

# Multiple Neurofibromas with Hypertrichosis in a Filipino Patient with Neurofibromatosis 1

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## ABSTRACT

This is a case of an 11-year-old male who presented with multiple neurofibromas with hypertrichosis. Classic cutaneous neurofibromas, café-au-lait macules, axillary freckling, Lisch nodules, and scoliosis were also present fulfilling a diagnosis of Neurofibromatosis type 1. This is the first report of multiple neurofibromas with hypertrichosis in the Philippines. Hypertrichosis overlying a neurofibroma is rarely reported and the mechanism remains to be elucidated.

*Key Words: neurofibromatosis 1, hypertrichosis, neurofibromas*

## INTRODUCTION

Neurofibromatosis type 1 (NF 1) is a genodermatosis caused by mutations in the NF 1 gene that encodes the tumor suppressor protein neurofibromin.<sup>1</sup> This autosomal dominant disorder affects approximately 1 in 4,000 individuals.<sup>2</sup> This disease can be diagnosed clinically with cutaneous neurofibromas as a hallmark finding. These usually present as skin-colored papules or nodules. This report presents a patient who presented with typical cutaneous neurofibromas but also presented with multiple patches with hypertrichosis that were histopathologically consistent with neurofibromas.

## CASE

An 11-year-old male consulted for multiple brown patches on the trunk with overlying hair. At birth, the patient had a dark brown to black patch at the lumbosacral portion of his back. It remained stable in size and asymptomatic but developed thin hair after four years. At that time, the mother also noted the appearance of multiple skin-colored papules on his upper back and multiple brown patches with thin hair all over the trunk. These increased in number but remained asymptomatic. They consulted several dermatologists and was managed as pityriasis versicolor and hypersensitivity reaction with unrecalled creams but all lesions persisted. Biopsy of the lesions was never done.

The patient was born full-term to a 26-year-old G1P1 mother without any fetomaternal complications. Immunization was complete and no other medical conditions were present. There was no history of seizures. The patient's development was at par with age but performed below average at school due to difficulty in reading. There were no family members with similar lesions.

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On examination, there were multiple skin-colored papules on the trunk extending to the thighs (Figures 1 and 2). There were multiple well-defined brown macules and patches located on the arms, abdomen, and back (Figures 3 and 4). There was axillary freckling (Figure 5). There was a black patch with hypertrichosis located midline at the lumbosacral region (Figure 6). Dermoscopy showed a brown reticular pattern with perifollicular hypopigmentation and terminal hair (Figure 7). There were multiple brown, slightly erythematous macules with overlying hypertrichosis on the trunk (Figure 8). Dermoscopy also revealed a reticulated brown pattern, perifollicular hypopigmentation but with some areas of erythema, and terminal hair growth (Figure 9).

Biopsy of three lesions was done. The first lesion was a skin-colored papule on the back which showed a well-circumscribed, unencapsulated proliferation of spindle-shaped cells with wavy nuclei arranged in an orderly fashion in a pale mucinous stroma surrounding adnexal structures, consistent with a neurofibroma (Figure 10). The black patch with overlying hair at the lumbosacral region (Figure 11) and the brown macules also with overlying hair on the abdomen (Figure 12) also revealed the same proliferation of spindle-shaped cells with wavy nuclei in a pale mucinous stroma with the former showing basal hyperpigmentation. Despite varying clinical presentations, all these lesions were histopathologically consistent with neurofibromas.



**Figure 1.** There were skin-colored papules on the trunk extending to the thighs.



**Figure 2.** Closer view reveals multiple skin-colored papules, brown plaques and brown patches (café-au-lait macules).



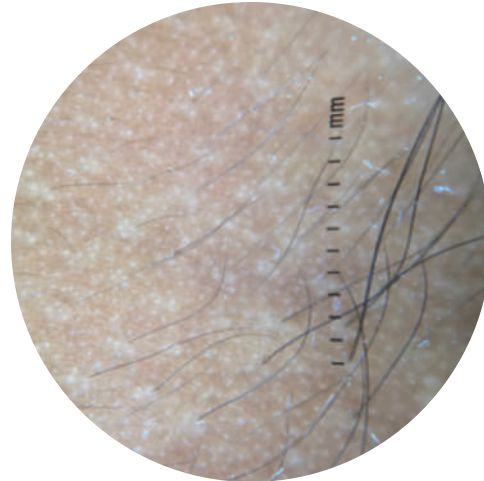
**Figure 3 and 4.** There were multiple brown macules and patches located on the arms, abdomen and back.



