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A Histopathologic Study of Connective Tissue Diseases of Skin

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Abstract

Cutaneous involvement is a prominent feature in connective tissue disease and the skin lesions are extremely important in diagnosing and subclassifying patients with these conditions. Fifty cases of connective tissue diseases of skin were studied over a period of two years to analyze overlapping of histopathological features, possible transformation of one disease to the other and co-existing conditions. Routine Haematoxyline and Eosin (H&E) sections were studied along with special stains like Periodic Acid Schiff(PAS) and Verhoeff Vangiesson (VVG) wherever necessary. Fifty cases studied included 18 morphea, 9 systemic sclerosis (SS), 9 discoid lupus erythematosus (DLE), 7 acute cutaneous lupus erythematosus (ACLE), 4 subacute lupus erythematosus (SCLE), 2 lichen sclerosus et atrophicus (LSet A) and 1 case of poikiloderma atrophicans vasculare (PAV). Considerable overlapping of features were observed among skin lesions in acute, subacute and chronic lesions of lupus erythematosus and in cutaneous lesions of systemic sclerosis and morphea. In conclusion, as there is a considerable overlapping of histopathologic features in connective tissue diseases of skin, often it is necessary to use other diagnostic tools like serological and immunological study in conjunction with histopathology with the background of clinical history for a conclusive diagnosis.

Keywords: Connective Tissue Diseases of Skin; Histopathologic Features; Overlapping Features; Co-Existence.

Introduction

The term connective tissue disease has evolved from older designation of "collagen disease" and "collagen-vascular disease" and constitutes a group of multisystem diseases that are remarkably diverse and at the same time clinically similar in many aspects [1].

Although the connective tissue diseases were originally grouped because they shared the pathologic feature of an acquired alteration in vascular and connective tissue structures, it has been the additional overlapping or sharing of many clinical and laboratory features that has maintained this classification. Diagnosing and subclassifying these cutaneous lesions are extremely important [1].

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Materials and Methods

This was a prospective histopathologic study of connective tissue diseases of skin undertaken by the department of pathology, J.S.S.Medical college, Mysuru, Karnataka. The study includes 50 cases of clinically diagnosed/suspected cases of connective tissue disease of skin who attended the department of dermatology in a period of two years. A brief history was taken and dermatological examination was carried out to evaluate the type, distribution, configuration and topography of lesions. Clinically established/suspected cases were biopsied. After routine processing and paraffin embedding of formalin fixed tissue Haematixyline and Eosin (H&E) sections

were studied. Special stains, periodic acid Schiff (PAS) and Verhoeff vangiesson (VVG) were used wherever necessary.

Various histopathological changes were studied with clinical correlation. The cutaneous lesions of lupus erythematosus (LE) was further classified into discoid, subacute and acute (DLE, SCLE and ACLE) LE according to the classification made by Gillian and Sontheimer (1981)[2].

A diagnosis of Scleroderma was made based on the criteria described by Fleischmajor R et al (1972)[3].

Two cases of L Set A and one case of PAV were diagnosed based on histopathological findings described by Jaworsky, (1997) [4].

Results

Among fifty cases of connective tissue diseases of skin studied morphea (18cases) was the commonest, followed by systemic sclerosis SS (nine cases), discoid lupus erythematosus (DLE) (nine cases), acute cutaneous lupus erythematosus (ACLE) (seven cases), subacute cutaneous lupus erythematosus (SCLE) (four cases), lichen sclerosus et atrophicus (LSetA) (two cases) and one case of poikiloderma atrophicans vasculare (PAV) (Table 1).

Cutaneous lesions of connective tissue diseases were commonly seen in the middle age group between 21-50 years (Table 2) and common among females with a male: female ratio being 1:2.6 (Table 3). Table 4 shows sex distribution in individual disease.

