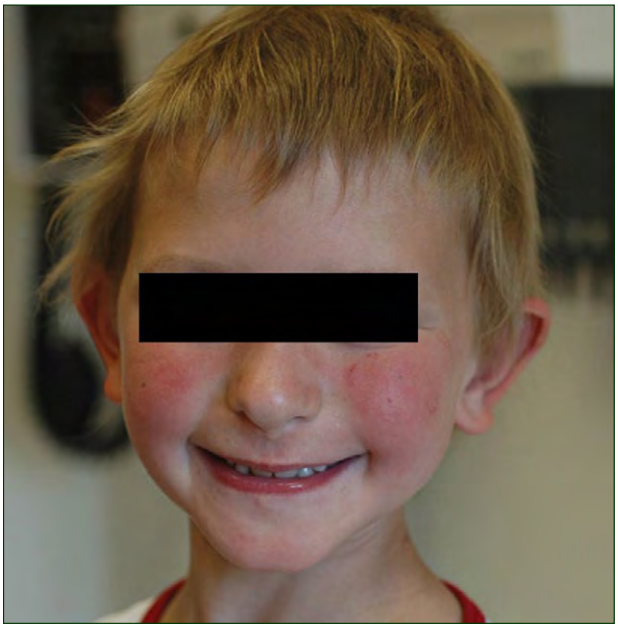
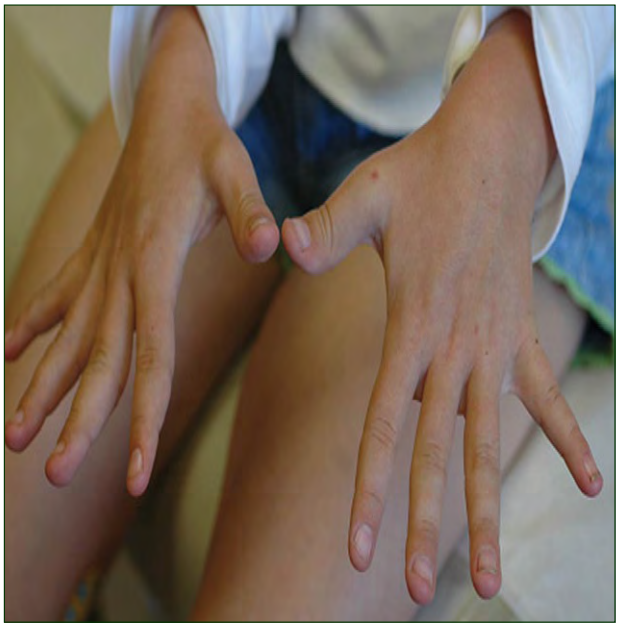
What Is Your Diagnosis?





A 7-year-old girl was referred for evaluation of slow-growing scalp hair (left). She had never required a haircut and denied abnormal hair breakage or hair falling out from the root. Her medical history was unremarkable, except for delayed onset of speech as a toddler. There was no family history of similar features or consanguinity. Review of systems was notable for brittle nails (right), hyperextensible joints, and a hoarse voice; there were no dental, cognitive, or sweating abnormalities.

PLEASE TURN TO PAGE 73 FOR DISCUSSION

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The authors report no conflict of interest.
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The Diagnosis: Trichorhinophalangeal Syndrome Type I

Physical examination revealed a girl of normal stature (37th percentile) with short blond hair and a hoarse voice. Facial features included a bulbous, pear-shaped nose; elongated philtrum; thin upper lip; prominent ears; and lateral eyebrow thinning (Figure 1). Hand examination showed thin nails and brachydactyly (Figure 2). Mild joint hyperextensibility also was noted. A hair pull test and hair mount revealed no abnormalities.

Radiographs of the hand demonstrated cone-shaped epiphyses of the middle phalanges of the second through fifth digits and the proximal phalanges of the first and fifth digits (Figure 3), consistent with trichorhinophalangeal syndrome (TRPS). There were no exostoses. Sequencing of the TRPS 1 gene, *TRPS1*, revealed a 5 base pair (bp) deletion in exon 5 (2291_2295delTGGTG) resulting in a novel frameshift mutation from codon 764 and premature stop codon 785.

Trichorhinophalangeal syndrome is a rare autosomal-dominant genetic disorder with high penetrance but variable expressivity and is characterized by hair, skeletal, and craniofacial abnormalities.[1-7] Patients have slow-growing, sparse scalp hair; increased telogen hairs; a high frontal hairline; medial eyebrow thickening; and lateral eyebrow thinning.[1,2,7] Hair mount may demonstrate reduced diameter and hairs with tapered tips but no hair-shaft defects.[2] Axillary

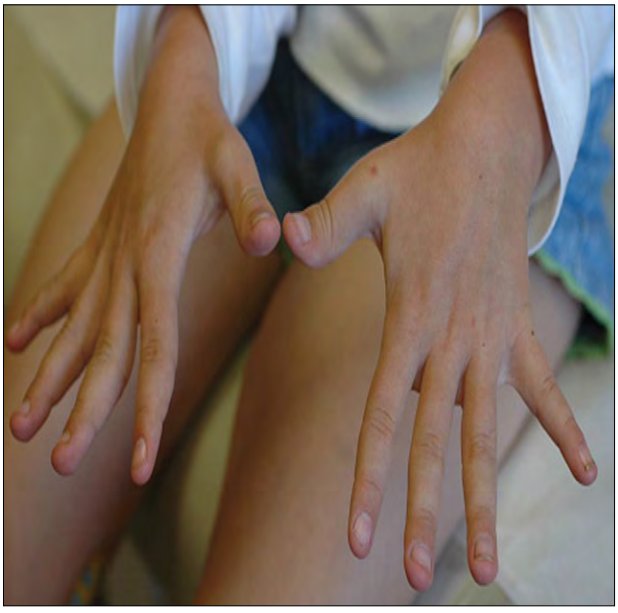

Figure 2. Thin nails and brachydactyly.

