HISTOMORPHOLOGICAL SPECTRUM OF CHANGES IN THREE CLINICAL STAGES OF VITILIGO - ACTIVE, QUIESCENT AND IMPROVING

P. N. BEHL * AND B. K. PRADHAN †

Summary

42 cases of vitiligo were studied histologically. The histological spectrum of changes have been described with particular reference to the clinically recognised 3 stages of vitiligo e.g., active, quiescent and improving.

Vitiligo is an acquired idiopathic depigmentary disorder, which, though worldwide in distribution, is very common in India, Egypt and other tropical countries. It causes great social embarrassment to dark skinned people. Various aspects of vitiligo have been extensively studied, but the exact cause of this common dermatological problem remains yet to be firmly established. The present work deals with the spectrum of histomorphological changes in a vitiliginous skin in relation to the three clinically recognised stages of vitiligo.

Material and Methods

42 vitiligo patients were selected for histological studies. The cases were divided into 3 clinical types namely active, quiescent and improving. Table I shows the number of cases included and their sex distribution in each variety (Table 1).

TABLE 1
Patients of vitiligo in each clinical stage

Clinical stages	No. of cases	Sex distribution Male	Female
Active	20	13	7
Quiescent	10	7	3
Improving	12	5	7
Total	42	25	17

A case was considered to be active when the vitiliginous patches were found to show signs of increase in size of the lesion, the border being ill-defined and not hyperpigmented. In a quiescent stage the white patch was characterised by constancy in its size over a considerable period of time, the border remaining well defined and hyperpigmented. The improving stage showed signs of repigmentation, in either follicular or peripheral pattern the initial lesion thus decreasing in size. The improvement could have been spontaneous or due to treatment. Clinical criteria employed in recognising the stages of vitiligo are enumerated in Table 2. However, the division of cases into active, quiescent and improving was based on the predominant number of lesions of a particular stage in a patient, because patients having lesions predominantly of one

Read at the International Symposium on Pigmentary Disorders and IVth Annual Conference of I A D V & L held in New Delhi in February 1976.

* Director
† Pathologist
Skin Institute, 5A Mathura Road, Jangpura
New Delhi-110014

Received for publication on 25—3—1977

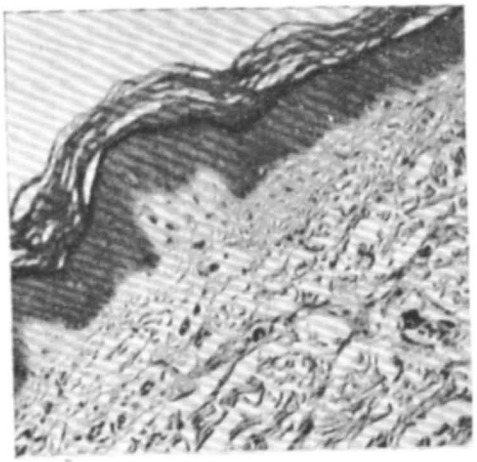

Fig. 1 The epidermis of the vitiliginous skin (right side) is relatively thin and flattened. The basal layer is devoid of melanin (H & E × 100)

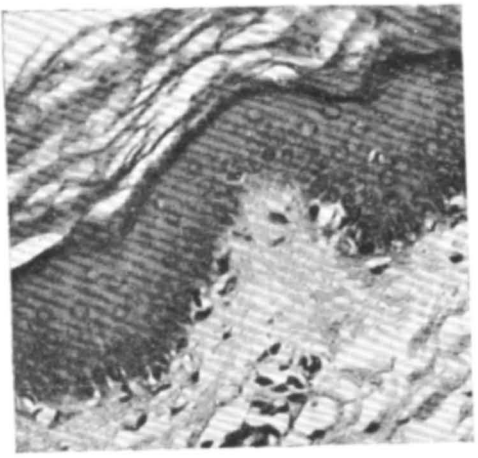

Fig. 2 A normal skin showing large number of basal clear cells (H & E × 100)

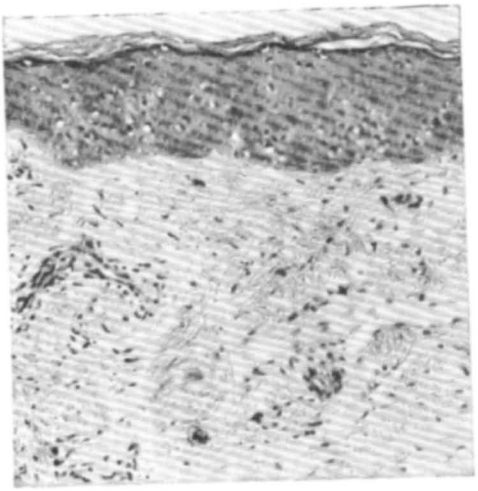

Fig. 3 A vitiliginous skin showing absence of melanin and occasional clear cells in the basal layer. The suprabasal zone contains large number of clear cells (H & E × 100)

