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CASE REPORTS

Trichothiodystrophy: PIBIDS Syndrome

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Abstract. Trichothiodystrophy comprises a heterogeneous group of autosomal recessive entities. This fact gives rise to different interrelated neuroectodermal disorders. From a structural point of view these features are the result of the low tissue sulfur content. We report a case of trichothiodystrophy initially classified as Tay syndrome that based on clinical features, complementary exams as well as on the disease evolution was labeled as PIBIDS syndrome.

Key words: trichothiodystrophy, sulfur deficit, PIBIDS.

TRICOTIODISTROFIA: SÍNDROME PIBIDS

Resumen. La tricotiodistrofia conforma un grupo heterogéneo de entidades determinadas genéticamente por un patrón autosómico recesivo. Este hecho va a dar lugar a diferentes alteraciones que comparten un mismo origen neuroectodérmico. Desde el punto de vista estructural estas manifestaciones se caracterizan por ser consecuencia del bajo contenido de azufre tisular. Presentamos un caso de tricotiodistrofia clasificado inicialmente como síndrome Tay, pero en función de las manifestaciones clínicas y pruebas complementarias, así como de la evolución de la enfermedad, fue finalmente etiquetado como síndrome PIBIDS.

Palabras clave: tricotiodistrofia, déficit de azufre, PIBIDS.

Case Description

We present the case of a 4-month-old preterm female infant with hair and nail defects and extremely dry, ichthyosiform skin since birth. On examination, she had progeria-like facies and very brittle hair (Figures 1 and 2), and fish-like skin, with palmoplantar involvement (Figure 3). There was growth retardation, the child's weight, length, and head circumference were all below the third percentile, and the child's length–weight ratio was clearly abnormal. Mental development was normal. During the routine check-up visits, the mother reported that the child had photosensitivity problems and there were noticeable lentigines.

The patient's medical history was remarkable for enterocolitis due to *Campylobacter* and 2 episodes of pneumonia, both uncommon in patients of this age. In view of this history, we performed cytogenetic and immunological studies at an early stage. The findings of both were unremarkable.

Complementary examinations revealed microcytic hypochromic anemia, which we classified as β thalassemia trait due to the high number of red blood cells, the reduced mean corpuscular volume of the cells, and the family history.

Samples were taken for a full hair analysis. The trichogram revealed intermittent pili torti and trichoschisis due to

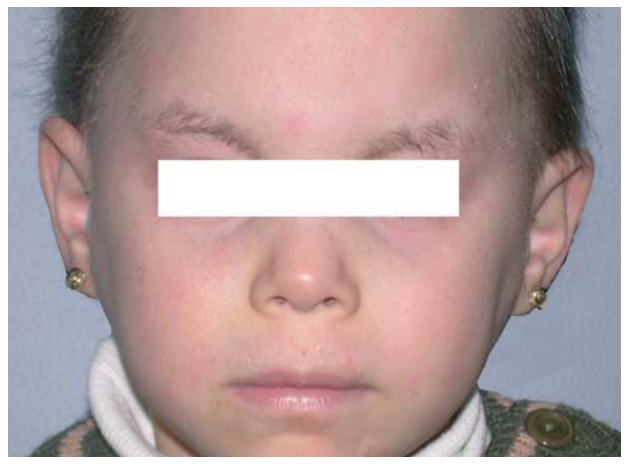

Figure 1. Progeria-like facies

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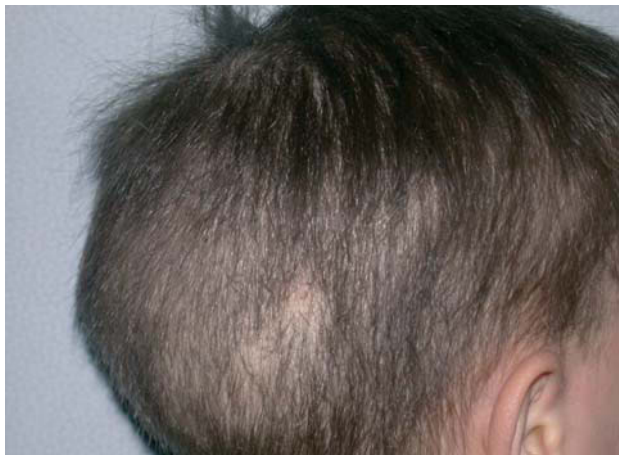

