

ORIGINAL ARTICLES

Cutaneous manifestations of rheumatoid arthritis

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Abstract

Rheumatoid arthritis (RA) is a multisystem autoimmune disease, affecting the joints predominantly, and extra-articular sites like skin, lungs, heart etc. The American College of Rheumatology (ACR) in collaboration with the European League Against Rheumatism (EULAR) in 2010, revised the 1987 ACR classification criteria for RA. The criteria covered four areas (joint involvement, serodiagnosis, acute phase reactants, duration of arthritis) and established a point value on a scale of 0 to 10. Patients with a value of 6 or higher are classified as having RA.

Although there are a number of studies on each of these factors, there is a paucity of studies on the cutaneous manifestations in RA patients. The present study explores cutaneous manifestations in RF-positive patients (predominantly female) in their fourth decade of age. Drug-induced and other miscellaneous side effects accounted for majority of the lesions. A significant correlation between nevi, striae and RA has been observed in this population.

Key words: Rheumatoid arthritis, Autoimmune, Cutaneous, Nevi, Stria

Introduction

RA is a multi-system autoimmune disease of unknown etiology, with articular and extra-articular manifestations. The disease predominantly affects females with two to three times higher prevalence in comparison to males between the fourth and sixth decade of life.¹ It runs an insidious course, associated with significant disability, reduced quality of life, varied prognosis and a shortened life span compared to the general population.² The American College of Rheumatology (ACR) in collaboration with the European League Against Rheumatism (EULAR) in 2010, revised the 1987 ACR classification criteria for RA. The criteria covering four areas, namely joint involvement, serodiagnosis, acute phase reactants and duration of arthritis, have established a point value on a scale of 0 to 10. Patients with a value of 6 or higher are classified as having RA.³ Though RA is predominantly a disease of the joints, extra-articular manifestations are known to occur, affecting organs like skin, lungs, heart, eyes, kidney, blood

etc. Of these, skin manifestations are the most common presentation. Several classifications of skin lesions, based on clinical or histo-pathological or their combination, have been proposed.⁴⁻⁶ The lesions of cutaneous manifestations can be broadly grouped as following:

- Specific to RA: RA nodules, RA vasculitis
- Non-specific to RA: Purpura, leg ulcers, urticaria etc.
- Common dermatological disorders overlapping with RA
- Drug-induced adverse effects

Knowledge of some of these skin lesions can help in assessing the prognosis and severity of the disease, while some others might give a clue to the possibility of adverse reactions due to drugs used in treating RA. A review of the relevant literature has revealed that there are very few studies to understand the relationship between the skin lesions and the disease, especially in the Indian

population. Hence, a systematic study was undertaken to investigate the features of cutaneous manifestations and their clinical significance in RA patients.

Materials and methods

The present cross-sectional study was conducted between June 2012 and October 2013. A total of 120 patients were included in the study and all of them were positive for rheumatoid factor (RF). Patients with other co-existing collagen vascular disorders, and those positive for ANA (antinuclear antibody) were excluded from the study. A detailed medical history of each of the subjects, including presence of cutaneous manifestations, such as rheumatoid nodules, purpura, livedo reticularis, plaques, papules, and vasculitic ulcers were recorded and an informed consent was obtained at the beginning of the study. Thorough physical and dermatological examinations, covering the skin, mucosa, scalp, hair, nails, genitalia, palms and soles, were carried out and the findings were recorded. Additional investigations were carried out wherever necessary.

