Trichothiodystrophy with Cerebral Hypomyelination

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Trichothiodystrophy (TTD), or sulfur deficient brittle hair, is a rare autosomal recessive disorder that may serve as a clinical marker for a neuroectodermal symptom complex.

We report a 17-month-old girl affected by TTD. Since birth, the parents had noticed sparse and coarse scalp hair. The diagnosis was based on the presence of brittle hair, alternating dark and light bands (tiger-tail appearance) of the hair shaft under polarizing microscopy, and trichoschisis under scanning electron microscopy. Apart from that, no other symptoms were present. However, she had experienced convulsions, 2 years after the diagnosis of TTD, and a cranial MRI showed cerebral hypomyelination. We suggest that a careful examination of patients with TTD should be performed in order to detect any other related abnormalities. (Ann Dermatol 17(2) 98~101, 2005)

Key Words: Trichothiodystrophy, Trichoschisis, Cerebral hypomyelination

INTRODUCTION

The term trichothiodystrophy (TTD) was used by Price et al.[1] in 1980 to describe a neuroectodermal symptom complex, characterized by sulfur-deficient hair. Often, severe neuroectodermal disorders are associated, but none are a constant feature[2,3]. Mental retardation is the most frequent neurologic finding, but autism, hypomyelination, seizure, hyperreflexia, pyramidal signs, gray matter heterotopia and acute necrotizing encephalopathy have also been reported[2-4]. To our knowledge, only one case of TTD, which had no associated disorder, has been reported in the Korean literature[5]. Herein, we report a rare case of TTD with cerebral hypomyelination.

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CASE REPORT

A 17-month-old Korean girl presented with sparse and brittle hair on the scalp, which had been present since birth. She was the first child of nonconsanguineous parents. Pregnancy and birth were uneventful. No disease of the skin, hair, or immune system had been previously recognized in relatives of the parents. The hair on the scalp was short, brittle, sparse and fine. Localized alopecia was seen in mechanically-stressed areas, such as the temporal and occipital part of the scalp (Fig. 1). Eyebrows and eyelashes were also fine and thinned. Apart from these, no other symptoms were seen. No significant scaling or nail changes were found and there was no evidence of photosensitivity. Pediatric and neurological evaluation had shown normal growth and mental development. Light microscopy examination of the hair showed trichorrhexis nodosa and clean-cut transverse fractures (trichoschisis). Polarizing microscopy showed alternating bright and dark bands giving the shafts a tiger-tail pattern (Fig. 2). Electron microscopy revealed trichoschisis, trichorrhexis nodosa, absence of cuticle, ridges and grooves (Fig. 3). We diagnosed the condition as TTD without associated disorders, and only recommended

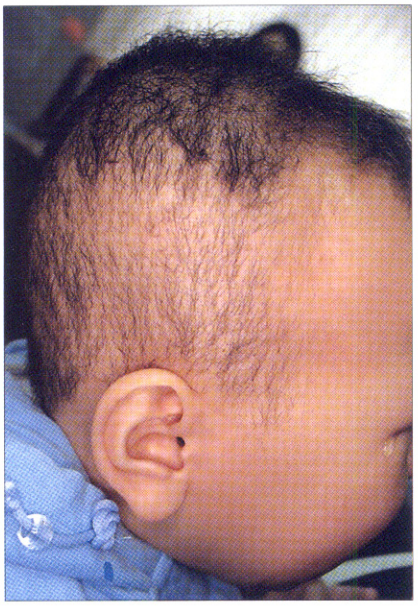

Fig. 1. Clinical examination shows brittle, short and sparse hair on the scalp.

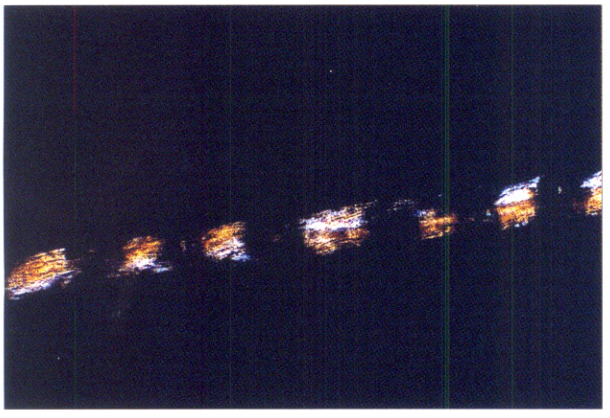

Fig. 2. Polarizing microscopy of hair shows the 'tiger-tail' pattern.

physical stress or chemical trauma of the hair should be minimized, because no effective treatment for TTD is known.