Figure 2. Characteristic hair appearance, very brittle

Figure 3. Fish-like scales on skin, including palms and soles

trichorrhexis nodosa (Figure 4). The elemental analysis showed a slight sulfur deficiency in the hair in the frontoparietal region; the deficiency was more evident at the back of the head, where over 50% of the hairs were affected (Figure 5).

In view of the clinical and other findings, we made an initial diagnosis of trichothiodystrophy and Tay syndrome given the existence of ichthyosiform erythroderma, hair abnormalities, and growth retardation. The subsequent observation of photosensitivity and multiple lentigines on the face led us to suspect PIBIDS (photosensitivity, ichthyosis, brittle, sulfur-deficient hair, intellectual impairment, decreased fertility, and short stature).

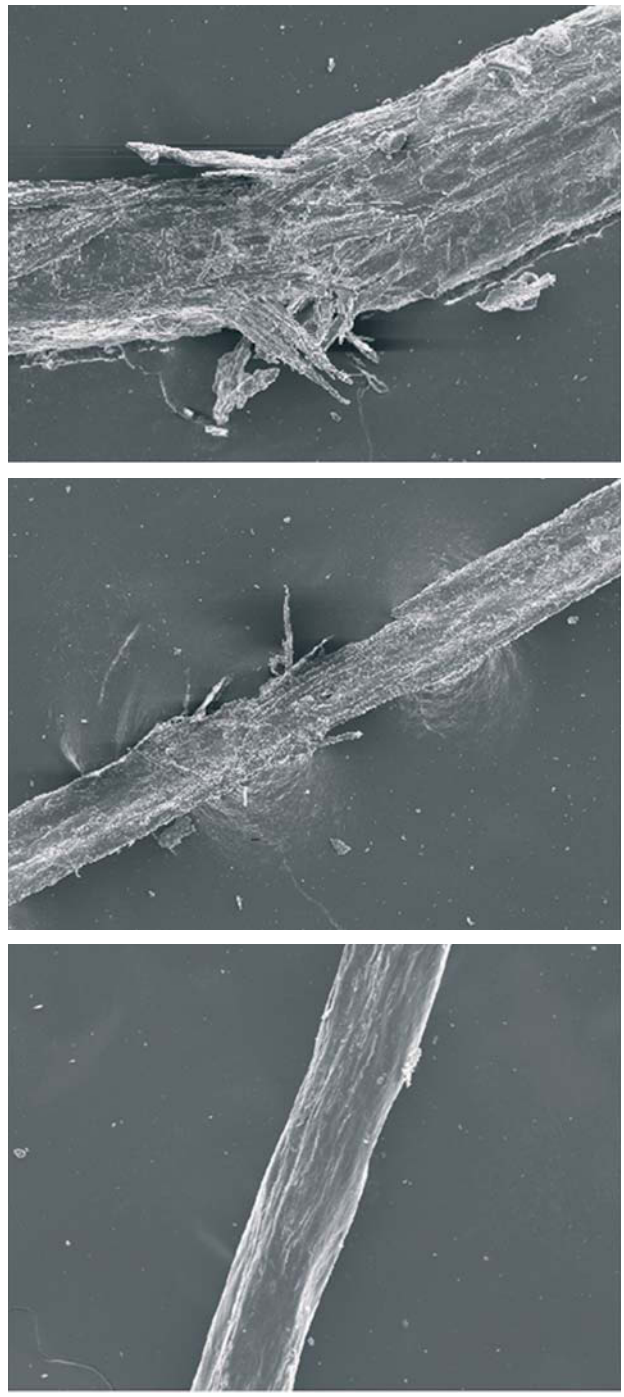

Figure 4. Trichoschisis (trichorrhexis nodosa) and pili torti in the trichogram

Discussion

The term trichothiodystrophy comes from the Greek *tricho* (hair), *thio* (sulfur), *dys* (alteration), and *trophe* (form). The disorder is caused by a sulfur deficiency in tissues of neuroectodermal origin. The associated photosensitivity is the result of a defect in the nucleotide excision repair (NER) system,[1,2] which is responsible for repairing DNA. A defect in any of the 11 genes that regulate general transcription factor IIH (TFIIH) activity can lead to increased risk of skin cancer

due to ultraviolet radiation-induced cutaneous hypersensitivity. Different clinical characteristics, which, combined, form varying syndromes, are observed depending on whether NER function, transcription function, or both simultaneously are affected (Figure 6). The 3 disorders that are most frequently related to defective NER are xeroderma pigmentosum, Cockayne syndrome, and trichothiodystrophy (PIBIDS).[3,4]

