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STUDY OF PATTERN ANALYSIS IN INFLAMMATORY DERMATOSES- A PROBLEM SOLVING APPROACH

Pathology

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ABSTRACT

BACKGROUND: Histopathology using skin biopsy is still the basis of diagnosis for most neoplasms and many inflammatory dermatoses despite molecular advances.

METHODS: The patients of all age group with clinical diagnosis of inflammatory lesions were included in the study.The cutaneous lesions of 190 patients were biopsied using punch biopsy technique with the aim to diagnose and categorize them using Ackerman AB'S (1978) algorithmic classification for inflammatory dermatoses.and to study their relative frequency.

RESULTS: Categorization of the lesions into 9 major basic patterns using AB Ackerman's criteria for pattern analysis with definite diagnosis was done in 175 cases out of 190 patients. Male preponderance was noted with maximum cases in 31-40 yrs of age group with most frequently observed diagnosis of leprosy with commonest pattern of nodular and diffuse dermatitis.

Conclusion: Use of pattern analysis makes the histological diagnosis easier and reproducible.

KEYWORDS

Inflammatory dermatoses,Punch biopsy,Pattern analysis.

INTRODUCTION

Skin biopsy is one of the most important tools in dermatology.The histologic diagnosis of skin lesions is essential for confirmation of a clinical diagnosis and in the management of patients.[1] Knowledge of the microanatomy of the skin and the biological behaviour of various inflammatory dermatoses and in addition,the use of a systematic approach during histological evaluation are essential to narrow the differential diagnosis, thereby achieving the most accurate and appropriate diagnosis.[2]

In dermatopathology, the most predictive diagnostic patterns are recognized through the scanning lens of the microscope, suggesting a list of possible 'differential diagnosis'.Then features that are more readily recognized at higher magnification suggest a further definitive diagnosis.Categorization of the lesions was done into **9 major** basic patterns using **AB Ackerman's** criteria.[3] Understanding these tissue reaction and inflammatory patterns help to simplify the diagnosis and make them clinically meaningful.[4]

METHODS

Total 190 patients of all ages, attending or referred to skin and venereal disease OPD were taken for the study for the duration of two years after due permission from ethical committee and consent of the patient.

The patients of all age group having various symptomatic skin lesions where clinical diagnosis was inflammatory dermatoses were included in the study.Known HIV, seropositive patients with dermatological manifestations, were not included in the study, as they are known to acquire unusual cutaneous lesions leading to histological misdiagnosis.

'Skin biopsy' was sampled knowing complete clinical details including local examination findings and other relevant clinical details and systemic examination findings using punch biopsy technique by the dermatologist using either 3 mm, 4 mm or 6 mm punch The biopsy specimen received was then immediately placed in formalin fixative (10% buffered formation) and was processed as routine histopathology samples. Serial sections and special stains were done as and when required like **AFB, FF, PAS, Masson's Trichome, Reticulin, Congo Red.**

The skin biopsy was interpreted using **Ackerman AB's (1978)**[5] algorithmic classification for inflammatory dermatoses and put into one of the 9 major tissue reaction patterns as:

Sr.No	Pattern	Abbreviation
1	Superficial perivascular dermatitis	SPD
2	Superficial and deep perivascular dermatitis	SDPD
3	Nodular and diffuse dermatitis	NDD
4	Vasculitis	VD
5	Intraepidermal vesicular and pustular dermatitis	IVPD
6	Subepidermal vesicular dermatitis	SEVD
7	Folliculitis and perifolliculitis	FP
8	Fibrosing dermatitis	FD
9	Panniculitis	PD

Then in each pattern, further subcategorization was done using minor criteria which included:--Changes in epidermis, in dermoepidermal interface, in dermis, involvement of subcutaneous tissue and Clinical information.This lead to narrowing down of the list of differential diagnosis and arriving at final diagnosis.

