Ichthyosis, Brittle Hair, Impaired Intelligence, Decreased Fertility and Short Stature (IBIDS Syndrome)
-A Case Report and Review of the Literature

Chi-Ling Lin  Gwo-Shing Chen

IBIDS is a syndrome characterized by ichthyosis, brittle hair, impaired intelligence, decreased fertility and short stature. It is a subtype of trichothiodystrophy. We presented an 11-year-old girl whose clinical features fit into the IBIDS syndrome. She had congenital ichthyosis, brittle hair, intellectual impairment, possibly decreased fertility, short stature and the typical facial features of micrognathia and prominent ears. The hair showed a trichoschisis-like pattern at light microscopy and alternate banding at polarizing microscopy. Herein, we report a case and review available literatures. (Dermatol Sinica 25: 236-241, 2007)

Key words: IBIDS syndrome, Trichothiodystrophy, Trichoschisis, Brittle hair, Congenital ichthyosis
INTRODUCTION

The nosography of complex neuro-cutaneous syndromes has recently been identified. In 1970s, Allen and Jackson et al. described a recessive autosomal syndrome associating brittle hair, intellectual impairment, decreased fertility, and short stature (BIDS).1, 2 Price et al. referred to brittle hair as trichothiodystrophy characterized with fragility, low sulphur content, abnormal hair pattern under polarization microscopy as alternative light and dark bands, and ichthyosis.3 Then, Jorizzo et al. proposed a unifying concept as IBIDS (ichthyosis, brittle hair, intellectual impairment, decreased fertility, and short stature).4 Later in a few years, Crovato et al. added one 'P' for photosensitivity and proposed the acronym PIBIDS.5

This reported patient, as most previously reported cases with the diagnosis of IBIDS syndrome, presented symptoms mainly in tissues of ectodermal origin (epidermis, hair and nervous system) and tissues of mesodermal origin (connective tissue-bone and gonads).

CASE REPORT

This 11-year-old girl was the third child of non-consanguineous parents. She was born through natural spontaneous delivery. Her appearance at birth was unremarkable, with normal weight and height.

During neonatal period life, generalized ichthyotic dry skin appeared gradually. Hypothyroidism was discovered by laboratory examination (TSH:1.0 μU/ml, T3:143.7 ng/dl, T4:15.1 μg/dl). Tc-99m pertechnetate thyroid scan revealed functioning thyroid gland in the normal location. Chromosome study showed normal female karyotype.

During the following years, the patient had slow growth rate despite fair appetite and adequate caloric intake. Mild to moderate mental retardation became apparent at the age of seven. Serial psychometrics showed IQ scores around 76. Radiological examination of both wrists showed bony maturation be at 13 months old when her chronological age was 4 years old; the bone age was 30 months old when she was 5
years and 3 months old. Significant retardation of bone age was impressed.

At the age of 10 to 11 years old, large polygonal tan-colored scales were noted on the limbs, particularly on the lateral and extensor aspects. They were most prominent on the shins and arms (Fig. 1). Large amounts of dry scales were noticed on the trunk. The scalp hair was sparse, short, curled and brittle, especially on the vertex (Fig. 2). There was moderate frontal recession of the scalp hair. Eyebrows were sparse and relatively short. Prominent ears and a regressed chin formed an elder-like face (Fig. 2, 3). Her height and weight were 132.0 cm (1 SD below the mean for her age) and 45.0 kg (2 SD above the mean for her age) respectively. The nails and teeth were of normal appearance. The remainder of the physical examination was unremarkable.

Surveying her family members, her mother had similar dysmorphic face, short stature (130.5 cm) and sparse hair. Her father and two elder sisters appeared normal.

