

Clinical and Trichoscopy Features in Trichorhinophalangeal Syndrome: A Multicenter Retrospective Study

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ABSTRACT Introduction: Trichorhinophalangeal syndrome (TRPS) is a rare autosomal dominant genetic disorder characterized by trichological, craniofacial, and skeletal abnormalities. To date, limited data are available on hair involvement in TRPS, especially those focusing on trichoscopy.

Objective: We aimed to describe the epidemiology and the clinical and trichoscopy features of TRPS.

Methods: We performed a retrospective multicenter study using chart review and images from six patients with a confirmed diagnosis of TRPS. Hair density (hair/field; field 13×1.4 mm) was classified as high (>30), medium (21-30), low (11-20), very low (5-10), or hairless (<4). The distance between follicular units, ranging from 1.0 mm to 1.4 mm, was considered normal.

Results: Most patients were females, with a median age of 12 at diagnosis. Hair density ranged from very low to medium. All female patients presented a high occipital hairline. Our patients had exclusively non-terminal hairs and no case with high hair density, following the literature, which describes thin and sparse hairs. Hair density was related to a higher proportion of single hair units, while the distance between follicles was within normal limits.

Conclusion: TRPS is notably uncommon, with hair alterations being important for diagnosis, where trichoscopy serves as a valuable tool. Our study found a normal hair diameter relationship (frontal \geq occipital) in females, while the male patient exhibited frontal-occipital inversion. Low hair density may result from an increased number of single hair units rather than from follicular distance. The high occipital hairline is proposed as a diagnostic pearl, warranting further studies to validate our findings.

Introduction

Trichorhinophalangeal syndrome (TRPS) is a rare autosomal dominant genetic disorder characterized by trichological, craniofacial, endocrinological, and skeletal abnormalities [1,2]. It is classified into three types (I-III), each exhibiting varying degrees of clinical features, including a prominent nose, craniofacial dysmorphism, and limb abnormalities such as brachydactyly. Genetic studies have identified mutations in the TRPS1 gene as a key contributor to the condition [1,2]. The management of TRPS requires a multidisciplinary approach, focusing on symptomatic treatment and genetic counseling for affected individuals and their families [1,2,3]. Its trichological findings include thin, sparse, or brittle hair, severe hypotrichosis, or diffuse non-scarring alopecia [1,3].

To date, limited data are available on hair involvement in TRPS, especially those focusing on trichoscopy.

Objective

This multicenter retrospective study aimed to describe the epidemiology, clinical features, and trichoscopy of TRPS.

Methods

We performed a retrospective review of chart data and images from four different specialized trichology centers. Six patients with a confirmed diagnosis of TRPS were enrolled. Figure 1 provides clinical and trichoscopy pictures of TRPS patients, demonstrating our main findings. Trichoscopy had

