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Case Report

Short stature with congenital ichthyosis

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Abstract

PIBIDS syndrome (photosensitivity, ichthyosis, brittle hair, intellectual impairment, decreased fertility and short stature) is a variant of trichothiodystrophy. It is a rare form of autosomal recessive congenital ichthyosis. Short stature is a vital component of PIBIDS syndrome. We present the cases of two siblings in whom we diagnosed PIBIDS syndrome. On evaluation for short stature, they were found to have severe vitamin D deficiency, which on correction led to the patients having considerable gain in stature. With this case, we would also like to propose that vitamin D deficiency could be one of the treatable causes of short stature in PIBIDS syndrome.

Background

PIBIDS syndrome is an acronym which stands for photosensitivity, ichthyosis, brittle hair, intellectual impairment, decreased fertility and short stature. This is a rare autosomal recessive form of congenital ichthyosis and it is a variant of trichothiodystrophy. Short stature is an important feature of PIBIDS syndrome. We report the cases of two siblings who presented to us in the endocrinology clinic with short stature and congenital ichthyosis.

Case presentation

A 13-year-old boy of Indo-Aryan ethnicity was brought to the endocrinology clinic by his parents with symptoms of poor gain in height since 3 years of age (patient 1). The patient was born full term via spontaneous vaginal delivery and had normal birth weight. The birth length was not known. After the birth, the patient's mother noted that a clear membrane was covering the entire body of the patient, which slowly shed off and was followed by peeling of the skin (Collodion membrane). Apart from this, there were no other complications during the neonatal period.

Since the age of 3 years, the parents noticed that the patient was shortest among all the children in the school. There were no previous weight recordings or growth charts available. The patient had no history suggestive of any other chronic systemic illness and no symptoms suggestive of malabsorption, type 1 diabetes, rickets, hypothyroidism or Cushing's syndrome.

The patient had normal milestones and the parents recall that he started walking on his first birthday. The patient continued to have shedding of skin, hair and nails. He had intolerance to both cold and heat because of his skin condition. The patient also had skin irritation on exposure to sunlight. He had dryness of skin and often the skin appeared like scales of a fish.

The patient had undergone extensive investigation and treatment for his skin condition. He had received

a number of topical creams, ointments and shampoos. He also received Ayurvedic, Unani and Homeopathic medications. Details of his earlier treatment were not available at the time of examination. The patient had been asked to apply an emollient to keep the skin moist.

The mother had no significant medical disorder during the prenatal and antenatal periods. The patient was born full term via spontaneous vaginal delivery and had normal birth weight. Apart from the skin condition, there was no history of excessive floppiness or asphyxia. There was no history of oedema of the hands or feet at birth, as well as no history of hypoglycaemia or seizures. There was no history of cryptorchidism. The patient was exclusively breastfed from birth until 6 months of age. The parents reported that the patient avoided healthy home food in preference to junk food. He used to get less sunlight exposure compared to children of his age because of his sensitivity to sunlight. The patient had been given all the vaccines as prescribed in the vaccination programme.

The first-born patient was a product of a consanguineous marriage (the parents were first cousins of each other). The mother gave no history of abortions. There was no history of neonatal or sibling deaths. The patient had a 9-year-old younger brother who suffered from a similar skin condition and short stature (patient 2).

There was no history of any endocrine illness in other family members. The parents had a history or normal timing and tempo of puberty. The patient had normal appetite and sleep. He had normal social interaction with his peers. Parental behaviour and attitudes were normal.

On physical examination, the patient appeared short and immature for his age. The limbs appeared proportionate. The patient had a height of 127.5 cm (<3rd centile on the Indian Academy of Pediatrics growth chart) and height Z-score of −3.61, which suggests extreme short stature. The height-age was around 8 years. The weight was 26 kg with weight-age of around 8 years (figure 1). The arm span was 130 cm. The upper segment/lower segment ratio was 1:1. The patient had normal blood pressure, pulse, temperature and respiratory rate.