RESULTS

Total 190 skin biopsies of all ages with clinically diagnosed inflammatory dermatoses were included in the study. Only one case was found to be inadequate for interpretation. Male preponderance was seen in present study (60%) with maximum cases in 31-40 yr of age group. Maximum cases were of Borderline tuberculoid leprosy followed by Tuberculoid leprosy. (Table 1)

Table I List of diagnosis of all cases in present study

Sr. No.	Cases	No.of patients	Percentage
1	Borderline tuberculoid leprosy	25	13.16
2	Tuberculoid leprosy	19	10
3	Inconclusive	14	7.39
4	Lepromatous leprosy	13	6.85
5	Borderline lepromatous leprosy	9	4.75
6	Bullous pemphigoid	6	3.16
7	Discoid lupus erythematosus	6	3.16
8	Lupus vulgaris	6	3.16
9	Pemphigus vulgaris	6	3.16
10	Lichen planus	5	2.64
11	Morphea	5	2.64
12	Psoriasis	5	2.64
13	Cutaneous amyloidosis	4	2.10
14	Indeterminate leprosy	4	2.10
15	Lichen sclerosus et atrophicus	4	2.10
16	Pemphigus foliaceus	4	2.10
17	Pseudolymphoma	3	1.59
18	Sarcoidosis	3	1.59
19	Ashy dermatosis	2	1.05
20	Erythema multiforme	2	1.05
21	Erythema nodusum	2	1.05
22	Hailey-Hailey disease	2	1.05
23	Histoid leprosy	2	1.05
24	Hypertrophic lichen planus	2	1.05
25	Linear IgA dermatosis	2	1.05
26	Necrobiosis lipoidica	2	1.05
27	Panniculitis	2	1.05
28	Pityriasis rosea	2	1.05
29	Prurigo nodularis	2	1.05
30	Tuberculoid leprosy with type 1 reaction	2	1.05

31	Lichen striatus	2	1.05
32	Sweet's syndrome	2	1.05
33	Darier's disease	1	0.52
34	Dowling Dego's disease	1	0.52
35	Epidermolysis bullosa	1	0.52
36	Erythema induratum	1	0.52
37	Erythema nodosum leprosum	1	0.52
38	Inadequate	1	0.52
39	Infective vasculitis	1	0.52
40	Kyrle's disease	1	0.52
41	Actinic lichen planus	1	0.52
42	Lichenoid lesion favouring drug eruption	1	0.52
43	Allergic contact dermatitis	1	o.52
44	Lupus profundus	1	0.52
45	Midborderline leprosy	1	0.52
46	Necrotising vasculitis	1	0.52
47	Panniculitis with vasculitis	1	0.52
48	Perforating folliculitis	1	0.52
49	Pityriasis rubra pilaris	1	0.52
50	Scleroderma	1	0.52
51	Scrofuloderma	1	0.52
52	Tuberculosis verrucosa cutis	1	0.52
53	Urticaria pigmentosa	1	0.52
	TOTAL	**190**	**100**

All 190 adequate cases were classified according to AB Ackerman's criteria into 9 major basic patterns.This basic patterns include Superficial perivascular dermatitis (SPD), Superficial and deep perivascular dermatitis (SDPD), Nodular and diffuse dermatitis (NDD), Vasculitis dermatitis(VD),Intrepidermal vesicular and pustular dermatitis (IVPD), Subepidermal vesicular dermatitis (SEVD),Folliculitis and Perifolliculitis(FP),Fibrosing dermatitis(FD) ,Panniculitis (PD) (Table II)

Table II Split up of cases according to major tissue reaction pattern

Sr. No.	Tissue reaction pattern	No. of cases	Percentage
1	SPD	48	25.40
2	SDPD	14	7.41
3	**NDD**	**86**	**45.50**
4	VD	2	1.06
5	IVPD	13	/-6.88
6	SEVD	9	4.76
7	FP	2	1.06
8	FD	6	3.17
9	PD	9	4.76
	TOTAL	**189**	**100**

Maximum cases were of Nodular and diffuse dermatitis reaction pattern (NDD) followed by Superficial perivascluar dermatitis (SPD). Least number of cases was of pattern Vasculitis (VD) and Folliculitis and Perifolliculitis (FP).