Histopathological examination of the skin from left lower leg at the age of 1 month (the time of generalized ichthyotic dry skin appeared) showed hyperkeratosis and absent the granular layer (Fig. 4). It was compatible with ichthyosis. Histopathological examination of the skin from the scalp at the age of 11 years showed degenerative changes in the hair matrix (hydropic change of basal layer; hyalinization and myxoid change of basement membrane) and pigment incontinence of the hair bulbs focally. No prominent inflammation was seen. It was compatible with the clinical pattern of diffuse alopecia.

Light microscopy revealed hair shafts with an undulating wavy contour. The pigment granules in the cortex had a similar wavy distribution. Abrupt changes in hair shaft diameter were present in some areas (Fig. 5A). Therefore, pili torti, trichorrhexis nodosa and trichoschisis (clean transverse fractures of the scalp hair shafts) were highly suspected. Polarized illumination showed alternating bright and dark zones (tiger tail or bamboo hair, Fig. 5B). Examination
of hairs from each member of her family, and from normal children of the same age, did not show this pattern. Analysis of the sulfur content and amino acid of the hair was not yet performed.

The following investigations were within normal limits: full blood count with differential white cell and platelet count, erythrocyte sedimentation rate, serum biochemistry, growth hormone and immunoglobulin levels, VDRL, electrocardiogram and chest X-ray. The analysis of the amino acid of the plasma were generally in normal levels. The ophthalmologic examination didn’t discover cataract or any other pathological findings. The odontological examination showed normal pattern of teeth eruption. The photosensitivity test using UVA (maximal dosage: 55 J/cm²) and narrow-band UVB (maximal dosage: 500 mJ/cm²) didn’t revealed photosensitivity.

DNA sequencing was performed with the blood samples provided by the patient and the other family members (parents and two sisters). We examined the DNA sequence of the patient’s genes (ERCC2/XPD, TTDA and ERCC3/XPB, which had been identified with mutations in patients with IBIDS syndrome before) and compared it to the normal sequence. However, no remarkable change (or mutation) was found except some polymorphisms. As a result, we were not able to identify a putative mutation from our gene analysis.

After receiving the pulsed corticosteroid therapy monthly for 3 consecutive months, a few new grown hairs appeared, but they remained fragile and broke easily. Therefore, systemic therapy with corticosteroids was with little effect.

DISCUSSION

The acronym IBIDS describes ichthyosis, brittle hair, impaired intelligence, decreased fertility and short stature. This rare and heterogeneous genodermatosis belongs to a group of disorders that has in common a hair defect termed trichothiodystrophy. Trichothiodystrophy, a sulfur-deficient brittle hair syndrome, is characterized by fragile hair that breaks easily. IBIDS, featuring skin lesions, is one of the subtypes of the trichothiodystrophies.

The mechanical weakness of the hair shaft might result from a sulfur deficiency in the shaft of the defective hair. This suggested a relative absence or imbalance in the incorporation of certain sulfur rich amino acids utilized in the process of protein synthesis of hair. Ideally, the patient should have a sulfur study of the hair to confirm the diagnosis of trichothiodystrophy. However, even without such a study, the phenotypic similarity of the patient to those with tri-

Table 1: Summary of the Examinations of Hair in the Previously Reported Cases of IBIDS, PIBIDS or Tay Syndrome

