NEURONAL STUDIES IN VITILIGO

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Summary

48 cases of vitiligo including 6 cases of segmental zosteriformis variety were subjected to histological examination to study the peripheral nerves. All the 3 components of the peripheral nerve viz; axis cylinders, myelin sheath and Schwann cell nuclei were examined with special stains. No structural damage to the nerve either in vitiliginous or adjacent normal skin or below the junctional area could be demonstrated even in lesions of long duration. Hence the implication of organic damage to the nerve fibres in the aetiology of vitiligo, as has been suggested in the literature, requires reconsideration.

Introduction

Several suggestions have been put forward from time to time to explain the aetiology of vitiligo, the more recent of which are auto-immunity, trophoneurosis and self-destruction theory of melanocytes. It was observed that vitiliginous patches, atleast in some of the cases, appear in crops with their distribution in relation to dermatomes. Besides this, difference in occurrence of depigmented patches between healthy and neurologically defective portions of the body in the same individual has also been pointed out[1]. The finding of increased skin temperature and sweat production over vitiliginous patch in comparison with normal skin which is indicative of cholinergic influences, possibly resulting from diminished sympathetic activity in depigmented areas lead further to the suggestion of implicating nerve in the causation of vitiligo[2]. The above suggestions were based on clinical grounds and physiological studies. Earlier Shao, Chan-Gen[3] described dystrophic changes in the nerve trunks and terminals associated with vitiligo lesions of varying duration by employing Bielchowsky Gros silver impregnation technique. The difference in intensity of staining reaction of nerve fibres compared with those of normal skin, thickening and varicose dilatation of finer axons, a significant decrease in all nerve elements, were accepted by him as evidence of nerve dystrophy. Breathnach et al[4] by electronmicroscopic studies found degenerative and regenerative changes in terminal regions of a small proportion of nerves supplying central and marginal areas of vitiliginous lesions and considered that the affected neurites are probably autonomic in functions.

In view of the above suggestions in the literature, the present work was designed to study all the components of a peripheral nerve i. e. axis cylinder, myelin sheath and Schwann cells, in a depigmented patch by employing special stains and to detect structural damage to the nerves, if any.

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Material and Methods

48 cases of vitiligo were included in the series. Out of these 6 were of segmental zosteriformis variety. The marginal portion of the vitiliginous patch was the site for biopsy. Biopsies were taken by a punch biopsy needle having a diameter of 7 m. m. Each circular piece of skin had a portion of normal as well as vitiliginous skin which was bisected by a sharp blade into two equal halves; each half representing both vitiligo and normal skin portion. One half of the tissue was subjected to DOPA staining[5] to see the DOPA reaction of the depigmented patch in comparison to the normal skin. The other half of the tissue was

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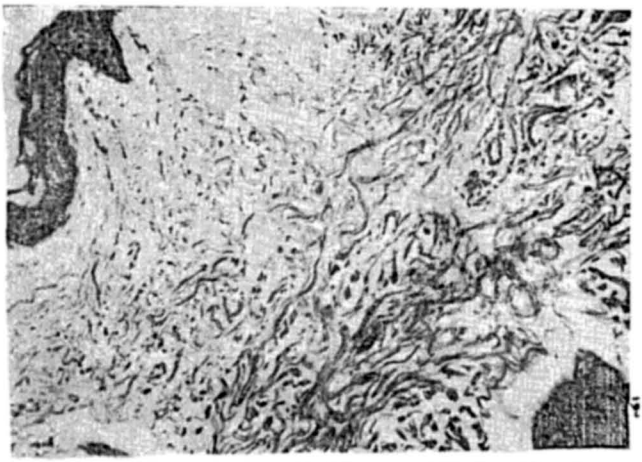