In SPD out of total 48 cases, Discoid Lupus Erythematosus (DLE) contribute to maximum of 6 cases along with inconclusive cases . (Table III)

Table III Pattern 1:- Split up of cases showing superficial perivascular dermatitis reaction pattern (SPD)

Sr.No.	Cases	Number	Percentage
1	**Discoid lupus erythematosus**	6	12.5
2	Inconclusive	6	12.5
3	Lichen planus	5	10.41
4	Psoriasis	5	10.41
5	Lichen sclerosus et atrophicus	4	8.34
6	Cutaneous amyloidosis	4	8.34
7	Erythema mutiforme	2	4.17
8	Hypertrophic lichen planus	2	4.17
9	Ashy dermatosis	2	4.17
10	Pityriasis rosea	2	4.17
11	Prurigo nodularis	2	4.17
12	Lichen striatus	2	4.17
13	Allergic contact dermatitis	1	2.08
14	Dowling Dego's disease	1	2.08
15	Actinic lichen planus	1	2.08
16	Lichenoid lesion favouring drug eruption	1	2.08
17	Pityriasis rubra pilaris	1	2.08
18	Urticaria pigmentosa	1	2.08
	TOTAL	**48**	**100**

Now Cases with SPD pattern were classified with minor tissue reaction patterns into cases with Lichenoid reaction (LR)-24 cases, Vacuolar reaction (VR) - 8 cases, Psoriasiform reaction (PR)- 6 cases and Spongiotic reaction (SR) -3 cases .(Table IV)

Table IV Split up of cases of superficial perivascular dermatitis reaction pattern (SPD) with minor tissue reaction pattern

Sr.No	Minor tissue reaction pattern	No.of cases	Percentage
1	**Lichenoid Reaction pattern (LR)**	**24**	**58.54**
2	Vacuolar Reaction pattern (VR)	8	19.52
3	Psoriasiform Reaction pattern (PR)	6	14.63
4	Spongiotic Reaction pattern (SR)	3	7.32
	TOTAL	**41**	**100**

Lichenoid reaction patterns includes conditions such as Lichen planus (5 cases) ,Lichen sclerosus et atrophicus and Cutaneous amyloidosis (4 cases) followed by Lichen striatus, Ashy dermatosis,Prurigo nodularis and Hypertrophic lichen planus (2 cases) and Actinic Lichen Planus (1 case)

Vacuolar reaction pattern was seen in Discoid Lupus Erythematosus (6 cases) and Erythema Multiforme. (4 cases)

Psoriasiform .reaction pattern was seen in total 6 cases which includes 5 cases of Psoriasis and 1 case of Ptyriasis rubra pilaris .

Second tissuee reaction pattern was SDPD. It includes maximum no of inconclusive cases (8 cases) along with Indeterminate leprosy (4 cases) and Sweet's syndrome (2 cases).

Third tissue reaction pattern was Nodular and diffuse dermatitis pattern including total 86 cases including various types of leprosy as follows. (Table V) & (Table VI)

Table V

Sr. No	Cases	Number	Percentage
1	**Borderline tuberculoid leprosy**	25	44.64
2	Tuberculoid leprosy	19	33.92
3	Borderline lepromatous leprosy	9	16.08
4	Tuberculoid leprosy with type I reaction pattern	2	3.58
5	Midborderline leprosy	1	1.78
	TOTAL	**56**	**100**

Pattern 3:-Split up of cases showing nodular dermatitis reaction pattern (NDD-ND)

Table VI

Sr.No	Cases	Number	Percentage
1	**Lepromatous leprosy**	13	43.34
2	Lupus vulgaris	6	20
3	Pseudolymphoma	3	10
4	Sarcoidosis	3	10
5	Histoid leprosy	2	6.67
6	Erythema nodosum leprosum	1	3.33
7	Scrofuloderma	1	3.33
8	Tuberculosis verrucosa cutis	1	3.33
`	**TOTAL**	**30**	**100**

Pattern 3:-Split up of cases showing diffuse dermatitis reaction pattern (NDD-DD)

VR Pattern was seen in two cases with each case of Necrotising and Infective vasculitis.

