Clinical Characteristics of Tricho-Rhino-Phalangeal Syndrome Type I in Taiwanese

Chung-Chu Ning, Mark Ming-Long Hsu, J. Yu-Yun Lee, and Sheau-Chiou Chao

Abstract: Tricho-rhino-phalangeal syndrome type I (TRPS-I) is a malformation syndrome characterized by distinctive craniofacial and skeletal abnormalities. Only one case of TRPS-I has been previously reported in Taiwan. This retrospective study analyzed the clinical, roentgenographic, and histopathologic findings in seven patients with a diagnosis of TRPS-I who were treated at a hospital in Tainan during a 6-year period from 1994 to 1999. Physical examination revealed fine, sparse, and short scalp hair, a pear-shaped nose, long philtrum, thinning of the lateral portion of the eyebrows, and brachydactyly of the thumbs and big toes. The stature and intelligence of these patients were normal. Histopathologic examination of the scalp in two patients showed hypotrichosis without inflammation or scarring. Roentgenographic evaluation of both hands and feet showed cone-shaped proximal epiphyses of the middle phalanges in all patients. The findings of this report suggest that TRPS-I is not rare among Taiwanese, although the island-wide incidence is not known. The diagnosis of this syndrome in our department was greatly facilitated by our prior experience with treatment of the first patient in this series because TRPS-I is readily recognizable by its characteristic clinical and roentgenographic features. The identification of these features is important to the facilitation of genetic and cosmetic counseling. In addition to the typical craniofacial manifestations, all patients in this study showed brachydactyly of the big toes. This additional feature appears to offer an easy way to recognize the syndrome clinically.

Methods

The medical records of all patients with a diagnosis of TRPS treated at National Cheng-Kung University Hospital during the period from 1994 to 1999 were reviewed. The diagnosis of TRPS was made on the basis of clinical and roentgenographic findings.

Tricho-rhino-phalangeal syndrome type I (TRPS-I) is a malformation syndrome characterized by distinctive craniofacial and skeletal abnormalities. It is inherited as an autosomal dominant trait, although autosomal recessive and sporadic cases have also been reported. A triad of characteristic abnormalities, first described by Klingmüller [1], were later named tricho-rhino-phalangeal syndrome by Giedion [2]. TRPS-I patients have sparse and slow-growing scalp hair, a bulbous tip to the nose, a long flat philtrum, a thin upper vermilion border, and protruding ears. Skeletal abnormalities include cone-shaped epiphyses at the phalanges, hip malformations, and short stature. In this report, we describe the clinical, roentgenographic, and histopathologic features of seven patients with TRPS-I diagnosed during a 6-year period at our hospital.
Results

TRPS was diagnosed in seven patients, all of whom had type I TRPS (Table). Two patients were a mother and her daughter, one patient had familial TRPS (autosomal dominant), and the other four were isolated cases. Patient 3 was the subject of the only previous report on TRPS in Taiwan [3]. Physical examination revealed fine, sparse, and short scalp hair (Fig. 1A and B), a pear-shaped nose (Fig. 1D and E), a long philtrum, thinning of lateral eyebrows, and brachydactyly of the thumbs and/or big toes in all patients (Fig. 2A and B). There was no exostose or microcephaly. Stature and psychomotor development were normal for age in all patients. Histopathologic examination of the scalp in two patients showed hypotrichosis without inflammation or scarring (Fig. 3). The sweat and sebaceous glands were normal in all patients. Roentgenographic examination of both hands and feet showed cone-shaped proximal epiphyses of all middle phalanges in all patients (Fig. 2C and D). No patients in this series complained of hip pain or showed Perthes-like change on hip roentgenogram.

Discussion

TRPS can be categorized as type I, II, or III. TRPS-I is characterized by sparse hair, bulbous nose, mild skeletal dysplasia with cone-shaped epiphyses, short stature, and shortening of the metacarpals and metatarsals. TRPS-II includes the characteristics of TRPS-I, with exostoses, mental retardation, and skin abnormalities [4]. Sugio and Kajii first described TRPS-III in 1984 [5]. It differs from TRPS-II in that patients have normal intelligence and an absence of exostoses and from TRPS-I by the severe shortness of all phalanges and metacarpals.