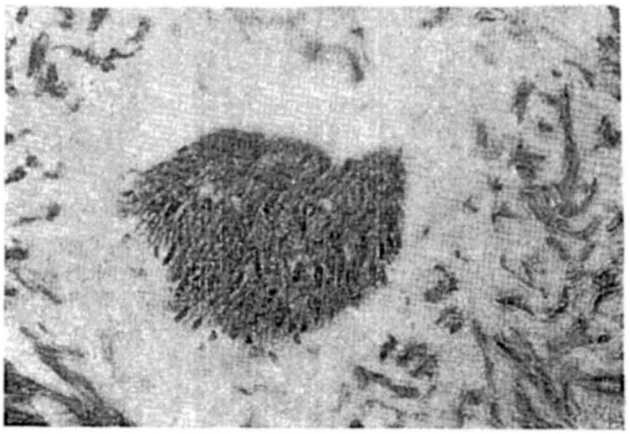

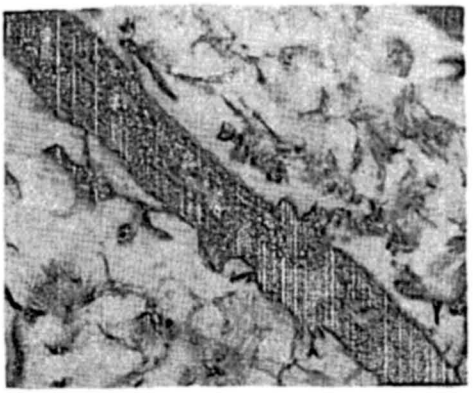

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Fig. 1 The basal layer on the left side (Vitiliginous portion) is DOPA negative in comparison with the DOPA positive basal layer on the right (normal skin portion) (DOPA X 100).

Fig. 2 A nerve bundle is seen in the right lower corner under a normal skin showing pigmented basal layer in silver stain (Bodian X 100).

Fig. 3 Same nerve bundle as is seen in Fig. 2. The axis cylinders (black zig zag lines) running between the oval Schwann cell nuclei are seen (Bodian X 250).

Fig. 4 A long nerve bundle under junctional area shows intact axis cylinders and Schwann cell nuclei (Bodian X 250).

