e-ISSN: 0975-1556, p-ISSN:2820-2643
Available online on www.ijpcr.com
International Journal of Pharmaceutical and Clinical Research 2024; 16(2); 1087-1091
Original Research Article

Unusual Presentation of Hypertrichosis and Hyperpigmented Cutaneous Lesions in Neurofibromatosis

Aum Sanjay Bapat[1], Kamala Kant Bhoi[2], Priya Pathak[3], Manali Madhukar Shinde[4], Naresh Verma[1]

[1]Junior Resident, Department of General Medicine, Shri Balaji Institute of Medical Science, Raipur, Chhattisgarh-492001, India
[2]Consultant and Assistant Professor, Department of Neurology, Shri Balaji Institute of Medical Science, Raipur, Chhattisgarh-492001, India
[3]Assistant Professor, Department of Pathology, Shri Balaji Institute of Medical Science, Raipur, Chhattisgarh-492001, India
[4]Independent Medical Researcher, Pune, Maharashtra-411019, India

Received: 04-12-2023 / Revised: 05-01-2024 / Accepted: 22-01-2024
Corresponding Author: Dr. Manali Madhukar Shinde
Conflict of interest: Nil

Abstract:
This case report presents an intriguing instance of Neurofibromatosis (NF) with an atypical combination of hypertrichosis and hyperpigmented cutaneous lesions, challenging conventional diagnostic paradigms. The patient, a 14-year-old male, exhibited multiple soft tissue lesions associated with café-au-lait spots and facial freckling. Histopathological analysis confirmed a benign peripheral nerve sheath tumor, favoring Neurofibroma. Notably, the coexistence of hypertrichosis and hyperpigmentation expands the phenotypic spectrum of NF. This case underscores the clinical heterogeneity of NF, emphasizing the importance of recognizing such unique presentations for accurate diagnosis. The diagnostic process, including imaging and immunohistochemical analysis, contributes to differential diagnosis and accurate management strategies. This report highlights the significance of reporting and understanding rare NF manifestations.

Keywords: Neurofibromatosis, Hypertrichosis, Hyperpigmented lesions, Café-au-lait spots, case report.

Introduction

Neurofibromatosis (NF) encompasses a spectrum of genetic disorders characterized by the development of benign tumors originating from neural crest cells. [1] Among its diverse clinical manifestations, hypertrichosis and hyperpigmented cutaneous lesions stand out as uncommonly associated features. [2] In this case report, we present an intriguing instance of NF where a patient exhibited an unusual combination of hypertrichosis and hyperpigmented cutaneous lesions, challenging the conventional diagnostic paradigms of this disorder. [3] This atypical presentation not only underscores the clinical heterogeneity of NF but also emphasizes the significance of recognizing and investigating such unique manifestations for improved disease comprehension and patient management. [4]

Patient and observation

Patient Information: A 14-year-old male presented to the outpatient department with multiple soft tissue lesions distributed across his body. These lesions had been noticed since birth and had gradually increased in size over the years. Additionally, the patient experienced overlying hairy growth surrounding the lesions. The patient reported becoming symptomatic two years prior, specifically noting an increase in size and hair growth of the left tibial lesion. Decreased appetite was also reported. There was no history of seizure, mental retardation, fever, skeletal deformities, or sensory deficits. [5,6]The patient denied any other health concerns. The patient was a single child born to non-consanguineous parents and exhibited normal developmental and growth milestones. There was no history of birth asphyxia or similar lesions within the family.[7]

Clinical Findings

Upon physical examination, the patient's weight was 41 kg, height 121.92 cm, and BMI 27.6 kg/m². Multiple hyperpigmented cutaneous lesions with overlying hypertrichosis were observed on both upper and lower limbs (Figure 1). These lesions were rubbery in consistency, except for a lesion on the left tibia, which was hard and painful, and had increased in size over the past two years alongside increased hypertrichosis (Figure 2). Caféau-lait spots were noted on the torso and back (Figure 3),

and the patient exhibited facial and axillary freckling (Figure 4). Ophthalmoscopic examination revealed no significant abnormalities.