However, she was admitted for convulsions at the age of 3. Cranial magnetic resonance imaging (MRI) was performed, which revealed hypersignal lesions on T2-weighted images which mainly involved the thalamus, brainstem (midbrain and pons), and frontal periventricular white matter, compatible with hypomyelination (Fig. 4).

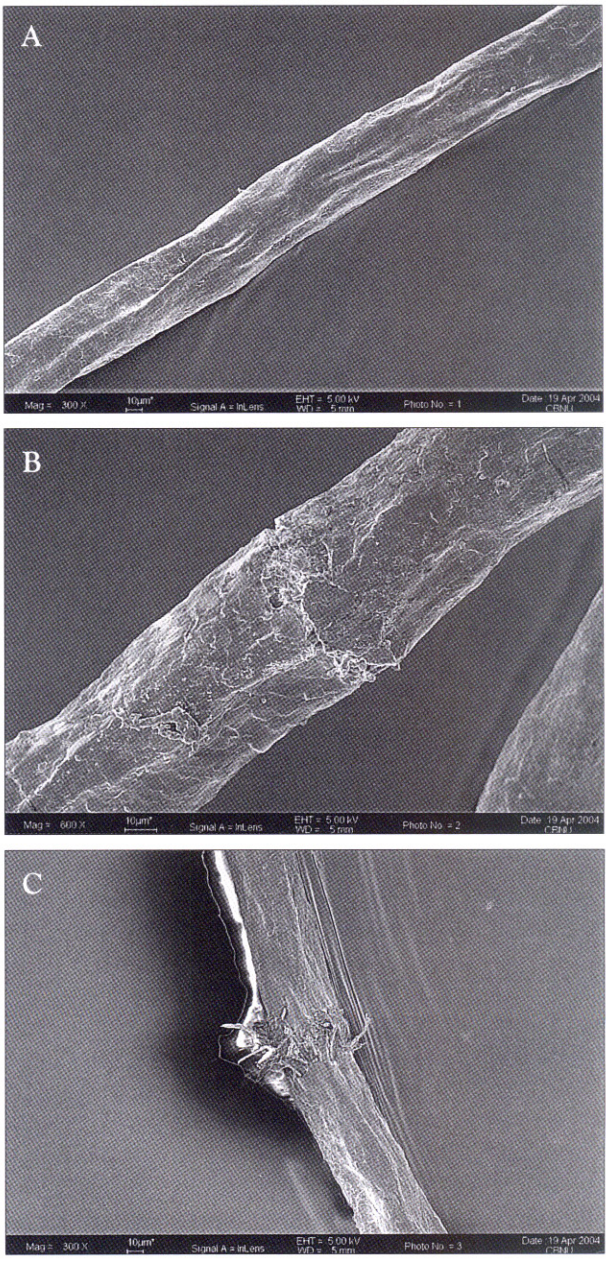

Fig. 3. Findings on scanning electron microscopy. Severe cuticular degeneration with ridges and grooves (A), trichoschisis (B) and trichorrhexis nodosa (C).

DISCUSSION

TTD is a rare autosomal recessive disorder characterized by sulfur deficient brittle hair, which may be isolated or associated with a wide spectrum of neuroectodermal abnormalities[6]. For the diagnosis of TTD, Itin et al.[2] suggested that a low hair sulfur