There is great variability in the clinical signs of TRPS-I even among family members. It is possible that some milder cases might be missed. The nose may be slightly enlarged or fleshy and almost trunk-like, although it may occasionally be normal in appearance (Fig. 1D–F). The fingers may be obviously deformed with broadening of the joints in some patients, while the abnormalities may only be detectable by roentgenographic study in others [4]. The hypotrichosis varies from complete baldness, through alopecia similar to male-pattern baldness, to a slight thinning and slow growth [6]. In this report, Patient 4 was almost bald, while Patient 2 had only slight thinning. Biopsy specimens of the scalp from Patients 3 and 4 showed a decrease in the number of pilosebaceous follicles without obvious hair structural abnormalities. Similar findings have been reported previously [7]. Cone-shaped epiphysis is an important feature of TRPS but is also found in 12 to 25% of normal individuals [8]. Roentgenographically, this condition is characterized by a deformity of the end of a phalanx whose central conical projection of the epiphysis causes a depression of the adjacent metaphysis. Cone-shaped epiphysis in TRPS is a universal finding and may be the only abnormality discovered in family members [9]. McCloud and Solomon have suggested that roentgenographic studies of hands and feet be performed in all individuals with sparse, slow-growing scalp hair and also in their family members to determine the true incidence of TRPS [9]. In this series, roentgenographic study of hands and/or feet showed cone-shaped epiphysis in all patients. Perthes-like changes of the hips may cause significant disability [10]. Le Saout et al reported that hip dysplasia was present in about 50% of cases of TRPS [11], while Noltrop et al reported this finding in 76% of cases [12]. None of the patients in this series had Perthes-like changes, suggesting that this feature may have a racial specificity.

TRPS is more than a simple cosmetic abnormality in affected families. It has been reported to be associated with endocrine alteration, including hypothyroidism [13], diabetes...
Tricho-rhino-phalangeal Syndrome Type I

Fig. 1. Hair alterations in tricho-rhino-phalangeal syndrome type I (TRPS-I) ranged from A) almost bald in Patient 4, through B) thinning in Patient 1, to C) only a slight thinning of the scalp hair in Patient 2. The nose in TRPS-I may be D) almost trunk-like, as in Patient 4, E) slightly enlarged or fleshy, as in Patient 7, or occasionally F) normal in appearance, as in Patient 1.

Fig. 2. Brachydactyly of A) the thumbs (Patient 1) and B) the big toes (Patient 6) in tricho-rhino-phalangeal syndrome type I patients. Roentgenograms of C) the hand in Patient 2 and D) the toes in Patient 3 show cone-shaped epiphyses (white arrow) of the middle phalanges.

Fig. 3. Histopathologic examination of the scalp in Patient 3 shows hypotrichosis without inflammation or scarring. (Hematoxylin and eosin, x40).

tes mellitus [13], idiopathic hypoglycemia, renal disease [14], ureteral reflux [15], and heart disease [13, 16, 17]. Patients with TRPS are more likely to have significant psychologic problems because of their unusual appearance. Patient 3 had repeatedly attempted suicide because her scalp hair was sparse [3]. Hence, psychologic evaluation and support for patients and their families should be an integral part of disease management [16].

Ludecke et al [18] and Hou et al [19] localized the TRPS-I gene to 8q24. Momeni et al positionally cloned a gene, designated TRPS1, that has 7 exons and encodes a zinc-finger protein [20]. They identified six different nonsense mutations in 10 unrelated TRPS patients. Their findings suggest that haploinsufficiency for this putative transcription factor causes TRPS-I.

In this series of Taiwanese TRPS-I patients, we found that, in addition to the typical craniofacial manifestations, all patients had brachydactyly of the big toes. Identification of this abnormality provides an easier way to recognize the syndrome than roentgenographic identification of cone-shaped epiphyses.

References