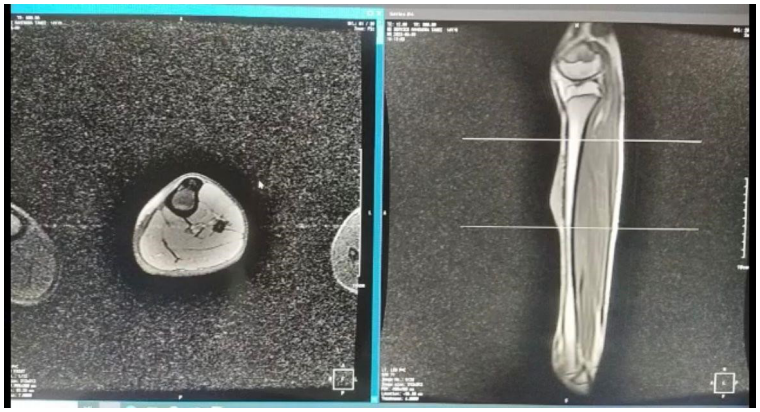

Figure 1. Magnetic Resonance Imaging Finding of the left leg.

Timeline of Current Episode

The patient initially presented with multiple soft tissue lesions since birth, which gradually increased in size and developed hypertrichosis. Symptomatic changes, including growth and increased hair on the left tibial lesion, were observed two years ago. The patient also reported a decrease in appetite.

Diagnostic Assessment

Comprehensive diagnostic testing was conducted to evaluate possible central nervous system or spinal cord involvement. MRI Brain revealed no evidence of intracranial hemorrhage, mass effect or midline shift (Figure 5). The electroencephalogram was within normal limits. MRI done for whole spine screening revealed a well-defined, encapsulated predominantly T2 hyperintense centrally necrotic/cystic right upper mediastinal soft tissue lesion measuring 9 x 6.5 x 1.5cm (Figure 6). Ultrasound of the presenting area revealed the following:

1. Left forearm - Predominantly echogenic area with internal serpiginous hypoechoic areas collectively measuring 2.9 x 0.9cm.
2. Left leg - Predominantly hypoechoic area measuring 8.5 x2.7 cm present subcutaneously and showing internal flow on color doppler study.

The MRI of Left leg (Plain + Contrast) revealed a multi-lobar, hypodermal, elongated 10 x 5.6 x 2.1cm, soft tissue with moderately enhancing signal intensity lesion involving the antero-medial aspect of proximal leg without osseous involvement or abnormal flow voids (Figure 1).

Upon gross examination of the histopathology sample of the Left leg lesion, following findings were observed:

1. Two skin covered soft tissue pieces.
2. Larger measuring 9.5 x 6 x 2cm. Outer surface shows two nodular lesions. No ulceration present.
3. Smaller measuring 2.5 x 1.7 x 1cm.

The microscopic examination of the histological specimen revealed that the sections show skin with a dermal based lesion composed of irregular shaped groups of bland dermal spindle cells with wavy nuclei and pale eosinophilic cytoplasm (Figure 7). Thick collagen separates the cluster of spindle cells. There was no nuclear atypia, activity is not appreciated. Foci of myxoid change seen. Overlying epidermis appears atrophic. Lesion seen extending upto the subcutis. No evidence of malignancy seen. The overall histopathological analysis of a lesion on the left leg favored the diagnosis of benign peripheral nerve sheath tumor, suggestive of Neurofibroma.

Diagnosis

The patient was diagnosed with Neurofibroma based on clinical presentation, physical examination, and histopathological findings.

Therapeutic Interventions

The patient was managed symptomatically till the surgery was undertaken. Following drugs were given:

1. Inj. Ceftriaxone 1 gram twice a day,
2. Inj. Linezolid 600 milligrams twice a day,
3. Inj. Pantoprazole 40 milligrams twice a day,
4. Inj. Tramadol 1 ampule as and when needed if pain was intolerable.
5. Inj. Ondansetron 4 milligrams as and when needed.

Later the patient was posted for excision of the left lesion by the department of plastic surgery. The mass was excised under spinal anesthesia and the sample was sent for biopsy.

Follow-up and Outcome of Interventions

Patient did not come for follow-up. He had financial restraints. He visited the hospital only because there was an intolerable pain associated with the lesions.

Patient Perspective

The patient was satisfied with the treatment he received. He was happy that the interventions relieved him of the pain and cosmetic disfigurement caused by the lesions. He had financial restraints, nevertheless he appreciated that the doctors conducted the necessary diagnostic procedures and came up with a definitive diagnosis for his condition. He considered it fortunate that sharing the details of his condition will benefit the interest of academicians and the researchers of the scientific community.