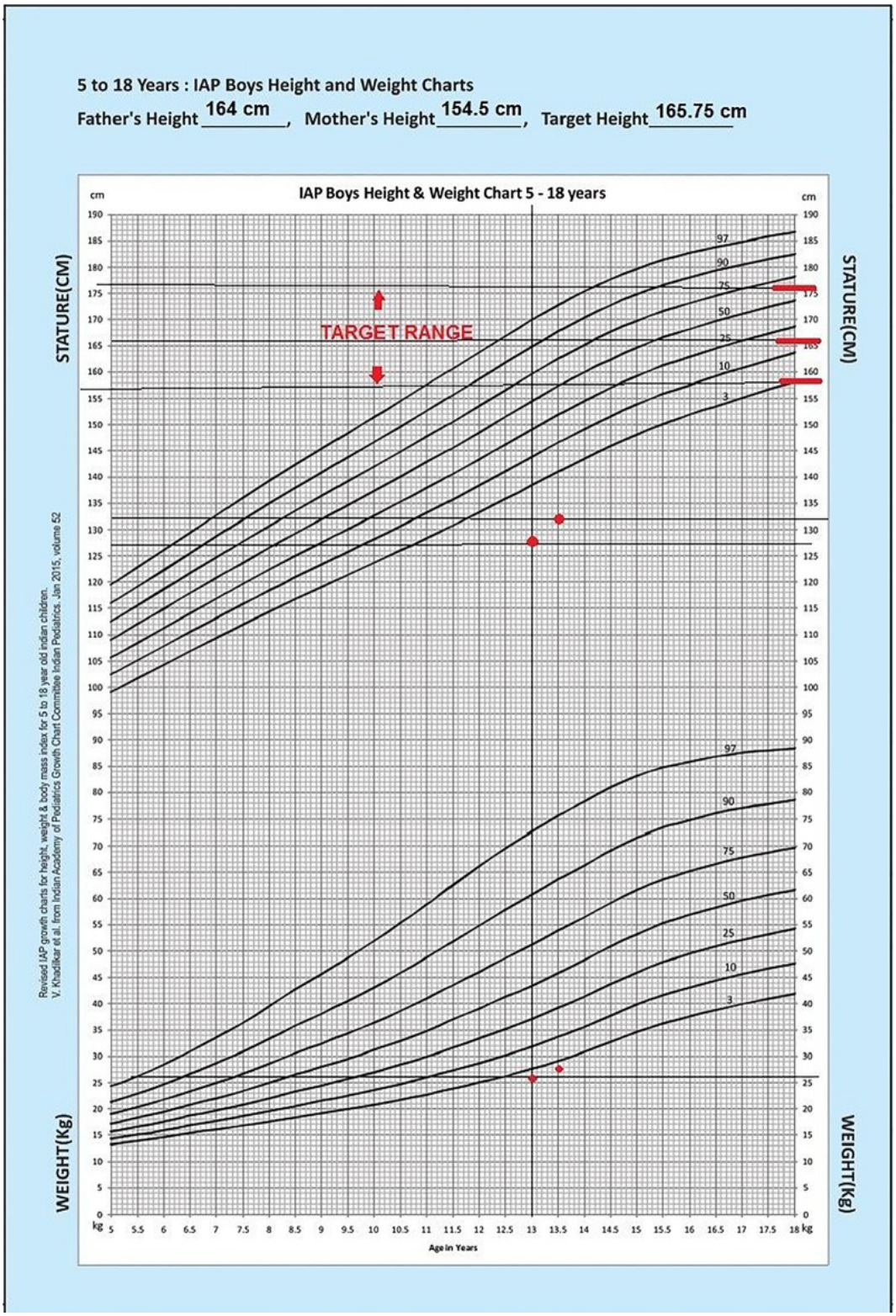

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Figure 1

Growth chart of patient 1. The patient had a height of 127.5 cm at the age of 13 years at the time of initial presentation. The height increased to 132.5 cm on follow-up after 6 months. The target height (calculated from using the formula: mean of father's and mother's height+6.5 cm) was 165.75 cm with a target range of 157.75–173.75 cm. His weight was 20 kg at presentation which increased to 23 kg on follow-up after 6 months.