Table 1: Distribution of connective tissue diseases of skin

Disease	No. of cases	Percentage
DLE	9	18
SCLE	4	8
ACLE	7	14
Scleroderma	9	18
Morphea	18	36
LSetA	2	4
Poikiloderma atrophicans vasculare	1	2
Total	50	100

Table 2: Age distribution of 50 cases of connective tissue diseases studied

Age group	DLE	SCLE	ACLE	Scleroderma	Morphea	LSetA	PAV	Total
0-10	-	-	-	-	2	-	-	2
11-20	-	-	-	1	3	-	-	4
21-30	3	1	-	2	9	-	-	15
31-40	5	2	1	-	-	1	-	9
41-50	-	1	4	5	4	1	1	16
51-60	-	-	1	1	-	-	-	2
61-70	1	-	1	-	-	-	-	2
Total	9	4	7	9	18	2	1	50

Table 3: Sex distribution of 50 cases of connective tissue diseases studied

Sex	No. of Cases	Percentage
Male	14	28
Female	36	72
Total	50	100

Table 4: Sex distribution in individual disease

Disease	Male		Female		M:F	Total No. of Cases
	No. of Cases	%	No. of Cases	%	Ratio	
DLE	4	44.4	5	55.6	1:1.2	9
SCLE	-	-	4	100	0:4	4
ACLE	3	42.9	4	57.1	1:1.3	7
Scleroderma	1	11.2	8	88.9	1:8	9
Morphea	4	22.1	14	77.8	1:3.5	18
LSetA	1	50	1	50	1:1	2
PAV	1	100	-	-	1:0	1

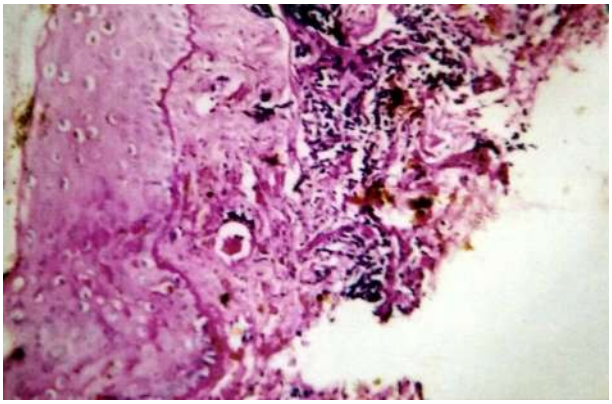

Fig. 1: Discoid lupus erythematosus showing basement membrane thickening (PAS, 10x10)

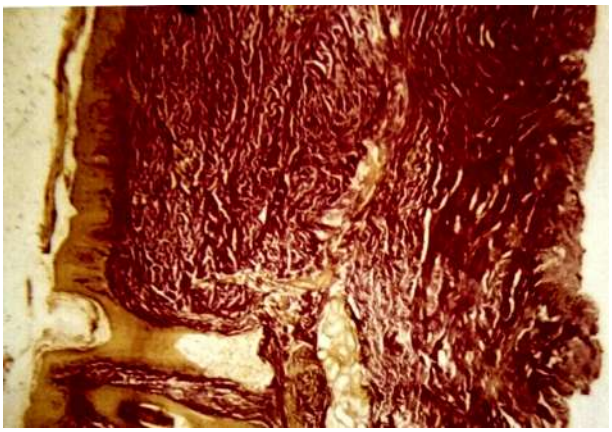

Fig. 2: Scleroderma showing compact dermal collagen and replacement of subcutaneous tissue by collagen (VVG, 10x10)

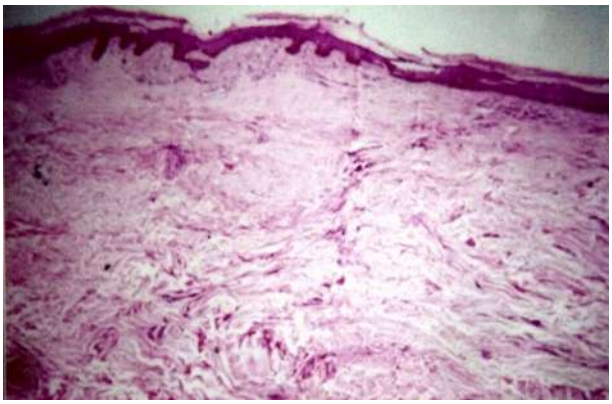

Fig. 3: Lichen sclerosus et Atrophicus showing hyperkeratosis, thinning of epidermis, dermal oedema, homogenization of upper dermal collagen (H&E, 10x10)

Discussion

Cutaneous involvement is a prominent feature in the connective tissue diseases and the skin lesions are extremely important in diagnosing and subclassifying patients with these conditions [1]. Classification of cutaneous lupus erythematosus(LE) can be divided into two broad categories; LE specific skin lesions and LE nonspecific but connective tissue disease-related skin lesions. LE specific skin lesions are chronic cutaneous LE which includes different forms of discoid lupus erythematosus (DLE), subacute cutaneous lupus erythematosus (SCLE) and acute cutaneous lupus erythematosus (ACLE) which includes different clinical forms[1]. Lupus erythematosus is a disease that affects multiple organ systems with broad range of clinical manifestations, may take the form of an isolated cutaneous eruptions often without any systemic involvement as seen in DLE, as an uncommon, non-scarring variant of LE often associated with mild systemic features (SCLE) or as acute cutaneous lesion of systemic LE (ACLE) [4,5,6]. Hence it is extremely important to diagnose different cutaneous forms of LE.