The term trichothiodystrophy was coined by Price between 1979 and 1980 on the basis of a series of cases that had been described by Pollit, Jenner, and Davies (1968). The corresponding patients had mental and growth retardation and trichorrhexis nodosa. Shortly afterwards (1970), Brown et al described a specific hair defect (trichoschisis), alternating birefringence, and low sulfur levels.

Tay (1971) coined the term Tay syndrome, which he described as trichothiodystrophy in association with ichthyosiform erythroderma and slow mental and physical growth. Jorizzo et al (1982) suggested the term IBIDS to cover the association with ichthyosis. Other signs that completed the clinical picture were described later, including osteosclerosis, reported by Chapmann (1988), who proposed the term SIBIDS, and photosensitivity,[5] reported by Crovato, Borrone, and Rebora (1983), who proposed the term PIBIDS (Table 1).

Clinical signs include brittle hair and photosensitivity due to a DNA repair deficiency in up to 50% of patients. The DNA repair deficiency is practically identical to that observed in xeroderma pigmentosum type D,[6] although there is no evidence of an increased risk of skin cancer in patients with trichothiodystrophy. Several other presentations of the disease have been described in isolated clinical cases.[7] These are summarized in Table 2 together with the more common presentations.

The only diagnostic changes that identify sulfur deficit are hair abnormalities and these are always present. Macroscopic changes are noticeable in the fronto-occipital region and microscopic changes in the occipital region. Optical microscopy reveals characteristic signs of trichoschisis, but other hair dystrophies such as atypical trichorrhexis nodosa or pili-torti-like abnormalties, may