<table>
<thead>
<tr>
<th>Case</th>
<th>Light microscopy</th>
<th>Polarizing microscopy</th>
<th>Electron microscopy</th>
<th>Amino acid analysis</th>
<th>Diagnosis</th>
<th>Present of year/ reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Trichoschisis</td>
<td>Alternating bright and dark zones</td>
<td>Not performed</td>
<td>Not performed</td>
<td>IBIDS or Tay syndrome</td>
<td>1991 / 12</td>
</tr>
<tr>
<td>2</td>
<td>Trichoschisis; trichorrhexis nodosa-like fractures</td>
<td>Alternating bright and dark zones</td>
<td>Amorphous debris and cavitation of cuticle</td>
<td>Markedly decreased sulfur content: 1.83 ± 0.43% (control: 4.61 ± 0.12%)</td>
<td>IBIDS or Tay syndrome</td>
<td>1988 / 8</td>
</tr>
<tr>
<td>3</td>
<td>Trichoschisis</td>
<td>Alternating banding</td>
<td>Not performed</td>
<td>Cystine deficiency</td>
<td>PIBIDS syndrome</td>
<td>1983 / 5</td>
</tr>
<tr>
<td>4</td>
<td>Pili torti; trichoschisis</td>
<td>Alternating bright and dark zones</td>
<td>Not performed</td>
<td>Sulfur content: 2.05% (normal: 4.00-5.00%)</td>
<td>IBIDS syndrome</td>
<td>1982 / 4</td>
</tr>
</tbody>
</table>
Fish-scales, brittle hair, stunted growth, infertility and short stature (IBIDS phenotype) - a case report and literature review

The hair shaft showed clean transverse fractures by light microscopy, which was termed trichoschisis. Examination with polarized light revealed regular alternating areas of birefringence and non-birefringence, suggesting a patterned abnormality of hair keratinization. These hair defects were considered diagnostic. The examinations of hair in the previously reported cases of IBIDS, PIBIDS or Tay syndrome are summarized in Table 1.

Lucky et al. had stated an association of UVB light sensitivity and trichothiodystrophy. A unifying concept was proposed by Crovato et al. as PIBIDS syndrome (photosensitivity and other features of IBIDS syndrome). Van Neste D et al. suggested that each patient with trichothiodystrophy should be explored for light sensitivity and DNA excision repair in order to establish a possible link with xeroderma pigmentosum. In this case, no light sensitivity due to UVA or UVB exposure was observed. The patient reported no remarkable history of sun-induced erythema, oedema or bullae on the exposed areas. The photosensitivity test using UVA and narrow-band UVB didn't revealed positive findings such as erythema or blister formation.

The patient's mother had the same characteristic abnormalities of a dysmorphic face, short stature and sparse hair as the girl. Other family members were unaffected. The girl's chromosome and gene analyses were normal. Therefore, the inheritance pattern is likely to be an autosomal recessive trait, as reported already in previous cases of IBIDS syndrome.

As can be seen from the girl and most previously reported cases, the patients with IBIDS presented symptoms mainly in tissues of ectodermal origin (epidermis, hair, nails, lens, nervous system and teeth) but also in tissues of mesodermal origin (connective tissue - bone and gonads). A group of syndromes with ectodermal and mesodermal defects should be considered in the differential diagnosis of patients with the features of the IBIDS syndrome. The Sjögren-Larsson syndrome is an autosomal recessive condition comprising non-bullous ichthyosiform erythroderma, spastic tetraplegia, mental retardation, epilepsy and (in 20-30% of cases) retinal pigment degeneration. The hair and nails are normal. Patients with Netherton's syndrome characteristically demonstrate ichthyosis linearis circumflexa in association with short, dry, lusterless hair showing trichorhexis invaginata. Many patients also have atopic manifestations such as urticaria or asthma, and a few have been mentally retarded. Nails, teeth and growth have been normal. In Conradi's syndrome, patients have a characteristic type of ichthyosiform erythroderma, cataracts, and stippled epiphyses on X-ray examination, with dwarfism and mental retardation occurring in some patients and follicular atrophoderma in others. Refsun's syndrome (heredopathia atactica polyneuritiformis) comprises retinitis pigmentosa, peripheral polynuropathy, cerebellar ataxia, deafness and ichthyosis as its major clinical components. Phytic acid has been shown to accumulate in the tissues, probably due to a deficiency in phytanic acid α-hydroxylase activity.

In this report, we have described the characteristic manifestations of IBIDS syndrome. The hair defect and the ectodermal and mesodermal abnormalities should attract the attention of the clinician and remind them the syndrome of features in combination as IBIDS.

REFERENCES