In the present study 20 cases of cutaneous LE were encountered. Nine were DLE, seven cases were ACLE and four cases were diagnosed as SCLE. Most of them were between 21-50 years of age. The male to female ratio was approximately 1:1.9 compared to 1:2.7 in a study conducted by Jerden MS et al (1990) [7]. As per the study of Bangert JL et al (1984)[8] the important features in distinguishing between DLE and SCLE were as follows : hyperkeratosis, epidermal atrophy, basement membrane thickening, density and depth of cellular infiltration, and follicular plugging.

McCright WG et al (1950)[9] who studied histopathology of 119 specimen of different forms lupus erythematosus stated that, though similar changes were noticed in different forms of the disease, there was some variation in the degree of changes. Jerdan MS et al (1990) [7] studied 63 patients of subsets of LE and histologically subtyped all the cases.

In the present study we subtyped all the cutaneous lesions of lupus eruthematosus into DLE, SCLE and ACLE histologically with clinical correlation. Features like basement membrane thickening, dense lymphocytic infiltration in the dermis were seen in chronic discoid lesions and features like basal cell vacuolation, subepidermal oedema, colloid bodies, mild lymphocytic infiltration in the dermis, were often found in acute and subacute lesions. PAS stain revealed the thickened basement membrane in all the cases of chronic cutaneous lupus erythematosus (DLE) (Figure 1), which was not found in SCLE and ACLE lesions.

PAS positive colloid bodies, [10] as large, eosinophilic round homogenous bodies formed as a result of degeneration of basal keratinocytes were seen in three cases of SCLE and in five cases of ACLE .The acute forms of cutaneous lesions of lupus erythematosus usually portray more oedema and less

infiltrate than the subacute type[11]. The combination of atrophy of the epidermis and marked liquefaction degeration of the basal layer is strongly suggestive of subacute lupus erythematosus [12]. In the present study it is found that, the acute and subacute cutaneous lesions of LE display similar histological features and distinguishing these two conditions based on histopatholgy alone was extremely difficult.

Scleroderma is a disease of the mesenchyme of unknown etiology and the symptoms and findings vary according to the location of the tissue involved, and may be limited or extensive [13]. Scleroderma and scleroderma-like conditions are classified broadly into Systemic sclerosis(SS), localized scleroderma (morphea), chemical induced scleroderma like conditions, eosinophilic fascitis, pseudoscleroderma and Graft-versus-host disease[1]. The present study of nine cases of systemic sclerosis(SS), findings underline female preponderance in these conditions (M:F ratio 1:8), as observed by Leinwand I et al (1954)[44], (M:F ratio 1:2.7) in a study of 150 cases and Fleischmajor R et al (1972)[3], (M:F ratio 1:2.3) who studied ten cases. There was a great variation in the age of onset, and majority of them were between 20 and 50 years of age.

Shono S et al (1991)[14] studied six cases of localized scleroderma (morphea) and all of them were women (M:F ratio 0:6) between 7 and 34 years of age. In the present study of 18 cases of morphea, 14 were females and the other four cases were males (M:F ratio 1:3.5). Majority of them were between 21 to 30 years of age. Morphea was seen more commonly in the younger age group, compared to the systemic form of the disease.

In earlier studies done by Jaworsky C (1997) [4] and O'Leary PA et al (1957)[15], it was found that, the histopathologic changes in SS and morphea are similar. Though the changes were minimal in morphea, often it is not possible to differentiate these two types of scleroderma histologically. In the present study compact connective tissue in the dermis and reduced fat around the eccrine sweat glands were seen in all the cases of SS and morphea. Compact connective tissue in the subcutaneous tissue was seen in all the nine cases of SS and in 15(out of 18) cases of morphea. Three cases of morphea showed panniculitis of subcutaneous fat. VVG stain done highlighted the collagen deposits in the dermis and subcutaneous tissue (Figure 2).