IVPD include Pemphigus Vulgaris (6cases), Pemphigus Foliaceus (4 cases), Hailey –Hailey disease (2 cases) and Darier's disease (1 case)

accounting total of 13 cases.

SEVD pattern include total 9 cases. Bullous Pemphigoid (6cases) , Linear IgA dermatoses (2 cases) and Epidermolyses bullosa (1 case).

FP reaction pattern was seen in Perforating folliculitis and Kyrle's disease .Each of one case.

FD reaction pattern was seen in total 6 cases. All 6 cases were of Morphea 9 case were showing PD pattern .Out of 9 cases 2 cases were of Necrobiosis lipoidica, Panniculitis and Erythema nodosum and one case each of Panniculitis with vasculitis,Lupus Profundus, Erythema induratum.

DISCUSSION

Out of 189 adequate skin biopsies of clinically diagnosed inflammatory dermatoses, 14 were inconclusive. In 175 cases final diagnosis was possible on histology by pattern analysis by algorithmic method based on pattern analysis as described by **Ackerman AB (1978).[5]and described by Kim IH and Kim SN (1987).[6]** Although in these 14 inconclusive cases we could classify them based on patterns, further interpretation was limited. Most of these cases belonged to SPD and SDPD pattern i.e. 6 & 8 respectively.

Commonest pattern in the present study was 3rd pattern of nodular and diffuse dermatitis i.e.86/189 (45.5%). Least number of cases was seen in each FP and VD tissue reaction pattern i.e.2/189 (1.06%).

We categorized these inflammatory diseases according to **Ackerman's AB's (1978)**[5] into 9 major tissue reaction patterns.

Patternwise Analysis -

1) Superficial perivascular dermatitis reaction pattern (SPD):-

First pattern of (SPD) included 48 cases.This group was subclassified based on changes in epidermis,dermis and at interface.[5] With this further subtyping was possible. Minor tissue reaction patterns include LR, VR, SR & PR pattern.

Out of 48 cases of SPD, 41 cases were classified with minor tissue reaction pattern, one was of urticaria pigmentosa and 6 were inconclusive cases.

Lichenoid Reaction Pattern (LR)-

The commonest lesion in LR was lichen planus. In all these cases, obscurring of the interface and hypergranulosis were the consistent findings.[7]

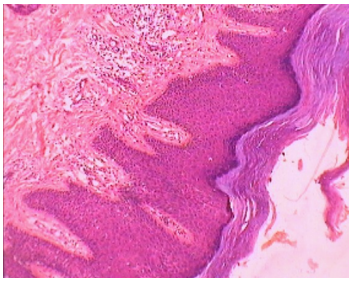

Fig1:-Histopathology of Lichen Planus showing Epithelial hyperkeratosis, irregular acanthosis, marked lymphocytic infiltrate underlying epithelium.(H&E 20)

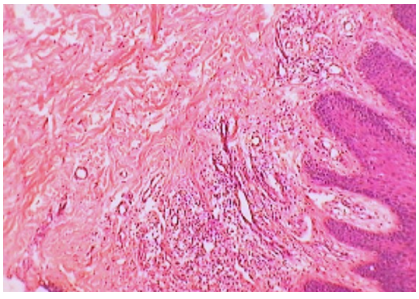

Fig 2:-Histopathology of Lichen Planus showing saw tooth appearences of rete ridges.Band like lymphocytic infiltrate fills papillary dermis.The infiltrate press against the undersurface of epidermis. (H&E 40)

Various other lesions in this reaction pattern were lichen sclerosus et atrophicus, lichen striatus, ashy dermatosis, prurigo nodularis.,cutaneous amyloidosis, hypertrophic lichen planus , actinic lichen planus and lichenoid drug eruption.

Other dermatosis included single case of actinic lichen planus and 2 cases of hypertrophic lichen planus.