Results

Out of the 120 patients included, 78 (65%) were female. All the patients belonged to the age range 11-74 years and the commonest age group was the 4th decade with 51 (42.5%) patients. The duration of the disease ranged from 6 months to 18 years. Disease duration of 6 to 10 years had been reported in 77 patients (64.2%). Out of these 77 patients, thirty-two patients with prolonged disease duration of 8-10 years were observed to have cutaneous changes. Rheumatoid nodules were seen in 7.5% and vasculitis in 5.8% patients. Two patients had livedoid vasculitis. One patient with rheumatoid arthritis had pyoderma gangrenosum associated with other manifestations of Behcet's disease. Non-specific cutaneous lesions like urticaria and photosensitivity were seen in two patients each. Careful evaluation was done to ensure that there are no other aggravating factors like food, infections and medications precipitating these disorders. Two patients also had onycholysis. Nail ridging and clubbing, considered as significant characteristic findings in RA patients, were not seen in any of these patients.⁷

The prevalence of various types of cutaneous manifestations in the present study sample is shown in figure 1. Miscellaneous disorders accounted for the majority of lesions in patients with RA. Among them, nevi accounted for most of the cutaneous lesions (about 40% of the patients). Based on the history the patient had both

congenital and acquired melanocytic nevi. The nevi were classified as small, medium and large, based on their size.⁸ Of these, small lesions measuring <1.5 cm were seen in 29.2% of the subjects. Intermediate-sized lesions measuring 1.5-20 cm was seen in 6.7%, and giant nevi measuring >20 cm were noted in 3.3% of the patients. One of the patients had numerous lesions. Ichthyosis and xerosis seen in 20 patients probably reflected the chronic disease state as well as poor nutritional status. Striae were seen in seven patients and very few of them had the striae away from the normally affected areas of the shoulder, groin, and elbows. Four patients had co-existing alopecia areata, aphthous ulcers and eczema. Psoriasis and lichen planus was seen in three and two patients respectively. Cushingoid features and acneiform eruptions were seen in eight and five patients respectively.

Discussion

There were a significantly high number of female patients among the recruited subjects for the study. This is not surprising as RA is two to three times common in females than males. A high percentage of the patients (64.2%) with longer disease duration had cutaneous manifestations, indicating possible correlation between chronicity and cutaneous changes.

In RA, the most widely recognized skin lesion is the rheumatoid nodule. Rheumatoid nodules are firm, dome-shaped, mobile, non-tender, skin-colored papules, typically seen at pressure areas throughout the skin and subcutaneous tissue.⁹ These were associated with severe arthritis, higher levels of RF, and an increased incidence of rheumatoid vasculitis.¹⁰

Using the classification proposed by Jorizzo and Daniels, the severity of vasculitis lesions observed in the present study, could be termed as mild to moderately severe lesions.¹¹ A relatively low incidence of specific rheumatoid lesions has been observed in the present study, and this is comparable with the literature data that cutaneous manifestations are seen in about 25-35% of patients. The variation in the rate of incidence can be attributed to two factors. Firstly, this is a cross-sectional study and the patient may not have disease activity at the time of evaluation. On the other hand, previous studies may not be the best representation, as racial differences may exist. To our knowledge, there has not been any study of susceptibility to cutaneous manifestations in Indian population.

