognosis of adhesive capsulitis after 4 months from beginning of disease.[8] In contrast, ganglion and tennis elbow had little systemic features of inflammation as expected. This was especially true when tennis elbow was initiated after a known and clear mechanical trauma to the site of injury. The results also showed anemia of chronic disease in the absence of known systemic problem may herald an indolent systemic rheumatic condition. Similarly, it could be true about unexplained osteoporosis in the absence of known precipitation factor which could be the first systemic consequence of chronic subclinical systemic

conditions. Association of more than one index of systemic inflammation strongly supports systemic nature of the apparently local condition.

Morning stiffness and nocturnal aggravation of symptoms of any duration may indicate occult inflammation or abnormal neuro-hormonal response leading to dysregulation of immune system.[9-11] Fatigue may also be the first manifestation of systemic inflammatory disease reflecting abnormal surge of inflammatory cytokines. Unlike previous belief, depression is not a pure psychologic problem and long-lasted depression as seen in FMS may also cause expression of inflammatory cytokines with systemic reactions.[12] Lee showed increased arterial stiffness in patients with FMS which may reflect some systemic consequence of this prototype of STRDs.[13] The only article dealing with inflammation in FMS is provided by Kadetoff.[14] Kobbe *et al.* studied on the role of fracture-associated soft tissue injury in the induction of systemic inflammation and remote organ dysfunction on mice.[15]

This study could be the first one on focusing systemic aspects of STRD. However, limitations could be the given results from a single center and rather small sample size in respect to diversity of STRDs. Considering full history and clinical evaluation, very low probability of occult sub-clinical infections may potentially be an issue of misinterpretation and over-estimation. On the other hand, by using highly sensitive tools for detecting occult inflammation (such as hs-CRP and individual pro-inflammatory cytokines), these observations might uncover more hidden aspects of inflammation in STRDs (under-estimation off-setting possible over-estimation mentioned above). The study highlights possible systemic aspects of apparently local and non-articular rheumatisms which merit further therapeutic consideration in refractory cases with STRDs.

CONCLUSION

Features of subtle systemic inflammation are positive in some cases of soft tissue rheumatism.

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