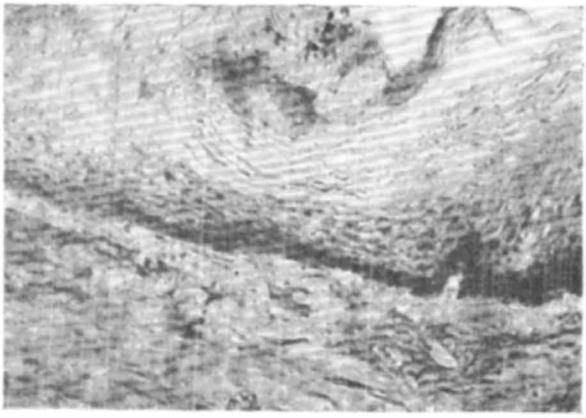

Fig. 4 A gradual diminution of DOPA reaction in the basal layer is seen in Active stage (DOPA × 100)

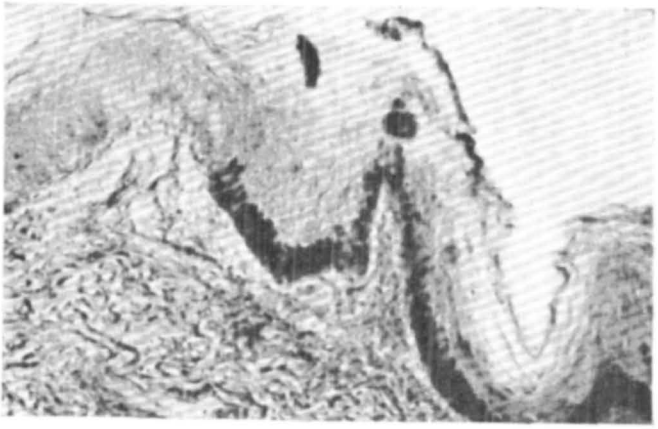

Fig. 5 There is an abrupt disappearance of DOPA positive reaction of the basal layer in Quiescent stage (DOPA × 100)

Fig. 6 In an Improving stage the basal layer shows foci of DOPA positive reaction (DOPA × 100)

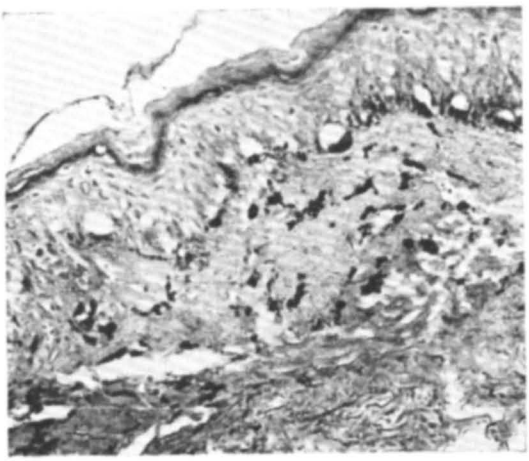

Fig. 7 DOPA positive cells are seen in the upper dermis under the vitiliginous skin in Improving stage (DOPA × 100)

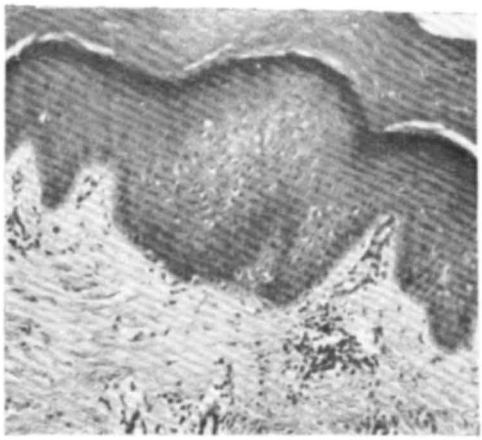

Fig. 8 The epidermis shows increase in thickness and the rete ridges are tending to form in Improving stage. The basal layer contains a few clear cells, but no melanin is seen (H & E × 100)