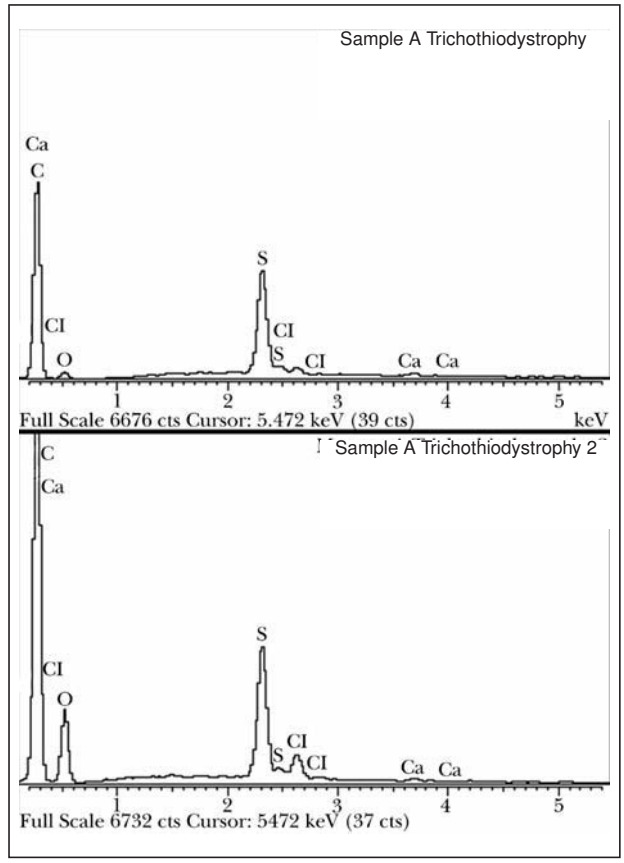

Figure 5. Sulfur deficiency (>50%).

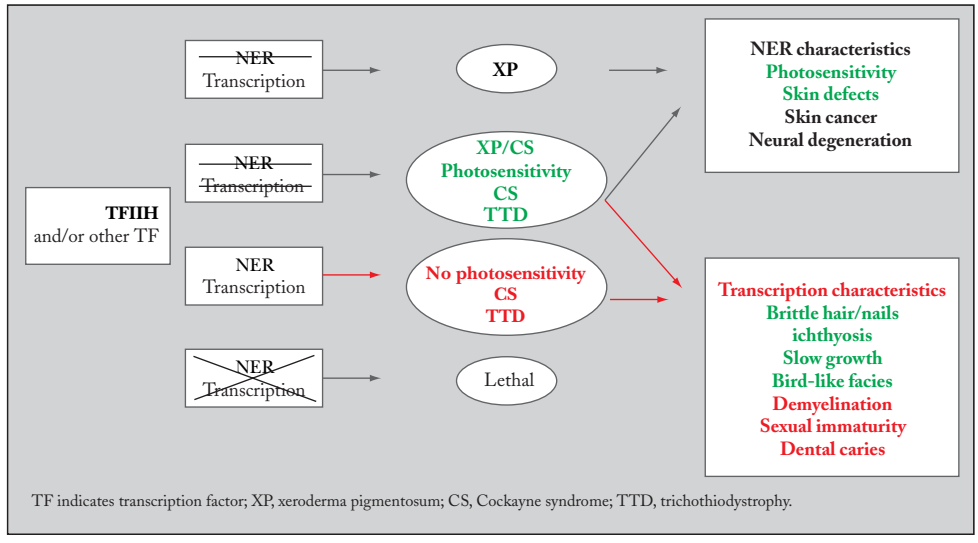

Figure 6. Nucleotide excision repair system. Genes involved and clinical presentations. Deleted = partial deficiency; cross = total deficiency

Table 1. Classification of Trichothiodystrophy by Clinical Presentations

Type	*Characteristics*	*Eponym/Acronym*
A	Hair ± nails	
B	Hair ± nails + mental retardation	Sabinas
C	Hair ± nails + mental retardation + folliculitis + slow bone growth ± caries	Pollitt
D	Brittle hair ± nails + infertility + growth retardation + short stature	BIDS
E	Ichthyosis + BIDS hair/nails + growth retardation + short stature ± impaired gonadal function ± lenticular cataracts + progeria + microcephaly ± ataxia ± calcifications of the basal ganglia + erythroderma and scale	Tay + BIDS
F	Photosensitivity + IBIDS	PIBIDS
G	Trichothiodystrophy with immunity defects Hair ±mental retardation + chronic neutropenia or immunoglobulin deficiency	Itin
H	Trichodystrophy with severe intrauterine growth retardation Hair + intrauterine growth retardation and failure to grow + developmental delay + recurrent infections + cataracts + hepatic angioendotheliomas	

Table 2. Clinical Presentations Associated With Trichothiodystrophy[2-4]