Informed Consent

The patient and his caregivers were counseled and explained in detail about the provisional diagnosis, planned investigations and procedure. Prior informed consent was taken from the patient and his caregivers. Patient also gave consent for his medical case to be summarized in writing for the purposes of medical teaching, presentation at a medical meeting, and/or publication in a medical journal.

Discussion

The presented case of a 14-year-old male with an unusual combination of hypertrichosis and hyperpigmented cutaneous lesions associated with Neurofibromatosis (NF) highlights the diverse and complex nature of this genetic disorder. Neurofibromatosis encompasses a range of clinical manifestations and the coexistence of hypertrichosis and hyperpigmentation in this case adds a novel dimension to the diagnostic considerations. [8,9] The following discussion delves into the relevant medical literature to contextualize this unique presentation and provide insights into its implications. The co-occurrence of hypertrichosis and hyperpigmentation in this patient prompts a closer examination of the neurocutaneous manifestations of NF. [10] Hypertrichosis, characterized by excessive hair growth, has been sporadically reported in association with NF, although the exact prevalence remains unclear due to its infrequent occurrence. Hypertrichosis in NF has been attributed to various factors, including the aberrant proliferation of hair follicles influenced by the underlying genetic mutations. In a similar context, a case report by Happle et al. described hypertrichosis and hyperpigmentation occurring in a mosaic distribution, reinforcing the concept of somatic mosaicism and its contribution to the observed phenotypic variation1. The current case underscores the importance of recognizing such distinct manifestations to enhance the clinical diagnosis of NF. [11]

Hyperpigmented cutaneous lesions, such as café-au-lait spots, are a hallmark of NF and are widely recognized as a diagnostic criterion. The presence of multiple café-au-lait spots in this patient aligns with the diagnostic criteria of NF, further corroborating the diagnosis. Interestingly, café-au-lait spots in NF have been linked to an underlying pathogenic variant in the NF1 gene. Studies by Kluwe et al. demonstrated a correlation between the size and number of café-au-lait spots and the presence of certain NF1 mutations, implicating genotype-phenotype associations2. [12] While our case does not delve into genetic testing results, this association could offer a potential avenue for further investigation into the underlying genetic basis of the patient's clinical presentation. The patient's neurological assessment, including MRI scans and EEG, exhibited no significant abnormalities, raising important considerations regarding the potential absence of central nervous system involvement in this presentation. [13,14] NF is classically associated with neural tumors such as neurofibromas and gliomas. The absence of such findings in this case challenges the conventional understanding of NF's clinical spectrum. In support of this, a study by Stumpf et al. reported atypical presentations of NF1, emphasizing the heterogeneity of manifestations3. [15,16] This underscores the necessity of vigilant clinical assessment and consideration of atypical manifestations to avoid overlooking potential cases of NF. Histopathological analysis of the lesion on the left leg revealed features suggestive of a benign peripheral nerve sheath tumor, favoring a diagnosis of Neurofibroma. The presence of Neurofibromas is a cardinal feature of NF, contributing to its classification as a neurocutaneous disorder. The immunohistochemical analysis, revealing positive immunoreactivity for S100 protein and CD34, further substantiates the diagnosis. These findings resonate with studies that have demonstrated S100 protein expression as a useful marker for neurofibromas, supporting their neural origin4. The reported morphological and immunohistochemical characteristics add to the growing body of evidence confirming the diagnostic utility of these markers. [17]

Furthermore, the differential diagnoses of Schwannoma and Hemangioma considered for the lesion on the left leg warrant discussion. Schwannomas are encapsulated nerve sheath tumors that also exhibit S100 protein immunoreactivity5. However, the presence of CD34 immunoreactivity, as observed in the presented case, helps differentiate

neurofibromas from Schwannomas6. In contrast, Hemangiomas arise from vascular endothelial cells and are typically characterized by CD34 negativity7. The comprehensive diagnostic assessment in this case, including imaging and histopathology, significantly contributes to the accurate diagnosis and differentiation of these entities. [18]

Conclusion

In conclusion, the intriguing case of a 14-year-old male with an unusual presentation of hypertrichosis and hyperpigmented cutaneous lesions associated with Neurofibromatosis highlights the complexity and clinical heterogeneity of this disorder. The clinical manifestations presented in this case expand the phenotypic spectrum of NF, shedding light on potential genotype-phenotype correlations and atypical presentations. This case underscores the significance of meticulous clinical assessment, histopathological analysis, and immunohistochemical evaluation in arriving at an accurate diagnosis. It also emphasizes the importance of recognizing and reporting unique presentations, which collectively contribute to advancing the understanding and management of NF and its varied clinical manifestations.