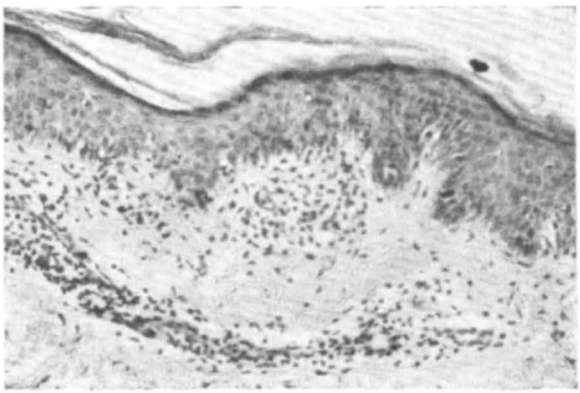

Fig. 9 There are mononuclear cells hugging on the epidermis at the junctional area between vitiliginous (left side) and normal skin (right side). The vitiliginous skin contains no pigment in the basal layer. Perivascular infiltrate in the upper dermis is seen below the area of mononuclear hugging (H & E × 100)

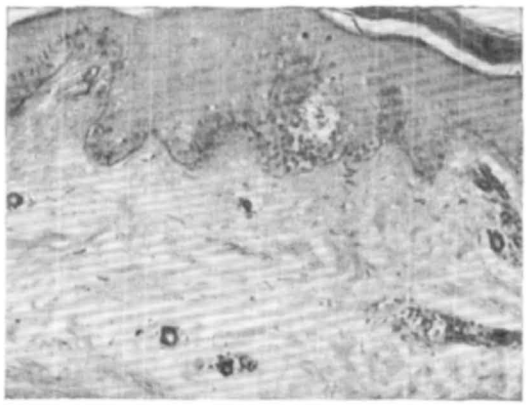

Fig. 10 The mononuclear cells at the border of the vitiliginous skin are lying within basal lamina (PAS × 100)

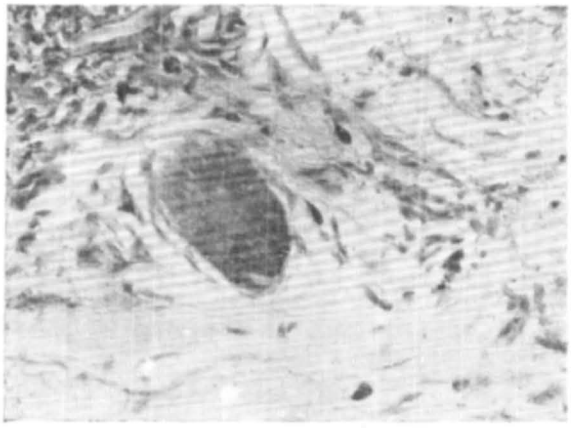

Fig. 11 Among the perivascular infiltrates, many mast cells (darkly stained) are seen. (Azure-A × 250)

TABLE 2
Clinical criteria for recognition of stages of vitiligo

Stages of vitiligo	Clinical features
Active	1. New lesions developing 2. Increasing size of the lesion 3. Border ill defined
Quiescent	1. No new lesion developing 2. The lesions are stationary in size 3. Border hyperpigmented and well defined.
Improving	1. Decrease in size of lesion 2. No new lesion developing 3. Border defined and signs of repigmentation present (follicular and peripheral)

stage did have in other parts of the body, few lesions showing features of other stages. Accordingly the biopsy was collected from that type of vitiliginous patch which constituted the maximum number of the same type of lesions in a particular patient.

Biopsy was taken by a punch biopsy needle having 7 m. m. diameter. The marginal area of the vitiliginous patch was the site for biopsy. Due care was taken to see that each piece of the biopsied material contained a portion of the vitiliginous as well as the adjacent normal skin. The circular piece of skin, thus obtained, was bisected into two equal halves, each half representing a part of vitiligo and also the normal skin. One half of the tissue was subjected to DOPA staining[1] and the other half submitted to routine processing. Paraffin blocks were made and cut at 5 μ thickness. Each block was subjected to serial sectioning and stained with haematoxylin and eosin. Azure—A stain[2] was employed on serial sections to study the mast cell population in the bulk of perivascular infiltrate.