The patient had hair which was lustreless and brittle and had progeria-like faces. He had no midline defect. The ear appeared deformed. The oral cavity had no enamel hypoplasia. The patient had no goitre. The skin had ichthyosis and desquamation was present. The nails appeared brittle (figure 2A, B). The chest appeared normal. The patient had no stigmata of rickets. The upper limb was normal and there was no rhizomelia, mesomelia, acromelia, wrist widening or Madelung deformity. The lower limb had no deformity. The brother of the patient (patient 2) had similar findings on physical examination.

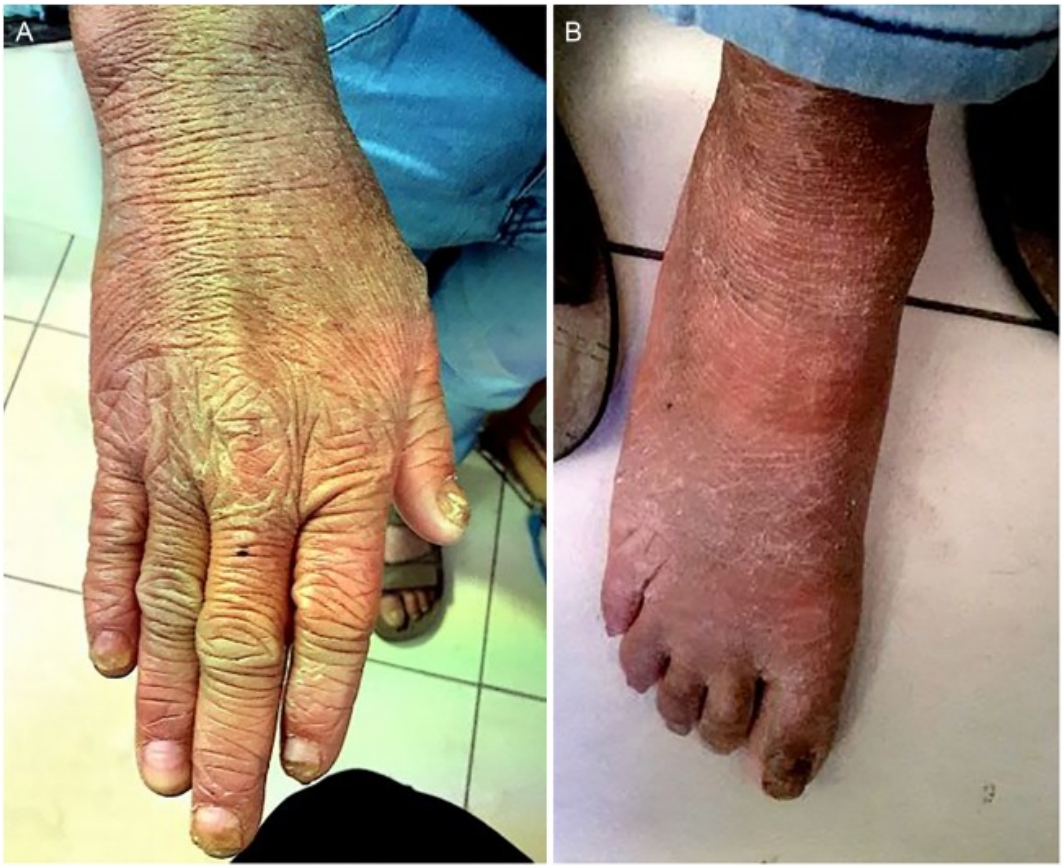

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Figure 2

(A and B) Hand and foot of patient 1 with hyperpigmentation, increased skin markings and skin thickening (lichenification) present on the dorsum of both hand and foot.

On developmental assessment, the patient had normal intelligence, gross motor skills, fine motor skills, language, social, visual and hearing. Dental development was normal. The patient had testicular volume of 3 mL and had no axillary hair or pubic hair, suggesting that the patient was prepubertal. The rest of the systemic examinations was normal. A dermatological consultation was also sought for the skin lesion.