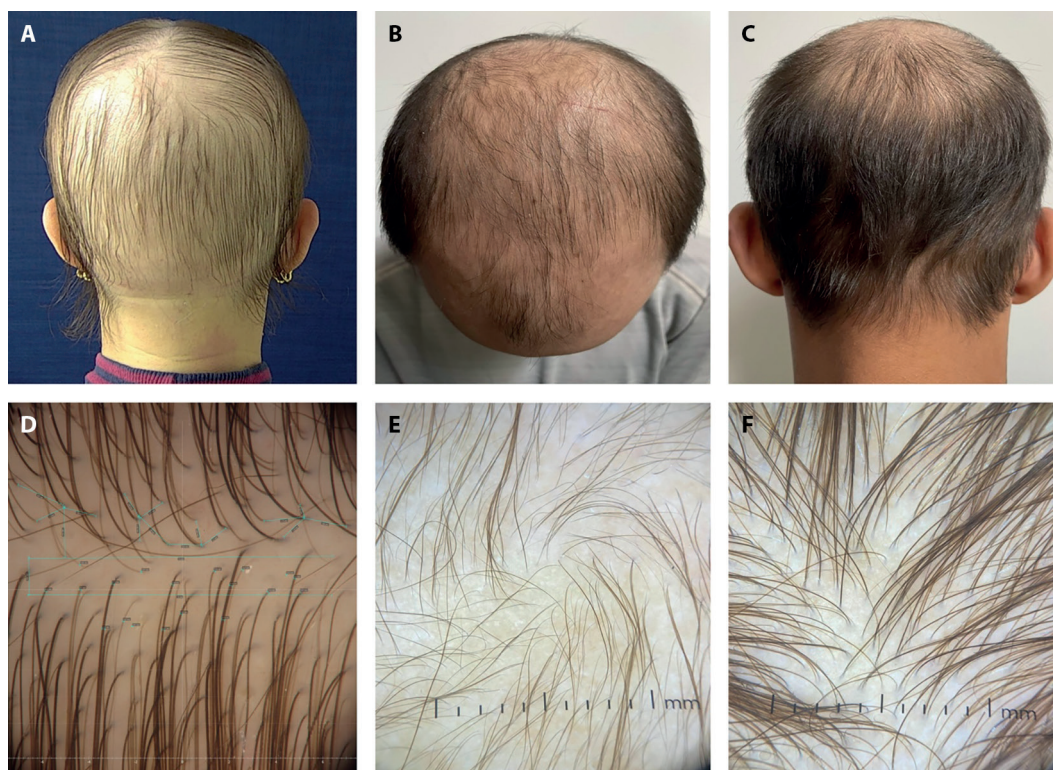


Figure 1. (A) Clinical presentation of trichorhinophalangeal syndrome (TRPS) in a female patient showing low hair density, thin hairs, and high occipital hairline. (B) An example of a male patient with TRPS presenting with reduced frontal and vertex hair density. (C) Occipital view of the same male patient with normal hair density. (D) Trichoscopic image from the occipital scalp showing exclusively non-terminal hairs ($<90\ \mu\text{m}$) and normal distance between follicles (range 1.19–1.50 mm; $\times 20$). (E) Manual trichoscopy from the frontal scalp of a male patient showing reduced hair shaft diameter and frontal-occipital inversion. (F) Manual trichoscopy of the occipital scalp of a male patient with normal hair diameter and frontal-occipital inversion.

been obtained with manual trichoscopy and Fotofinder and then grouped into scalp areas for analysis. Hair density (hair/field; field 13X1.4mm) was classified according to de Lacharrière et al., based on Fotofinder images, as high (>30), medium (21-30), low (11-20), very low (5-10), and hairless (<4) [4]. The distance between follicular units, ranging from 1.0 mm to 1.4 mm, was considered normal. [5]

Results

Most patients were females (n=5), with a median age of 12 at diagnosis (9–14 years old). All clinical and demographic data can be found in Table 1. All female patients presented a higher occipital hairline (Figure 1A). Under trichoscopy, hair density ranged from very low to medium. Single hair units

Table 1. Clinical and Trichoscopy Findings in Six Patients With Trichorhinophalangeal Syndrome.

Patients/Disease Characteristics	Categories or Statistics		Obtained Values	
			Female	Male
Phototype		I	0	
		II	1	
		III	3	
		IV	2	
		V/ VI	0	
Hair type		African or Asian	0	0
		Caucasian	5	1
Body mass index categories		Normal	3	1
		Overweight	1	0
		Obese	1	0
Other comorbidities		No	5	1
		Yes	0	0
Age at disease diagnosis		Median (interquartile range)	12 (2)	12 (0)
		Minimum; Maximum	9; 14	12; 12
Type of trichorhinophalangeal syndrome		1	4	0
		2	0	0
		3	0	0
		Unknown type	1	1
Family history of androgenetic alopecia		No	0	0
		Yes, paternal	4	1
		Unknown family history	1	0
Slow growth speed		No	0	0
		Yes	5	1
Yellow dots (frontal scalp)		≤ 4 per field (20x magnification)	4	1
		> 4 per field	1	0
Hair density (hair/field; field 13×1.4 mm)	<i>Frontal</i>	Hairless (<4)	0	0
		Very low (5-10)	1	0
		Low (11-20)	2	1
		Medium (21-30)	2	0
		High/Very high (>30)	0	0
	<i>Occipital</i>	Hairless (<4)	0	0
		Very low (5-10)	1	0
		Low (11-20)	2	0
		Medium (21-30)	1	1
		High/very high (>30)	0	0
		Unknown hair density	1	0