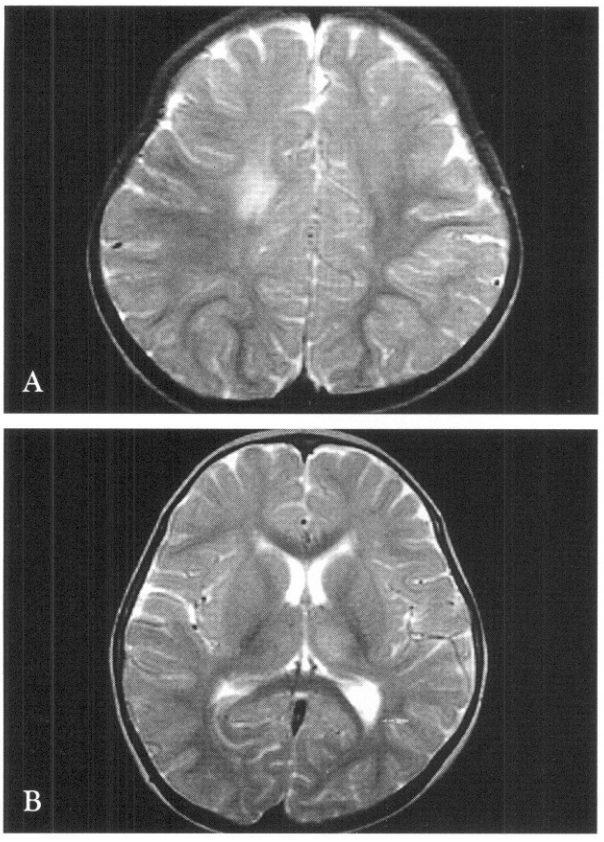

Fig. 4. T2-weighted axial MRI image revealed diffuse increased signal intensity in periventricular white matter of frontal lobe, right (A) and thalamus, left (B).

level must be associated with at least one of the following features; trichoschisis, alternating light and dark bands under polarizing microscopy, and absent or severely damaged hair cuticle under scanning electron microscopy. Amino acid analysis of hair shows a cysteine and high-sulfur protein content which is much lower than normal. We did not investigate amino acid level of hair, but trichoschisis is a marker and a very characteristic feature of the sulfur-deficient hair of TTD. Therefore, we could diagnose the condition as TTD, based on the presence of brittle hair, tiger-tail appearance of the hair shaft under polarizing microscopy and trichoschisis, absence of cuticle, ridges and grooves under scanning electron microscopy.

TTD has previously been referred to as BIDS (brittle hair, impaired intelligence, decreased fertility, and short stature), IBIDS (which also includes ichthyosis), PIBIS (which also includes photosensitivity), or Tay syndrome, depending on the range of manifestations in these heterogeneous disorders[3]. Depending on the extent of the sulfur deficiency, clinical features of patients with TTD show a highly variable range, from those with an isolated hair defect to those with short stature, mental retardation, ichthyosis, nail dystrophy, photosensitivity, cataracts, osteosclerosis, neurologic abnormalities or immunodeficiency[1,2,7]. The associated abnormalities are generally noted at birth, but TTD presenting with unusual progressive manifestations have been reported[8].

Recent advances in human genetics have shown that impairment of transcription factor, TFIIH, results in TTD. TFIIH has dual function in NER (nucleotide excision repair) and initiation of transcription. Approximately 50% of patients with TTD show photosensitivity. Nonphotosensitive patients exhibit the transcription defects with normal NER activity, whereas photosentitive patients exhibit disruption of the DNA repair functions. Most photosensitive patients have mutations on the XPD gene, rarely on the XPB gene or an unidentified TTD-A gene, but no gene has been isolated yet in the nonphotosensitive patients group[9].

The association of TTD and neurological involvement has been frequently reported. It included mental retardation, autism, spasticity, hypotonia, hyperreflexia and seizures[1-4,9]. MRI studies have also described the central hypomyelination, cortical atrophy with microcephaly, periventricular and subcortical heterotopia, partial callosal agenesis and callosal calcifications[10-13]. In our case, the patient experienced convulsions and a cranial MRI revealed multifocal T2-weighted hypersignal lesions involving mainly the thalamus, midbrain, pons and frontal periventricular white matter, which is compatible with hypomyelination. The pathophysiology of the central nervous system involvement in TTD is unknown, but the deranged synthesis of high-sulfur matrix proteins such as cysteine may affect synthesis, not only of hair and nail, but also of similar matrix proteins in other tissues including the nervous system.

We report a 17-month-old girl affected by TTD with cerebral hypomyelination. She had suffered with sparse and brittle hair since birth. Apart from that, no other symptoms had been noticed. However, she had experienced convulsions 2 years after the diag-

nosis of TTD, and a cranial MRI showed cerebral hypomyelination. TTD has rarely been reported, because brittle hair was regarded as a cosmetic problem. Only one case of TTD, which was isolated without the associated disorders, has been reported in the Korean literature[5]. However, TTD can be a clinical marker for a neuroectodermal symptom complex. We suggest that a careful examination of patients with TTD should be performed, in order to detect any other related abnormalities.

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