In the presence of photosensitivity, congenital ichthyosis and short stature were considered the possibility of PIBIDS syndrome.

Investigations

Investigations were carried out for the following purpose: (1) to find the cause for the short stature; (2) to affirm the aetiology of the skin lesion and (3) to find any association between the two.

The patient was evaluated on the basis of our established protocol for short stature. The bone age of the patient was 13 years (Tanner-Whitehouse method), which corresponded to the chronological age. An

X-ray of the wrist and hand suggested osteopenia. His liver and thyroid function tests were normal. The clonidine stimulation test for growth hormone was carried out which revealed normal growth hormone response to stimulation. Patient 2 also underwent similar investigations. Since no endocrine cause was found in patient 1, it was decided not to carry out the clonidine stimulation test in patient 2. Table 1 shows the detailed list of initial and follow-up investigations carried out for both patients.

Table 1

Detailed list of investigations done for patients 1 and 2 to evaluate for short stature

	Initial investigations (patient 1)	Follow-up after 6 months (patient 1)	Initial Investigations (patient 2)	Follow-up after 6 months (patient 2)	Normal range
Haemoglobin	12.7 g/dL		12.6 g/dL		11.5–15.5 g/dL
Serum creatinine	0.8 mg/dL		0.7 mg/dL		0.5–1.4 mg/dL
Free T4	1.3 ng/dL		0.95 ng/dL		0.5–2.0 ng/dL
Thyroid-stimulating hormone	2.0 mIU/mL		1.8 mIU/mL		0.5–5.0 mIU/mL
Clonidine stimulation test for growth hormone (GH)	1.2 ng/mL (baseline) 8.2 ng/mL (30 min) 10.5 ng/mL (60 min)				Peak GH >10.0 ng/mL—normal
25 hydroxy vitamin D	5.5 ng/mL	44.4 ng/mL	7.2 ng/mL	33.2 ng/mL	<20 ng/mL—deficient 21–30 ng/mL–Insufficient >30 ng/mL—sufficient
Parathyroid hormone	543 pg/mL	59.1 pg/mL	97 pg/mL	60 pg/mL	12–72 pg/mL
Serum calcium	7.73 mg/dL	9.65 mg/dL	8.7 mg/dL	10.2 mg/dL	8.2–10.4 mg/dL
Serum phosphorus	3.26 mg/dL	5.16 mg/dL	4.5 mg/dL	5.5 mg/dL	4.5–5.5 mg/dL
Alkaline phosphatase	568 IU/L	262 IU/L	206 IU/L	182 IU/L	114–390 IU/L
Aspartate aminotransferase/alanine transaminase	28/19 IU/L		28/18 IU/L		0–40 IU/L
IgA anti tissue transglutaminase	1.0 U/mL		0.8 U/mL		<4 U/mL
Serum IgA	102 mg/dL		98 mg/dL		42–295

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For confirming the diagnosis of trichothiodystrophy, the hair shaft was examined under polarised light microscopy. It showed a characteristic hair tiger-tail appearance which confirmed the diagnosis.

Genetic testing was offered for the children. However, owing to the prohibitive cost of the investigations, the parents did not consent to the tests.

Differential diagnosis

The patient was having short stature which was proportionate and did not have any dysmorphic features. Both the weight and height were below the 3rd centile with both the weight-age and the height-age of around 8 years. The bone age corresponded to the chronological age. In such a scenario, the most likely diagnosis would have been short stature due to undernutrition or secondary to chronic systemic illness.

A possibility of occult Cushing's syndrome because of the use of corticosteroid containing creams, ointments or medications was considered. However, the children had no clinical features suggestive of Cushing's syndrome apart from the short stature. Also, there was no history of use of any such therapies either by prescription or occult use.

Endocrine causes of short stature-like growth hormone deficiency and hypothyroidism lead to a delay in the bone age which was not seen in this case. Constitutional delay in puberty also leads to delay in bone age. Achondroplasia leads to a disproportionate short stature and Russell-Silver syndrome has characteristic dysmorphic features.