We found 4 cases of cutaneous amyloidosis which were confirmed by demonstration of amyloid with Congo red stain.[5] 2 cases each of prurigo nodularis and ashy dermatoses were also seen in this study, along with one case of Dowling Dego's disease. All were correlated with clinical diagnosis.

Vacuolar Reaction Pattern (VR)-

Our study included 8 cases of vacuolar reaction pattern (VR), of which 6 were of (DLE) and 2 cases were diagnosed as Erythema multiforme (EM). Microscopic feature of Cutaneous lupus erythematosus(LE) found vacuolation of keratinocytes and epidermal atrophy as the most consistent histological findings in DLE along with other features like hyperkeratosis and collagen damage. [8]

We found basilar keratinocyte unaccompanied by significant inflammatory infiltrate in our 2 cases of EM and reached the diagnosis by correlating with the clinical findings. [9]

Psoriasiform reaction pattern (PR)-

This pattern was seen in total 6 cases, of which 5 were classical Psoriasis and 1 case was of Pityriasis rubra pilaris (PRP). Psoriasis showed confluent parakeratosis and presence of neutrophils in the stratum corneum (Munro microabscesses), dilatation and tortuosity of capillaries in the papillae, acanthosis, elongation of rete ridges and parakeratosis.[10]PRP show follicular plugging,increased granular layer and acantholysis.[11]

Spongiotic Reaction pattern (SR) -

We found only 3 cases of spongiotic reaction pattern which included 2 cases of Pityriasis rosea & one case of Allergic contact dermatitis Histological features are not specific and include focal parakeratosis, hypogranulosis, spongiosis, papillary dermal edema, mild perivascular lymphohistiocytic infiltrate, exocytosis and extravasated erythrocytes in the papillary dermis.[12]

Presence of eosinophils in superficial perivascular region as strongly favouring the diagnosis of allergic contact dermatitis which was also observed by us in our study.[13]

2. Superficial and deep perivascular dermatitis reaction (SDPD):-

This pattern included total 14 cases, including 4 cases of indeterminate leprosy, 2 cases of Sweet's syndrome. Maximum inconclusive cases were found in this category i.e. 8 cases.

In the absence of specific alterations in epidermis, the changes like perivascular dermatitis become very nonspecific as skin has limited number of ways of reaction to any stimulus, making specific diagnosis difficult.[2]All the cases of indeterminate leprosy showed unremarkable epidermis with only perivascular and periappendigeal lymphohistiocytic infiltration**.**

3. Nodular and Diffuse Dermatitis (NDD):-

Maximum cases in our study i.e. (86/190) showed this pattern of inflammation. Depending on the spread of infiltrate, this is again divided into nodular and diffuse.[6] Present study showed 56/86 cases of nodular dermatitis (65%) and 30/86 cases of diffuse dermatitis (35%). Nodular dermatitis included all cases of leprosy mostly tuberculoid type showing granuloma formations whereas diffuse dermatitis included other granulomatous lesions in addition to leprosy.

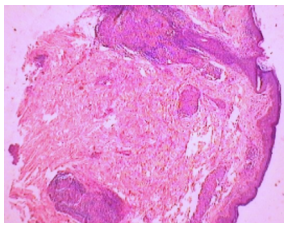

Fig3:-Histopathology of Borderline Tuberculoid leprosy showing

epidermis lined by stratified squamous lining epithelium with dermis showing adnexal structure with periadnexal inflammatory infiltrate.(H&E 20X)

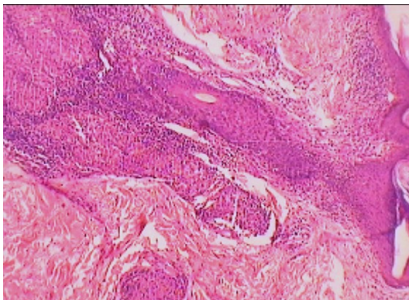

Fig 4: Histopathology of Borderline tuberculoid leprosy showing linear or irregular granulomatous inflammatory infiltrate observed at upper epidermis with ill defined granulomas(H&E 40X)