**Figure 5.** There was note of axillary freckling.



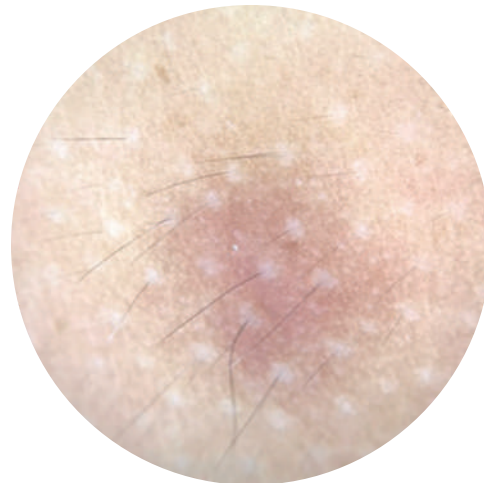
**Figure 6.** The black patch with hypertrichosis at the lumbosacral region.



**Figure 7.** Dermoscopy of the lesion showed a brown reticular pattern with perifollicular hypopigmentation and growth of terminal hair.



**Figure 8.** There were brown, slightly erythematous macules with hypertrichosis.



**Figure 9.** Dermoscopy of the lesion also revealed a brown reticular pattern with perifollicular hypopigmentation but with some areas of erythema and terminal hair.

The patient was referred to the Pediatric service and they agreed with the diagnosis of NF 1. He was assessed to have an intellectual disability based on the following: the patient was unable to recite the alphabet, do simple calculations, read simple words, and write dictated words. He was also assessed to have poor abstract thinking, and judgment. Ophthalmology noted multiple Lisch nodules on both eyes but did not identify any optic gliomas. No further imaging studies were recommended and no intervention was necessary for the current status. Radiographic examination showed thoracic dextroscoliosis and lumbar leftward asymmetry but no lytic changes or changes suggestive of underlying masses were noted.

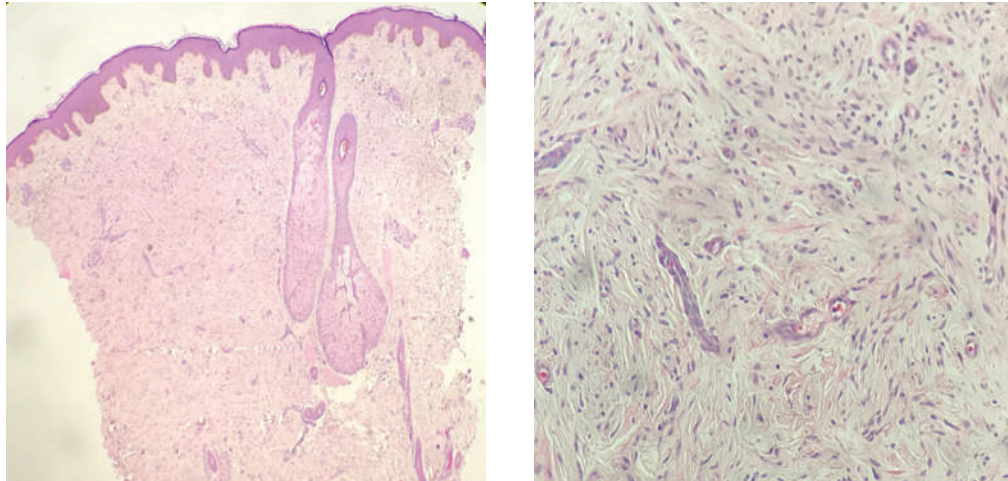
The diagnostic criteria by the National Institutes of Health Consensus Development Conference 1988<sup>2</sup> require the fulfillment of two or more diagnostic criteria to

establish the diagnosis of NF 1. Since the patient had more than six café-au-lait macules five millimeters and greater in size, greater than two neurofibromas, axillary freckling, and Lisch nodules, a definitive diagnosis was made. Moreover, scoliosis, impaired vision, and learning disability are findings attributable to NF 1.