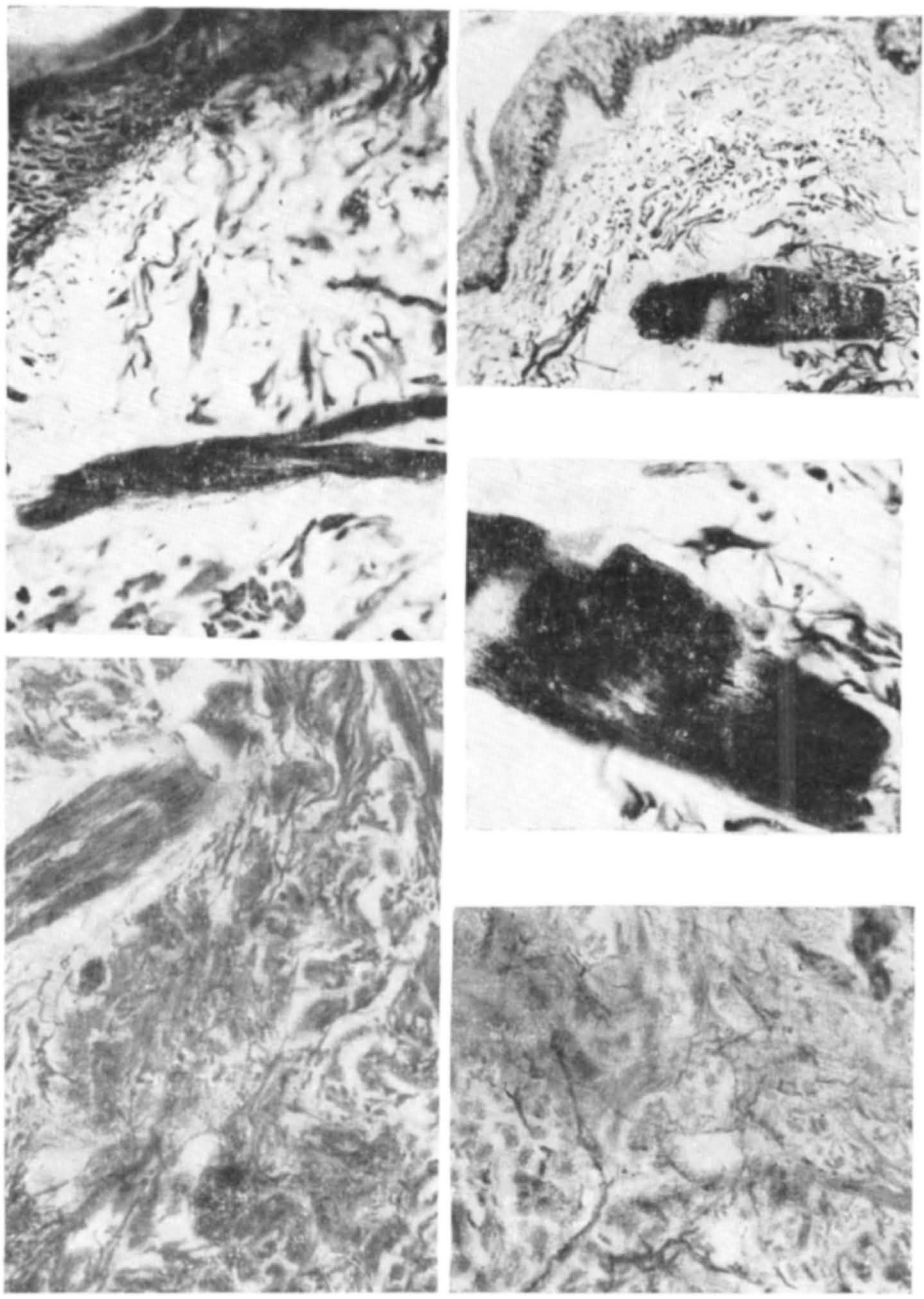

Fig. 5 A nerve trunk under vitiliginous skin (The basal layer is devoid of pigment) does not show any abnormality in axis cylinders and Schwann cell nuclei (Bodian X 250) (Lt. Top)

Fig. 6 The nerve bundle shows discontinuity in its course. This nerve lies under the normal skin showing pigmented basal layer in silver stain. This feature is considered artefactual (Bodian X 100). (Rt. Top)

Fig. 7 Same nerve bundle as is seen in Fig. 6. The fine axis cylinders and oval Schwann cell nuclei are seen at the margin of the interruption (Bodian X 250). (Rt. Mid.)

Fig. 8 Myelin positive fibres (irregularly running black fibres in the dermis) are seen under the vitiliginous skin showing no abnormality (Weil's Haematoxylin X 250). (Rt. Bottom)

Fig. 9 Discrete myelin positive fibres and a nerve bundle (in the right upper corner) containing parallel running myelin positive fibres are seen under junctional area. They show no abnormality (Weil's Haematoxylin X 250). (Lt. Bottom)

submitted to routine processing. Paraffin blocks were made and cut at 5μ thickness. Each block was subjected to an exhaustive serial sectioning and the sections were stained by H & E. Bodian stain[6] for demonstration of axis cylinders and Schwann cell nuclei, and Weil's haematoxylin stain[7] for myelin sheath of the peripheral nerves were employed on serial sections.

Observation and Discussion

The above procedure enabled us to study the nerves in vitiliginous skin in comparison to those in normal skin and to appreciate the relative differences. In DOPA staining, the depigmented skin was characterised by diminution or absence of DOPA reaction in the basal layer depending upon the duration of the lesion. In a lesion of recent origin stray DOPA positive cells or diminished DOPA positive reaction was seen in the basal layer. However, a long standing lesion manifested complete absence of DOPA positive cell (Fig. 1).

The Bodian stain demonstrated the course of axis cylinders and Schwann cell nuclei in a nerve twig or nerve bundle. Single neurites running randomly in the bulk of dermal collagen and in special locations like the outer root sheath of the hair follicle, could be clearly visualised. In nerve bundles of normal skin (close to the vitiliginous border), the course of the axis cylinders between the oval Schwann cell nuclei could be clearly appreciated (Figs. 2 & 3). Similarly the nerve bundles in the junctional area (Fig. 4) and the vitiliginous area (Fig. 5) did not reveal any detectable change in the axis cylinder or Schwann cell nuclei. It must be pointed out that even the lesions of several years' duration and the lesions of zosteriformis variety did not show any abnormality in the said components of the nerve bundle. There was no thickening or varicose dilatation of the axons. In some places, however foci of discontinuity in the path of axis cylinders were observed. This feature was not considered as pathological since in those situations the contour of the nerve bundle was maintained, and the arrangement of the Schwann cell nuclei was unaltered. Thus the sites of missing axis cylinders are considered as artefactual (Figs. 6 & 7), because it is understood that the peripheral nerves follow a zig zag course and the plane of cutting the section may not pass through the entire course of the nerve.

In Weil's Haematoxylin stain, the myelin sheath around the axons in a nerve bundle could be visualised, but this stain did not give a photographic contrast. Hence the solitary nerve fibres were chosen for photomicrography. The myelin positive fibres in the vitiliginous skin (Fig. 8) and junctional area (Fig. 9) did not show any appreciable change.

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