Various features for histological diagnosis taken into account for this included epidermal atrophy, epithelioid granuloma, distribution of lymphocytes, histiocytes and foam cells, infiltration of nerves, blood vessels, adnexa and presence of grenz zone.[14]

4. Vasculitis reaction pattern (VD):-
We found only two cases of vasculitis. One of necrotizing vasculitis and infective vasculitis each. Both cases showed classical histological features diagnostic of vasculitis. [15]

5. Intrepidermal vesicular and pustular dermatitis (IVPD):-
This group included total 13 cases, most of which belonged to pemphigus vulgaris i.e. 6 cases (46.15%), followed by pemphigus foliaceous i.e. 4 cases (30.77%), Hailey-Hailey disease i.e.2 cases (15.38%) and one case of Darier's disease (7.7%) Pemphigus vulgaris showed suprabasilar acantholysis, while pemphigus foliaceus showed acantholysis in superficial layers of the epidermis. [3][4] Vesiculobullous diseases can be diagnosed using general diagnostic approach combining clinical features, histological and immunological findings.[16]

2 cases of Hailey-Hailey disease were found in our study.These cases showed acantholytic dyskerototic cells in some foci, throughout the thickness of epidermis along with superficial perivascular infiltration by lymphocytes and eosinophils.[4]

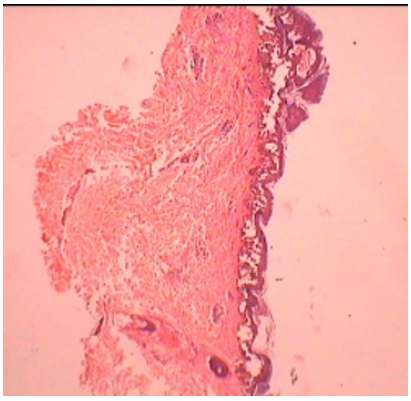

Fig 5:-Histopathology pf Hailey-Hailey disease with intraepidermal and suprabasilar acantholysis (H&E 20X)

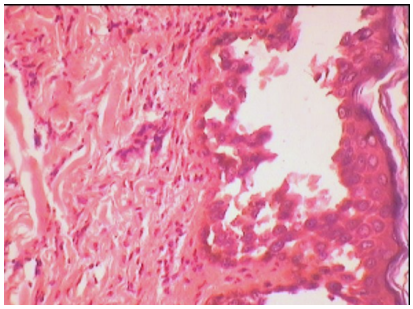

Fig 6:-High power view of Hailey –Hailey disease showing acantholytic cells with eosinophilic polygonal shaped cytoplasm with few intact iintercellular bridges giving dilapidated brick wall appearance.(H&E 40X)

One case of Darier's disease showed suprabasal acantholysis with no crust formation.[17]

6. Subepidermal Vesicular reaction pattern (SEVD):-
This group included 9 cases of which 6 cases were of bullous pemphigoid, 2 cases of linear IgA dermatosis and 1 case of epidermolysis bullosa.

Subepidermal split with superficial perivascular inflammatorywas seen in bullous pemphigoid [18]

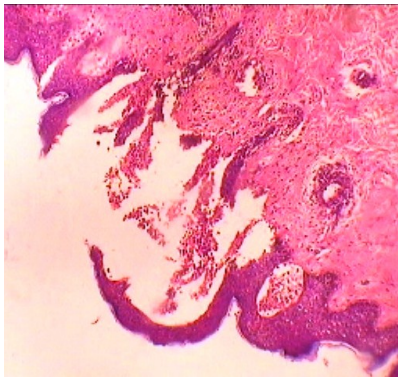

Fig 7:-Histopathology of Bullous Pemphigoid showing subepidermal blister with inflammatory infiltratrate.