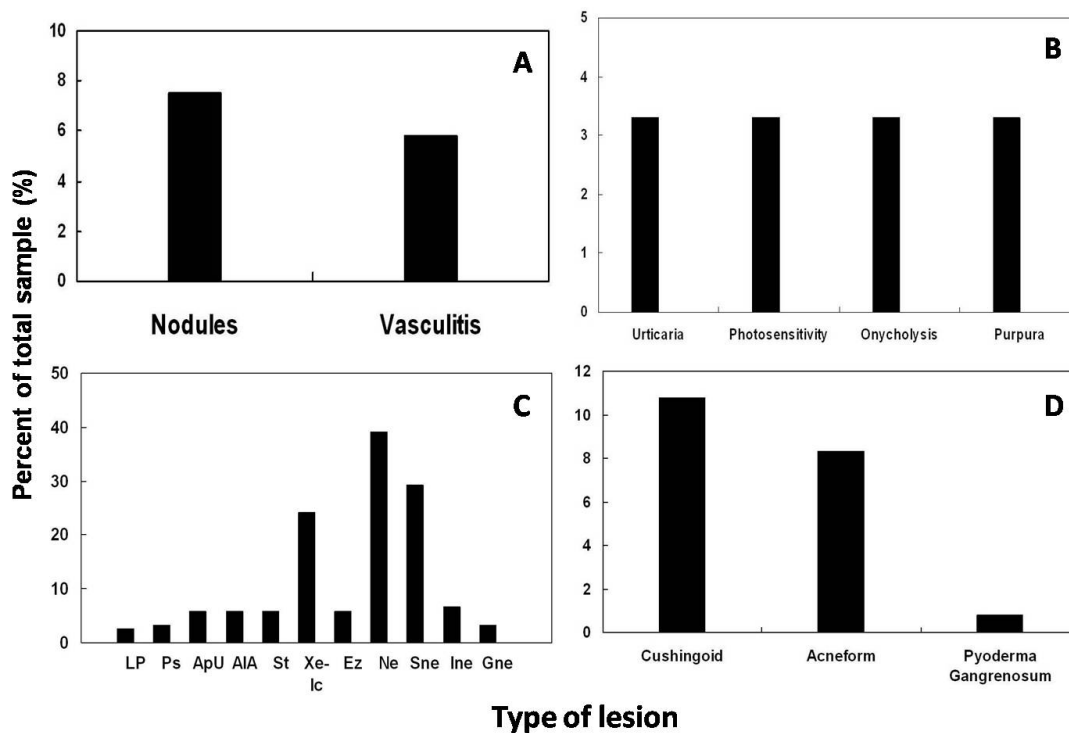
Genetics is known to play a role in the appearance of rheumatoid nodules. Those with HLA-DRw2 genetics were observed to have fewer nodules and lower RF titers.¹² It is estimated that the prevalence of congenital melanocytic nevi (CMN) varies widely from 0.5% to 31.7% in several studies.^{8, 13}

Nevi were the commonest lesion noted in the present study. Various cutaneous and extra-cutaneous associations have been associated with nevi.¹³ Nevertheless, there is no evidence correlating nevi with RA, and the significance of this association needs to be evaluated. In addition, the fact that nevus is also genetically mediated and that RA has a strong genetic association, corroborate the need for a better understanding of nevi in RA patients. Striae were seen in individuals who did not have a sudden change in the girth of the body contour. Significance of this seemingly unassuming lesion needs to be evaluated. Presence of alopecia areata has been attributed to the autoimmune nature of the RA patients.

Infective lesions predominated and included infections like herpes labialis and tinea versicolor. Probably, these lesions were reflecting the immune suppression of the individual due the medications used to manage the disease or the illness itself. Considering that RA is a chronic and severe disease associated with varying morbidity and mortality, it is natural that various drugs like NSAIDs, DMARDs, and biologics are used in controlling the activity of the disease. Therefore, it is also imperative that many side effects of these drugs can be expected to be encountered in these patients. Urticaria and angioderma were the most frequently observed symptoms in a previous study.¹⁴

Some patients presented with Cushingoid features and acneiform eruptions were probably iatrogenic. There is very high probability that the lesions were steroid-induced as the patient history revealed prior treatment with systemic steroids. Steroids are known to be used quite extensively in the management of RA in developing countries. Apart from steroids, no other probable adverse cutaneous drug effects

Fig 1: Characteristics of cutaneous manifestations. A. Specific lesions, B. Non-specific lesions, C. Miscellaneous lesions, D. Therapy-induced lesions



Abbreviations: LP- lichen planus, Ps- psoriasis, ApU- aphthous ulcer, AIA- alopecia, areata, St- striae, Xe- xerosis, Ic- ichthyosis, Ez- Eczema, Ne- nevi, SNe- small nevi, INe- intermediate nevi, GNe- giant nevi

were seen in these patients. Observation of these drug-induced side effects is a pointer to the need to carefully monitor for any side effects at the initial stages so as to limit the damage. Small number of subjects is the limitation of this study and larger studies, more appropriately case-controlled studies, are required to correlate the cutaneous changes with RA disease pattern.