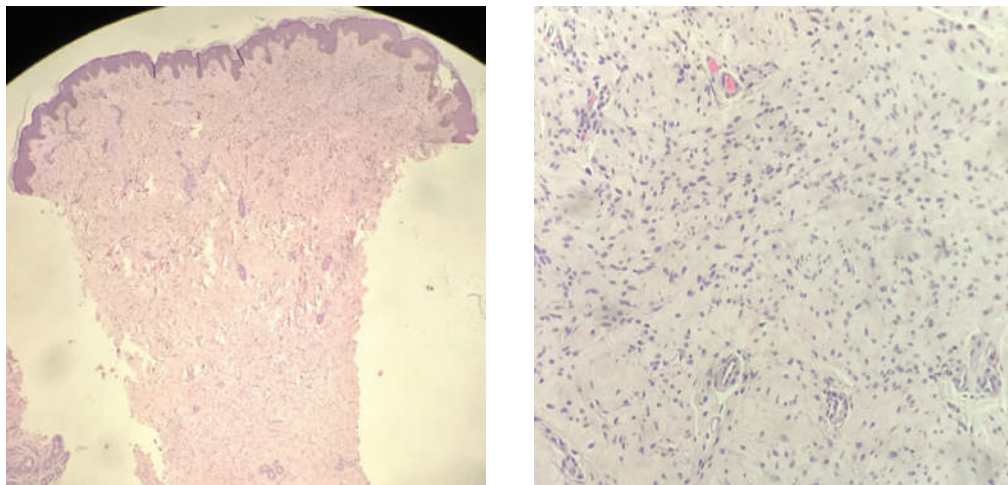
The patient and his guardian were educated about the nature and prognosis of the condition and the importance of regular follow-up to detect the development of complications and to address them accordingly.

## DISCUSSION

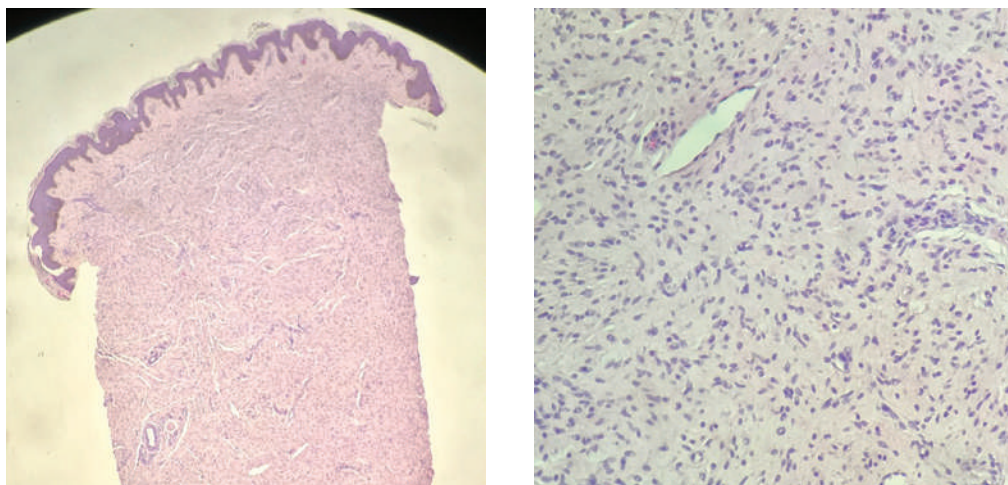
Neurofibromas with hypertrichosis are not commonly seen. Reports of such cases showed lesions that occurred singly and localized to the head and neck region and



**Figure 10.** H&E staining of the punch biopsy on a skin-colored nodule (scanning view and 20x magnification) that showed a well-circumscribed, unencapsulated proliferation of spindle-shaped cells with wavy nuclei in a pale mucinous stroma.