Competing interests

The authors declare no competing interest.

Authors' contributions

Aum Sanjay Bapat: Data collection and processing

Kamala Kant Bhoi: Analysis and therapeutic interventions

Priya Pathak: Histopathological findings

Manali Madhukar Shinde: Literature review and manuscript writing

Acknowledgements

Dr. Kamala Kant Bhoi bore the cost of immunohistochemical tests required for this patient.

References

1. Happle R, Mosaicism in Human Skin. Understanding Nevi, Nevoid Skin Disorders, and Cutaneous Neoplasia. Springer, 2014.
2. Kluwe L, Siebert R, Gesk S, et al. Screening 500 unselected neurofibromatosis 1 patients for deletions of the NF1 gene. Hum Mutat. 2004;23(2):111-116.
3. Stumpf D, Alksne J, Annegers J, Brown S, Conneally P, Housman D, et al. Neurofibromatosis. Conference statement. National Institutes of Health Consensus
4. Development Conference. Arch Neurol. 1988; 45(5):575-578.
5. Hasselblatt M, Jeibmann A, Riesmeier B, et al. Expression of the cell-cell adhesion molecule CD34 in pediatric embryonal tumors. Am J Surg Pathol. 2006;30(2):187-193.
6. Perry A, Brat DJ. Practical surgical neuropathology: A diagnostic approach. Churchill Livingstone, 2010.
7. Rodriguez FJ, Folpe AL, Giannini C, Perry A. Pathology of peripheral nerve sheath tumors: Diagnostic overview and update on selected diagnostic problems. Acta Neuropathol. 2012; 123(3):295-319.
8. Drolet BA, Esterly NB, Frieden IJ. Hemangiomas in children. N Engl J Med. 1999;341 (3):173-181.
9. Takahasi M. Studies on café au lait spots in neurofibromatosis and pigmented macules of nevus spilus. Tohoku J Exp Med. 1976 Mar; 118(3):255-73.
10. Benchikhi H, Zeller J, Wolkenstein P, Wechsler J, Vidaud D, Revuz J. Neurofibromes plexiformes nodulaires exclusifs. Une présentation exceptionnelle de neurofibromatose de type 1 [Exclusive nodular plexiform neurofibroma. An unusual case of neurofibromatosis type 1]. Ann Dermatol Venereol. 1995;122(9):601-3. French.
11. Mahé E, Zeller J, Wechsler J, Wolkenstein P, Revuz J. Grandes taches pigmentées pileuses au cours de la neurofibromatose de type 1: une forme atypique de neurofibromes [Large hairy pigmented spots in neurofibromatosis type 1: an atypical form of neurofibromas]. Ann Dermatol Venereol. 2001 May;128(5):619-21. French.
12. Bousema MT, Vuzevski VD, Oranje AP, Heule F, Stolz E, van Joost T. Non-von Recklinghausen's neurofibromatosis resembling a giant pigmented nevus. J Am Acad Dermatol. 1989 Feb;20(2 Pt 2):358-62.
13. Specht CS, Smith TW. Uveal malignant melanoma and von Recklinghausen's neurofibromatosis. Cancer. 1988 Aug 15;62(4):812-7.
14. Lantiéri L, Wolkenstein P. Les manifestations cutanées de la neurofibromatose de type 1 et leur traitement [Cutaneous manifestations of type 1 neurofibromatosis and their treatment]. Ann Chir Plast Esthet. 1998 Aug;43(4):445-54. French.
15. Sarica FB, Cekinmez M, Tufan K, Erdoğan B, Sen O, Altinörs MN: A rare case of massive NF1 with invasion of entire spinal axis by neurofibromas: case report. Turk Neurosurg 2008; 18:99-106.
16. Sandoval-Tress C, Nava-Jiménez G: Poliosis circumscripta associated with neurofibromatosis 1. Australas J Dermatol 2008;49:167-168.
17. Koplon BS, Shapiro L: Poliosis overlying a neurofibroma. Arch Dermatol 1968;98:631-63 3.

18. Calonje E, Lazar AJ, Luzar B. Tumors of neuroectodermal origin. In: Diagnostic Atlas of Cutaneous Mesenchymal Neoplasia. 1st ed. Elsevier; 2020. P. 437-538.