Hair
- Loss of eyebrows and/or eyelashes
- Loss of underarm, pubic, and/or body hair
- Abnormal nose and/or ear hair

Nails
- Dysplasia (onychodystrophy)
- Koilonychia
- Onychogryphosis
- Yellow nails
- Unguis inflexus

Skin
- Ichthyosis
- Follicular keratosis
- Collodion baby
- Erythroderma
- Photosensitivity (if DNA repair deficiency exists)
- Erythema
- Eczema
- Hypohidrosis
- Pruritus
- Telangiectasia
- Hemangioma
- Lipoatrophy
- Folliculitis
- Poikiloderma
- Cheilitis
- Hyperpigmentation
- Pyoderma
- Palmar pustules

Nervous system
- Mental retardation
- Autism
- Demyelination
- Spasticity/paralysis
- Ataxia
- Cerebral deficiency
- Intention tremor
- Motor disorders
- Pyramidal signs
- Hypotonia
- Peripheral neuropathy
- Hyperreflexia
- Reduced tendon reflexes
- Hemiparesis
- Tetraparesis
- Intracranial calcifications
- Partial agenesia corpus callosum
- Necrotizing encephalopathy
- Impaired ocular motility
- Dysarthria
- Irritability
- Lethargy
- Perimedullary or spinal fibrosis

Genital/urological
- Hypoplasia
- Undescended testicles
- Hypospadias
- Hydronephrosis
- Ureteral duplication
- Pyelocalyceal ectasia

Dysmorphology and miscellaneous
- Growth retardation
- Cranial dysplasia
- Microdolichocephaly
- Protruding ears
- Hypoplastic ears
- Periauricular pits
- Accessory lobes
- Thin nose
- Nasal obstruction
- Maxillary hypoplasia
- Dental abnormalities
- Caries
- Malabsorption due to jejunal atrophy
- White lingual plaques
- Gingival hyperplasia
- Bifid uvula
- Small mouth
- Double lip
- Frontal bossing
- Facial hemiatrophy
- Disproportionate trunk/limbs
- Short neck
- Progeria

Ocular
- Cataracts
- Conjunctivitis
- Nystagmus
- Photophobia
- Epicanthal folds
- Retinal dystrophy
- Entropion/extropion
- Hypotelorism
- Exophthalmos/enophthalmos
- Exstrophy
- Myopia
- Astigmatism
- Retrobulbar hemangioma
- Chorioretinal atrophy
- Retinal pigmentation
- Tortuosity of retinal vessels
- Strabismus
- Hypertelorism
- Bacterial keratitis
- Gland inflammation
- Meibomian
- Blepharitis
- Corneal opacity
- Microcornea

Cardiovascular
- Hemangioma
- Telangiectasia
- Circulatory insufficiency
- Hepatic angioendotheliomas
- Pulmonic stenosis
- Ventricular septal defect

Immunological/hematological
- Recurrent infections
- Neutropenia
- Anemia
- Hypereosinophilia

Pulmonary
- Pulmonary adenomatosis
- Asthma
- Bronchiectasis

Skeletal
- Geno valgum
- Coxa valga
- Valgus deformity of the great toe
- Cubital and tibial valgus deformity
- Deviation of fingers
- Contracture
- Zygodactyly
- Clinodactyly
- Limited range of motion
- Pectus excavatum
- Scoliosis
- Thoracic kyphosis
- Lumbar lordosis
- Reduced-size metacarpal bones

also be seen. Tiger-tail banding is noticeable under polarized light microscopy,[8] and affected hair always has 50% less sulfur than does normal hair.

As far as therapeutic advances are concerned, it is worth noting that an increasing number of new cases are diagnosed prenatally thanks to the detection of ultraviolet radiation-induced DNA synthesis defects in cultivated amniotic fluid cells, a discovery which may lead some parents to decide to terminate the pregnancy.[9]

Conflicts of Interest

The authors declare no conflicts of interest.

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