Presence of eosinophils admixed with neutrophils were seen in papillary dermis in 3 of our cases. Similar features with increased neutrophils were observed in linear IgA dermatosis. [4]

Epidermolysis bullosa in our study showed intact stratum corneum with vesicle formation at the basal layer. [4]

7. Folliculitis and Perifolliculis (FP):-
This pattern showed only two cases. One was clinically diagnosed as Kyrle's disease and other was a known diabetic with nephropathy. Histologically it showed epidermal invagination filled with parakeratotic plug. Epidermis was acanthotic with dyskeratotic cells in it. Subepithelial tissue showed marked inflammations.This condition simulates perforating follicutitis both clinically and histologically. Perforating folliculitis usually shows a retained hair and degenerated collagen. The case of perforating folliculitis in our study showed mixed inflammatory cell infiltrate including neutrophils . Presence of dyskeratotic cells in epidermal layers favours the diagnosis of Kyrle's disease. [5]

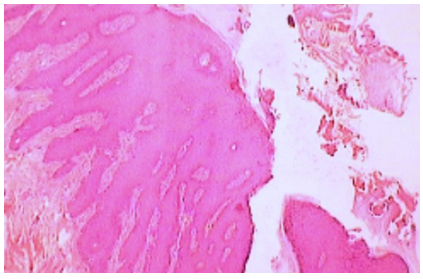

Fig 8:-Histopathology of Kyrle's disease with epithelial invagination with keratotic plug with basophilic cellular debris.

8. Fibrosing Dermatitis (FD):-
Present study included 6 cases of fibrosing dermatitis.5 of them were of morphea and 1 was of scleroderma. These conditions were associated with increased dermal collagen. The morphology varied depending on the stage of the lesion as **Ackerman AB (1978)**[5] has described early and late lesions in this pattern. Early inflammatory lesion showed vascular changes consisting of endothelial swelling and edema, mild periadenexal and interstitial inflammatory infiltrate among thick collagen bundles. Late lesions showed less inflammation

and more fibrosis with atrophy of the appendages.

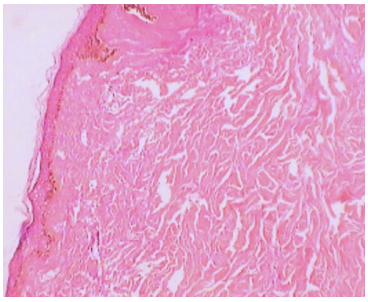

Fig9 –Histopathology of Morphea showing deeply eosinophilic collagen fibres in reticular dermis with reduced subcutaneous fat. (H&E 20X)

9. Panniculitis (PD):

This pattern included total 9 cases of which 2 cases were of necrobiosis lipoidica, both were seen in diabetic patients [5], seen in extremities. It showed lymphoplasmacytic infiltration in septa without vasculitis [5].3 cases were of panniculitis, one of which was associated with vasculitis. Two cases of erythema nodusum were also seen showing mostly septal inflammation [19] with associated vasculitis. Both of our cases showed granulomatous inflammation reaching into deeper dermis and subcutaneous fat causing lobular inflammation with associated element of small vessel vasculitis.

Similar features along with nuclear dust and signs of fat necrosis are seen in lupus profundus [5]. We observed one case of lupus profundus that was also correlated clinically.The type of inflammation was lobular panniculitis in this case. [20]

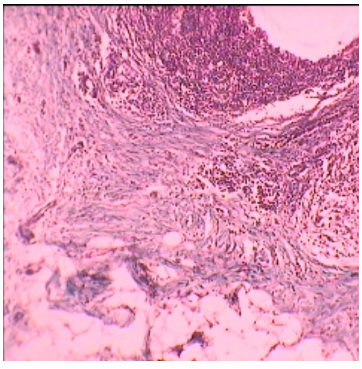

Fig 9:-Histopathology of Panniculitis showing sepatal inflammation involving septa with dense chronic inflammatory infiltrate (H&E 20X)

CONCLUSION-

In modern era of molecular techniques,histopathology still forms the basis for diagnosis of inflammatory lesions of skin. Use of pattern analysis makes the histological diagnosis easier and reproducible with better understanding of pathogenesis. It should be applied in every inflammatory condition to arrive the final diagnosis.

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