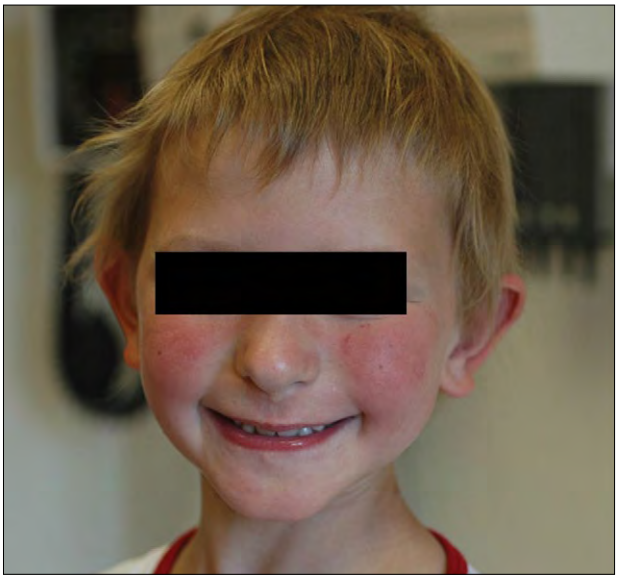

Figure 1. A 7-year-old girl with a pear-shaped nose, elongated philtrum, thin upper lip, prominent ears, and lateral eyebrow thinning.

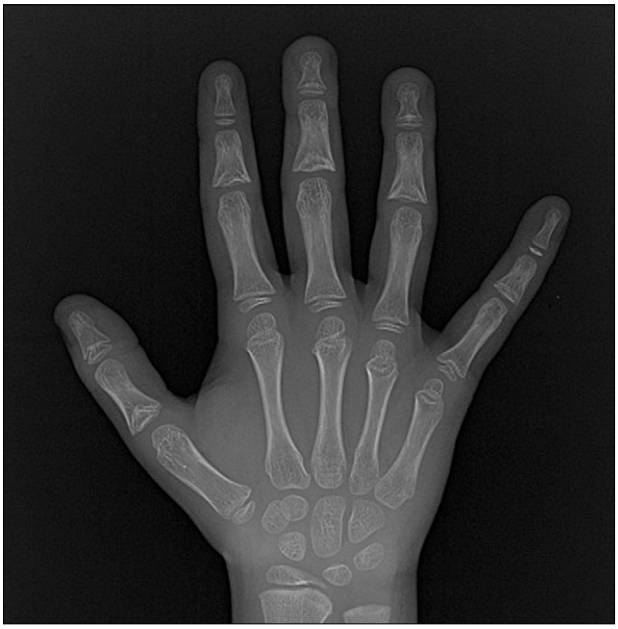

Figure 3. Radiography showed cone-shaped epiphyses of the middle phalanges of the second through fifth digits and the proximal phalanges of the first and fifth digits.

and pubic hair also may be sparse. Craniofacial anomalies include a pear-shaped nose, elongated philtrum, thin upper lip, protruding ears, tall forehead, triangular face, horizontal chin groove, micrognathia, high-arched palate, and supernumerary teeth.[1-3,7] Skeletal abnormalities include short stature, brachydactyly, cone-shaped epiphyses, swelling of proximal interphalangeal joints of the hand, clinodactyly, delayed skeletal maturity, hip malformations, scoliosis, lordosis, winged scapulae, and pectus carinatum.[3] Nails may be slow growing, brittle, and dystrophic, with variable leukonychia, koilonychia, or racket shape.[4] Endocrine abnormalities (ie, hypothyroidism, growth hormone deficiency, diabetes mellitus) rarely may occur.[3]

There are 3 subtypes of TRPS. Trichorhinophalangeal syndrome type I (TRPS1) (Giedion-Gurish) was first described and is most common.[5,6] Trichorhinophalangeal syndrome type II (TRPS2) (Langer-Giedion syndrome) has features of TRPS1 plus cartilaginous exostoses, mental deficiencies, loose skin in infancy, and microcephaly. Trichorhinophalangeal syndrome type III (TRPS3) (Sugio-Kajii syndrome) resembles TRPS1 but has more severe short stature, brachydactyly, and cone-shaped epiphyses. Although *TRPS1* gene defects cause all 3 subtypes, TRPS2 is a contiguous gene syndrome involving deletions encompassing *TRPS1* and the adjacent exostosin 1 gene, *EXT1;* TRPS3 solely results from mutations in exon 6 of *TRPS1*.[5,6] *TRPS1* encodes a putative zinc finger transcription factor.

Diagnosing TRPS is important for counseling about prognosis and inheritance as well as initiating orthopedic intervention if necessary. Treatment is limited for most manifestations. Surgical correction of the nasal anomalies can be undertaken after puberty.[8] Our patient's short hair was upsetting because people frequently mistook her for a boy. Minoxidil solution 5% was tried for several months, and although her hair initially seemed thicker, the length did not change and treatment was discontinued. Otolaryngologic evaluation of the patient's hoarse voice revealed small vocal cord nodules, but her hoarseness did not improve with speech therapy. A coarse deep voice may be characteristic of TRPS, though it has been uncommonly documented.[9]

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