Table1 continues

Table 1. Clinical and Trichoscopy Findings in Six Patients With Trichorhinophalangeal Syndrome. (continued)

Patients/Disease Characteristics	Categories or Statistics		Obtained Values	
			Female	Male
Frontal-occipital inversion		No	4	0
		Yes	0	1
		Unknown	1	0
Single hair unit (>20%)	<i>Frontal</i>	No	1	0
		Yes	4	1
	<i>Occipital</i>	No	1	1
		Yes	3	0
		Unknown single hair unit	1	0
Hair shaft diameter in categories	<i>Frontal</i>	Thin (30-40 µm)	1	1
		Medium/Intermediate (50-80 µm)	4	0
		Terminal (90 -110 µm)	0	0
	<i>Occipital</i>	Thin (30-40 µm)	3	0
		Medium/Intermediate (50-80 µm)	1	1
		Terminal (90 -110 µm)	0	0
		Unknown hair shaft diameter	1	0
Distance between shafts (mm)	<i>Frontal</i>	Median (Interquartile Range)	1.27 (0.11)	1.19 (0.0)
		Minimum; Maximum	1.15; 1.40	1.19; 1.19
	<i>Occipital</i>	Median (Interquartile Range)	1.26 (0.14)	1.50 (0.0)
		Minimum; Maximum	1.19; 1.40	1.50; 1.50

Note: All three continuous variables were tested, and variables were considered to be normally distributed based on Shapiro-Wilk normality test ($P>0.05$).

predominated, especially in the frontal scalp (five out of six patients). The mean distance between shafts was 1.25 mm (range 1.19–1.40) in the frontal scalp and 1.32 mm (range 1.19–1.50) in the occipital scalp. Hair shaft diameter analysis showed exclusively non-terminal hairs (<90 µm), regardless of the scalp area (Figure 1D). The mean shaft diameter of the frontal scalp was greater than of the occipital in all but one male patient, who exhibited frontal-occipital inversion (Figures B, C, E, and F).

Discussion

The clinical findings associated with TRPS exhibit considerable variability; however, the three recognized types (I-III) share certain manifestations. Notable skeletal abnormalities include short stature, brachydactyly, and shortened phalanges or feet. Physical examination plays a crucial role in the diagnostic process, particularly as many of the abnormalities presented are dermatological in nature. Additionally, affected individuals may exhibit facial dysmorphism, typically characterized by midline features. While hair and nail abnormalities are nonspecific, they have been documented in the literature [2].

An interesting finding that might be a clue to the clinical diagnosis of the syndrome in female TRPS patients is a higher occipital hairline, also observed by Seitz et al [1]. On trichoscopy, our patients had exclusively non-terminal hairs and no case with high hair density, following the literature, which describes thin and sparse hairs [2]. Lower thickness of hairs may be explained by the smaller duration of the anagen phase of the hair cycle, which is the syndrome's hallmark [3]. The differential diagnosis should encompass other genetic disorders characterized by abnormalities of the hair, nose, and limbs. In terms of dermatological findings, conditions such as monilethrix, ectodermal dysplasia, early-onset androgenetic alopecia, and hypotrichosis must be considered [6,7].

Based on our findings regarding hair density, we hypothesize that the lower hair density observed in TRPS patients is due to a higher proportion of single hair units rather than to a sparse distribution, since the distance between follicles remains within normal limits [5]. There was no increase in yellow dots in most cases. Future studies with scalp biopsy may confirm whether the low hair density derives from a decline in follicular density.

Limitations

Limitations of this study include the small sample size, lack of standardization of videodermoscopy images, and the absence of an age-matched control group.

Conclusion

Trichorhinophalangeal syndrome is notably uncommon, and hair alterations play an important role in its diagnosis, with trichoscopy identified as a helpful diagnostic tool. Our study revealed a normal hair diameter relationship (frontal \geq occipital) in all female patients, while the male patient exhibited frontal-occipital inversion. We further emphasize that the observed low hair density in TRPS patients may be attributed to an increased number of single hair units rather than to the distance between follicular units. Notably, the high occipital hair-line emerged as a diagnostic pearl that could assist clinicians in identifying this condition more effectively. This case series detailed the trichoscopic features of TRPS, including hair density, thickness, and the distance between shafts, while highlighting the need for further studies to confirm our findings.

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