As the skin lesions were present from birth, the dermatological differential diagnosis included congenital syndrome, Lamellar ichthyosis, Refsums syndrome, Sjögren-Larsons syndrome, X linked ichthyosis, bullous ichthyosiform erythroderma and non-bullous ichthyosiform erythroderma. Cockayne syndrome was also considered as a differential diagnosis since the patient had short stature as well as photosensitivity. However, since the patient had multiple features of PIBIDS syndrome with characteristic features on polarised light microscopy, the other conditions were ruled out.

Treatment

As the patient had severe vitamin D deficiency with secondary hyperparathyroidism, correction of vitamin D deficiency was the first priority. The patient was given cholecalciferol sachets in a dose of 60 000 units once a week for 8 weeks followed by once every fortnight.

As the patient had ichthyosis, he was prescribed topical emollients. The patient had photosensitivity for which he was advised photoprotection and was given a broad spectrum sunscreen. Oral non-sedative antihistamine fexofenadine was given in the dose of 120 mg once daily.

Outcome and follow-up

The children followed up with us after 6 months. Patient 1 had a height gain of 5 cm on follow-up with a growth velocity of 10 cm/year. The vitamin D and parathyroid levels had normalised. Patient 2 gained 4.4 cm in height (growth velocity of 8.8 cm/year) and also had normalisation of both vitamin D and parathyroid levels. The children continue to be on vitamin D supplements and are advised to follow-up again after 6 months.

On follow-up, the lichenification had reduced to a great extent. There was also a symptomatic improvement in photosensitivity and itching. Oral antihistamines were stopped, but the sunscreen lotion was continued.

Discussion

Trichothiodystrophy is a congenital disorder characterised by ichthyosis, brittle hair, intellectual impairment, decreased fertility and short stature. It is also known as Tay syndrome or PIBIDS syndrome. It is an autosomal recessive disorder. The classical finding of trichothiodystrophy is the presence of short and brittle hair which on examination by polarised microscopy gives a ‘tiger-tail’ appearance due to alternating dark and light bands. Trichoschisis may also be found. Our patient had photosensitivity, ichthyosis and short stature. So the possibility of trichothiodystrophy was considered. However, the intellectual development was normal.

Short stature is a vital component of PIBIDS syndrome and trichothiodystrophy. In a systemic review of reported cases of trichothiodystrophy, Faghri *et al* reported that 81% of cases have some growth

abnormality in the form of short stature and/or reduced weight. The authors also reported that 14% of the patients did not have any form of intellectual impairment.[1]

One of the important sources of vitamin D is sunlight. When ultraviolet B rays from the sun fall on the skin, provitamin D is converted to previtamin D.[2] It is our belief that the short stature in trichothiodystrophy may have some association with vitamin D deficiency. Vitamin D deficiency in our patients was severe and associated with secondary hyperparathyroidism. Correction of vitamin D deficiency also resulted in these children gaining a considerable amount of height. Frascari *et al* conducted a study on vitamin D deficiency in children with congenital ichthyosis. They reported that 88.7% of patients with congenital ichthyosis had vitamin D levels below the optimal level of 30 ng/mL.[2] A similar result was found in a study conducted by Ingen-Housz-Oro *et al*[3] who reported a prevalence of vitamin D deficiency in all the patients with congenital ichthyosis which they studied. Chouhan *et al*[4] studied 45 Indian children with ichthyosiform erythroderma due to keratinising disorders and found that vitamin D deficiency, secondary hyperparathyroidism and clinical rickets were more common in these children compared to matched controls. Vitamin D deficiency in children (Rickets) is well known to cause short stature. Vitamin D deficiency could be one of the treatable causes of short stature in trichothiodystrophy and other congenital ichthyosis syndromes.

Learning points

- Presence of photosensitivity, ichthyosis, brittle hair, intellectual impairment, decreased fertility and short stature points to a rare syndrome called PIBIDS syndrome (a form of trichothiodystrophy).
- Vitamin D levels must be checked in all children with congenital ichthyosis, especially those with PIBIDS syndrome.
- Vitamin D deficiency may be one of the treatable causes of short stature in PIBIDS syndrome.

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Footnotes

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