

Pigmentation in Plexiform Neurofibroma Following Blaschko's Lines: A New Observation

Plexiform neurofibroma is a rare variant of neurofibromatosis type 1. It is a known fact that distribution pattern of the neurofibroma lesions follows the dermatomes of the nerve fibers from which these lesions arise from.^[1] However, many of these patients also have patches of hyperpigmentation over the skin in the involved regions. It is not known whether these hyperpigmentation patches follow any pattern. In this article, we are presenting five cases of plexiform neurofibromas and their pigmentation patterns [Table 1].

The lesions started appearing in early childhood and they gradually progressed in size in all given patients. None of the patients had additional findings of NF1 except for the fourth patient who had café au lait spots and inguinal freckles. All patients underwent staged debulking. The post-operative period was uneventful, and all the patients were discharged on day 3 after surgery. Histopathological analysis in all the cases showed increased number of melanocytes (prominence seen in the basal layer) along with exocytosis of pigment in the upper layers also [Figure 1A and B]. In the deep reticular dermis and subcutaneous tissue were fascicles of slender spindle cells with S-shaped nuclei associated with thin and thick nerve bundles in the pattern of a diffuse and plexiform neurofibroma. Immunohistochemistry for S-100 showed diffuse nuclear positivity in the spindle cell population. Further staining with other stains like Melan-A or HMB-45 was not contemplated as the histological features and immunohistochemistry were strongly suggestive of neurofibromas and there were no features favoring

melanoma. According to Fetsch *et al.*,^[2] as these tumours have predominance of features of neurofibroma and less-defined melanotic elements, they can also be called as melanotic neurofibromas.

There are various anecdotal reports regarding pigmentation in plexiform neurofibromas.^[3] But none of these reports says anything regarding the distribution pattern of these pigmentations. All the five patients in our study had patches of pigmentation, and these were not exactly following the dermatomal distribution patterns. But they were found to be following Blaschko's lines of that region. This was confirmed by superimposing the photographs of the lesions with Blaschko's lines of the corresponding anatomical site [Figures 2 and 3]. According to the drawings in 1901 supplement to the Proceedings of the German Dermatological Society Meeting and illustrations of Blaschko's lines in face given by Bologna *et al.*,^[4] the lines of Blaschko follow an inverted V-pattern in the trunk which is evident in the lesion depicted in Figure 3 and an irregular pattern which is similar to the one traced in Figure 2 over the face. In this diagram, we can see that the pigmentation is limited to one side of the face and is limited to the confines of Blaschko's lines in the face. Blaschko's lines, named after Alfred Blaschko, are lines of normal cell development in skin. Usually inconspicuous in normal conditions, they become apparent during the manifestation of certain pigmented disorders of the skin such as epidermal nevus, hypomelanosis of Ito, etc.^[5] The cells of epidermis and its appendageal structures such as melanocytes, fatty hypoderm, or vascular structures

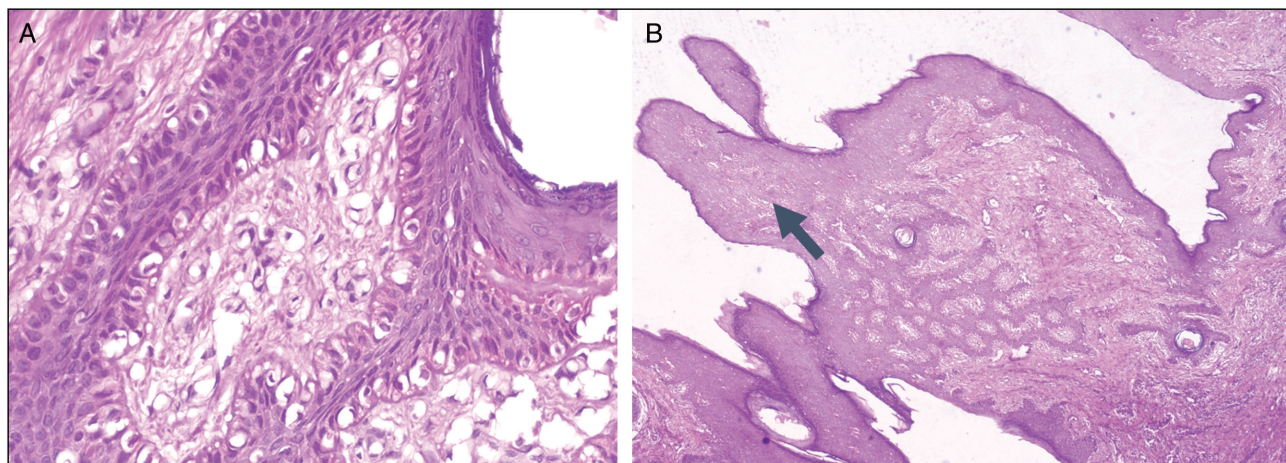


Figure 1: A: (200× H&E stain): HPE showing increased number of melanocytes in the basal layer resulting in increased pigmentation. B: (40× H&E stain) Photomicrograph with all layers of skin



Figure 2: Lesion over the left side of face of case 2 superimposed over the dermatomes and Blaschko's lines



Figure 3: Lesion over gluteal region of case 5 superimposed over the dermatomes and Blaschko's lines

may be involved together or separately in morphological conditions following the Blaschko's lines.^[6] Plexiform neurofibromas are lesions that originate from multiple nerve sheaths and they involve many additional types of cells apart from Schwann cells.^[1] Studies have shown findings of melanocytic hyperplasia in cases of pigmented neurofibromas.^[3] Blaschko's lines are presumed to trace the pathway of development of ectodermal cells.^[7] Hence this pattern of distribution of pigment adds to the evidence that there may be an abnormal group of mutated melanocytes. The histopathological findings are also reflecting the same

with increased number of melanocytes in these areas. Both Schwann cells and melanocytes are derived from neural crest cells. The causative mutation in Schwann cells, which manifest as plexiform neurofibromatosis, thus may be present in the melanocytes as well and this possibility is to be explored. Hence, this report highlights the relationship between proliferations of Schwann cells and melanocytes in the setting of plexiform neurofibromatosis. There are no reports in literature regarding risks of development of malignancies like melanoma and malignant nerve sheath tumors in melanotic neurofibromas. However, we can

Table 1: Demography and distribution pattern of the lesions

| Case no. | Age (years) | Sex | Location | Dermatomes involved |
|----------|-------------|--------|-------------------------------------|------------------------|
| Case 1 | 32 | Male | Left axilla and parascapular region | T4-T8 (left) |
| Case 2 | 18 | Male | Left side face | V1, V2, V3 (left) |
| Case 3 | 28 | Male | Left foot dorsum | L4, L5, S1 (left) |
| Case 4 | 22 | Male | Right side face | V1, V2, V3 (right) |
| Case 5 | 26 | Female | Bilateral gluteal region | L5, S1, S2 (bilateral) |

speculate that this risk can be less than 10% based on the following facts:

1. The overall risk for a patient with neurofibromatosis type 1 of developing a malignant peripheral nerve sheath tumor is estimated to be 4% or less.^[8]
2. The best estimates for malignant transformation in giant congenital nevi are between 4.6%^[9] and 6.3%.^[10]
3. None of our patients has had an adverse outcome so far.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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