Conclusion

In this cross-sectional study of Indian population, miscellaneous and drug-induced side effects formed a majority of cutaneous manifestations of RA. A significant association between nevi, striae and RA has also been observed. Possibility of cutaneous changes was more pronounced in chronic RA patients, and presence of cutaneous lesions infers chronic RA. Understanding the etiology and therapy for cutaneous manifestations of RA will be helpful in optimization of patient care.

Competing interests

The authors declare that they have no competing interests.

Disclosure

None

Citation

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References

1. Jorizzo JL, Greer KE, Callen JP. Miscellaneous disorders with

- prominent features involving the skin and the joints. Chapter 5. Dermatologic signs of internal disease. Third ed, Saunders. 2003.
2. Kobelt G, Jonsson L, Lindgren P, Young A, Eberhardt K. Modelling the progression of rheumatoid arthritis: a two-country model to estimate costs and consequences of rheumatoid arthritis. *Arthritis Rheum* 2002 Sep;46(9):2310-9.
 3. Aletaha D, Neogi T, Silman AJ, Funovits J, Felson DT, Neal S, et al. 2010 Rheumatoid arthritis classification criteria: an American College of Rheumatology/ European League Against Rheumatism collaborative initiative. *Arthritis Rheum* 2010 Sep;62(9):2569-81.
 4. Yamamoto T. Cutaneous manifestations associated with rheumatoid arthritis. *Rheumatol Int* 2009 Jul;29(9):979-88.
 5. Chen KR, Toyohara A, Suzuki A, Miyakawa S. Clinical and histopathological spectrum of cutaneous vasculitis in rheumatoid arthritis. *Br J Dermatol* 2002 Nov;147(5):905-13.
 6. Magro CM, Crowson AN. The spectrum of cutaneous lesions in rheumatoid arthritis: A clinical and pathological study of 43 patients. *J Cutan Pathol* 2003 Jan;30(1):1-10.
 7. Michel C, Cribier B, Sibilia J, Kuntz JL, Grosshans E. Nail abnormalities in rheumatoid arthritis. *Br J Dermatol* 1997 Dec;137(6):958-62.
 8. Ruiz-Maldonado R. Measuring congenital melanocytic nevi. *Pediatr Dermatol* 2004 Mar-Apr;21(2):178-9.
 9. Harris E Jr. Rheumatoid arthritis. *Curr Opin Rheumatol* 1994 May;6(3):287-9.
 10. Chu P, Connolly MK, LeBoit PE. The histopathologic spectrum of palisaded neutrophilic granulomatous dermatitis in patients with collagen vascular disease. *Arch Dermatol* 1994 Oct;130(10):1278-83.
 11. Jorizzo JL, Daniels JD. Dermatological conditions reported in patients with rheumatoid arthritis. *J Am Acad Dermatol* 1983 Apr;8(4):439-57.
 12. Sayah A, English JC. Rheumatoid arthritis: A review of the cutaneous manifestations. *J Am Acad Dermatol* 2005 Aug;53(2):191-209.
 13. Alikhan A, Ibrahim OA, Eisen DB. Congenital melanocytic nevi: Where are we now? Part I. Clinical presentation, epidemiology, pathogenesis, histology, malignant transformation, and neurocutaneous melanosis. *J Am Acad Dermatol* 2012 Oct;67(4):495.e1-17.
 14. Albrecht J, Atzeni F, Baldini C, Bombardieri S, Dalakas MC, Demirkesen C, et al. Skin involvement and outcome measures in systemic autoimmune diseases. *Clin Exp Rheumatol* 2006 Jan-Feb;24(1 Suppl 40):S52-9.