**Figure 11.** H&E staining of the punch biopsy the black patch at the lumbar region (scanning view and 20x magnification) that also showed a well-circumscribed, unencapsulated proliferation of spindle-shaped cells with wavy nuclei in a pale mucinous stroma.



**Figure 12.** H&E staining of the punch biopsy the brown macule with hair (scanning view and 20x magnification) still showed a well-circumscribed proliferation of spindle-shaped cells with wavy nuclei in a pale mucinous stroma.

**Table 1.** The National Institutes of Health Consensus Development Conference 1988 diagnostic criteria for Neurofibromatosis 1  
**Six or more café-au-lait macules over 5mm in greatest diameter in pre-pubertal individuals and over 15mm in greatest diameter in post-pubertal individuals.**  
**Two or more neurofibromas of any type, or one plexiform neurofibroma**  
**Freckling in the axillary or inguinal regions**  
 Optic glioma  
**Two or more Lisch nodules (iris hamartomas)**  
 A distinctive osseous lesions such as sphenoid dysplasia or thinning of long bone cortex, with or without pseudoarthrosis  
 A first degree relative with NF 1 by the above criteria

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*Two or more of the criteria have to be present in order to fulfill a diagnosis of Neurofibromatosis 1.*  
*Criteria in boldface were present in the patient reported.*

**Table 2.** Summary of studies on hypertrichosis and neurofibromas

Author (Year)	Age/Sex	Presentation	Other clinical findings of NF 1
Ettl and Koorneef (1995)	14/F	Hyperpigmented macule with hypertrichosis overlying a swelling from the right upper lid towards the forehead with proptosis	Axillary freckling Café au lait macules Lisch nodules Learning difficulties
	12/F	Hypertrichosis on the left half of face with worsening lid swelling	None
Wagamon and Mirmirani (2007)	7/M	Area of excessive hair growth on the forehead that blended with the anterior hairline with underlying subcutaneous fullness	Axillary freckling Café-au-lait macules Cutaneous neurofibromas NF 1-mother and grandfather
Na et al (2009)	17/F	Light brown plaque with terminal hairs on the post-auricular area	None
Cho (2012)	10/F	Brown plaque with terminal hairs on the posterior neck	None

occurred among the pediatric age group (Table 2).<sup>3-6</sup> In reported studies, the area with hypertrichosis signified an underlying plexiform neurofibroma. Some cases presented in association with NF 1 while others were sporadic. The current study is the first report of multiple neurofibromas with hypertrichosis in the Philippines.

The mechanism for hypertrichosis in association with neurofibromas remains to be elucidated. A study exploring the pathogenesis of cutaneous neurofibromas showed that these lesions contain multipotent precursor cells which may be derived from the multipotent cells of the hair roots, that are intimately associated with microscopic neurofibroma.<sup>1</sup> Given their spatial proximity, signals that stimulate the development of cutaneous neurofibromas may also stimulate follicular induction.

## CONCLUSION AND RECOMMENDATIONS

The multiple plaques with hypertrichosis are atypical presentations of neurofibromas. Punch biopsy confirmed the etiology of the lesions that were previously managed as common dermatoses. The diagnosis of NF 1 also provided a parsimonious explanation for the constellation of findings of café-au-lait macules, neurofibromas, axillary freckling, impaired vision, learning disabilities, and scoliosis.

Therefore, in a patient presenting with localized hypertrichosis, an underlying neurofibroma may be considered. Moreover, investigation of other clinical findings associated with neurofibromatosis must be carried out.

## Statement of Authorship

All authors approved the final version submitted.

## Author Disclosure

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