Observation and Discussion

The above procedure enabled us to study the vitiliginons skin in comparison with the adjacent normal skin and facilitated appreciation of relative changes. The vitiliginous skin was characterised by diminution or absence of pigment in the basal layer. In a lesion of recent origin, the basal layer showed diminished pigment which, however, in a long standing lesion was devoid of pigment. There was relative thinning and flattening of the epidermis on the affected side (Fig. 1). On examination of a section stained with haematoxylin and eosin, the melanocytes in a normal skin are found wedged in between the basal cells of the epidermis. They have a dark staining small nucleus and clear cytoplasm[3]. In our study, abundant clear cells (melanocytes) were found in the basal layer of the normal skin (Fig. 2). In some of the cases, increased number of suprabasal clear cells were found in the depigmented portion and the basal layer contained occasional or no clear cells in those situations (Fig. 3). It is mentioned that these suprabasal clear cells are considered as the Langerhans cells[4]. A lot of speculations exist regarding the origin and function of these cells, besides their relationship to melanocytes specially in disease under study [5,6,7,8,9]. In active stage the DOPA stain revealed a gradual transition of DOPA positive reaction from pigmented to depigmented side (Fig. 4), whereas a quiescent variety manifested an abrupt disappearance of DOPA reaction (Fig. 5). In improving cases, a gradual transition was the feature as in active variety. But here discrete foci of DOPA positivity was seen in the basal layer showing signs of improvement (Fig. 6). More striking was the presence of DOPA positive cells in the upper dermis (Fig. 7). What the source of these dermal DOPA positive cells in improving cases, whether they are fallen out epidermal effete melanocytes or are migrating from a new source, is a question to be answered. If they are effete melanocytes, the physiological DOPA reaction is unlikely to 'persist in an ageing cell. It has been suggested

that epidermal melanocytes originate from neural crest and migrate through the peripheral nerves to reach the basal layer of the skin[10]. Thus we presume that once improvement is set in, the Schwannian cells of the peripheral nerves are stimulated to leave the nerve and migrate through the dermis towards the epidermis to repopulate the basal layer. Hence the DOPA positive cells in the upper dermis are perhaps the migrating Schwannian cells. Since they are young and newly formed active cells, the physiological activity of DOPA reaction is likely to be present in them. Our recognition of 3 clinical stages of vitiligo is thus confirmed by DOPA reaction. The division of cases into clinical varieties has therapeutic and prognostic significance which will be dealt with at length in our subsequent publication.

Besides the DOPA reaction mentioned above, increasing thickness of the epidermis with rete ridges tending to form were also features of improvement (Fig. 8). Another interesting finding which was consistently found in 'active stage,' occasional in 'quiescent' and 'improving' stages, was the feature of mononuclear hugging occurring at the dermoepidermal junction of marginal area of vitiliginous patch (Fig. 9). These cells were predominantly small lymphocytes with occasional histiocytes and they were lying within the basal lamina on serial section examination (Fig. 10). The dermis below the border area (the junctional area between vitiliginous and normal skin) contained more number of blood vessels with perivascular infiltrates (Fig. 9) composed of lymphocytes, histiocytes and occasional plasma cells. Among these infiltrates, large number of mast cells were seen as evidenced by Azure-A stain (Fig. 11). The details and significance of this finding will be speculative at this stage and needs further work to establish the specificity of this tissue reaction.

Acknowledgments

The authors record their grateful thanks to Miss Usha Kiran and Miss Sudarshan Kalsi, Lab. Assistants, Skin Institute, for their all round technical help throughout the execution of this study. Thanks are also to Dr. N. R. Mahadevan for clinical help and Mr. Krishan Lal for having typed the manuscript. We are thankful to Mr. K. S. Jolly of the photographic section, Maulana Azad Medical College, New Delhi, for helping us in photomicrography.

REFERENCES

1. Drury RAB and Wallington EA : Carleton's histological technique, Oxford University Press, New York, 1967, p 250.
2. Drury RAB and Wallington EA : Carleton's histological technique, Oxford University Press, New York, 1967, p 214.
3. Lever WF and Lever GS : Histopathology of the skin, JB Lippincott Co., Philadelphia, 1975, p 16.
4. Lever WF and Lever GS : Histopathology of the skin, JB Lippincott Co., Philadelphia, 1975, p 20.
5. Masson P : Pigment cells in man, New York Academy of Science (Spec. publ), 4 : 15, 1948.
6. Birbeck SM, Breathnach AS and Everall JD : Electron microscopic study of basal melanocytes and high level clear cells (Langerhans cells) in vitiligo, J Invest Derm, 37 : 51, 1961.
7. Breathnach AS : The Langerhans cells. J Invest Derm, 44 : 201, 1965.
8. Breathnach AS and Wyllie LMA : Melanin in Langerhans cells, J Invest Derm., 45 : 401, 1965.
9. Breathnach AS, Silver WK, Smith J et al : Langerhans cells in mouse skin experimentally derived of its neural crest component, J Invest Derm, 50 : 147, 1968.
10. Leopold JG and Richards DB : The interrelationship of blue and common naevi, J Path, 95 : 37, 1968.