Lichen sclerosus (LS) encompasses the disorders known as lichen sclerosus et atrophicus (LSetA), balanitis xerotica obliterans and kraurosis vulvae [4]. In the present study of two cases of LSetA, one was a 32 year old male and the other patient was a 50 year old female (M:F ratio 1:1), compared to earlier such studies done by Shono S et al (1991)[14], (M:F ratio 2:1) and Citarella C et al (2003)[16], (M:F ratio 8:1). Histologically both the cases in the present study showed classic features,[4] like hyperkeratosis, liquefactive degeneration of basal cells, homogenization of upper dermal collagen and oedema of the upper dermis (Figure 3).

Poikiloderma atrophicans vasculare (PAV) may be seen in association with three genodermatoses; as a early stage of mycosis fungoides; in association with dermatomyositis and less commonly, lupus erythematosus[4]. One case of poikiloderma atrophicans vasculare (PAV) encountered in the present study was a 49 year old male. The histological features of the lesion showed classic features,[4] like thinning of epidermis, effacement of rete ridges, focal hydroipic degeneration of basal cells, exocytosis of lymphocytes and subepidermal oedema with mild lymphocytic infiltration.

Conclusion

As connective tissue diseases of skin overlap both morphologically and in distribution often the diagnosis is difficult. Though the histological features are distinct and specific in some, often there is a overlapping of features and it requires a combination of histopathology, serological and immunological study with the background of clinical history for a conclusive diagnosis.

References

1. Sontheimer RD, Euwer RL, Geppert TD, Cohen SB. Connective tissue diseases, Moschelle SL, Hurley HJ, Dermatology, Philadelphia: W.B Saunders Company; 2nd edition, 1985.
2. Gilliam JN, Sontheimer RD. Distinctive cutaneous subsets in the spectrum of lupus erythematosus. J Am Acad Dermatol 1981; 4:471-5.
3. Fleischmajer R, Damiano V, Nedwich A. Alterations of subcutaneous tissue in systemic scleroderma. Arch Derm 1972; 105:59-66.
4. Jaworsky C. Connective tissue diseases in Histopathology of the skin. Philadelphia; Lippincott Raven, 8th edition,1997.
5. Murphy JK, Stephens C, Hartley T, Das AK, Hughes GRV, Mckee PH. Subacute cutaneous lupus erythematosus – the annular variant. A histological and ultrastructural study of five cases.

Histopathology 1991; 19:329-36.

6. Pruneiras M,Montgomery H. Histopathology of cutaneous lesions in systemic lupus erythematosus. AMA Archives of Dermatology 1956; 74:177-89.
7. Jerdan MS, Hood AF, Moore GW, Callen JP. Histopathologic comparison of the subsets of lupus erythematosus. Arch Dermatol 1990; 126:52-55.
8. Bangert JL, Freeman RG, Sontheimer RD, Gilliam JN. Subacute cutaneous lupus erythematosus and discoid lupus erythematosus. Arch Dermatol 1984; 120: 332-7.
9. McCreight WG, Montgomery H. Cutaneous changes in lupus erythematosus. Archives of Dermatology and Syphilology 1950; 61:1-11.
10. Weedon David. The Lichenoid reaction pattern from skin pathology. Churchill Livingstone, Edinburgh, 1997.
11. Ellis FA,Bundick WR. Histology of lupus erythematosus. AMA Archives of Dermatology and Syphilology 1954; 70:311-324.
12. Lever WF. Histopathology of the skin. J.B. Lippincott, Philadelphia, 1949.
13. Leinwand I,Duryee AW, Richter MN. Scleroderma (Based on a study of over 150 cases). Ann Int Med 1954; 41:1003-1041.
14. Shono S, Imura M, Ota M, Osaku A, Shinomiya S, Toda K. Lichen Sclerosus et Atrophicus, Morphea, and coexistence both diseases. Arch Dermatol 1991; 127:1352-56.
15. O'Leary PA, Montgomery H, Ragsdale WE. Dermatohistopathology of various types of scleroderma. AMA Archives of Dermatology 1957; 75:78-87.
16. Citarella L, Masson C, Kerl H, Cerroni L. Lichen sclerosus with histopathologic features simulating early mycosis fungoides. Am J Dermatopathol 2003; 25(6):463-5.