Pseudohypoparathyroidism: a case report and family study

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IN 1942, ALBRIGHT and his associates described three patients with characteristic somatic features and hypoparathyroidism. Injection of parathyroid extract in these patients produced a poor phosphaturic response in comparison to that evoked in idiopathic hypoparathyroidism. They suggested, therefore, that these patients did not have a deficiency of parathyroid hormone (PTH) but rather an end organ refractoriness to the effects of PTH. This hypothesis was further supported by the finding of normal parathyroids in one of these subjects and they described the disorder as pseudohypoparathyroidism. This paper records the first case and family study of pseudohypoparathyroidism reported in Malaysia. Tan and Cheah reported a similar case from Singapore in 1967.

History

L.K.H., a 12-year-old Chinese male, was first admitted to the University Hospital, Kuala Lumpur, on 6th July, 1970 with a history of recurrent generalised fits since May 1969. His milestones were normal and he had an average school performance in a regular school. He had a febrile fit in 1958 at the age of six months, but had remained well from then till May 1969. Since then, he had suffered about 11 fits. There was no history of paraesthesiae or carpo pedal spasms.

Physical examination

His height was 127.5 cm. (less than 10th percentile on the Malaysian scale) (Chen) and weight 29.2 kg. (30th percentile on the Malaysian scale) (Chen). The patient was thus short and stocky. His facies was round (Fig. 1) and the fingers of both hands, particularly the fourth and the fifth digits, were short and thick (Fig. 2). The finger nails were short and broad, especially those of the thumbs. The eyes showed bilateral pseudopapilloedema, with no enlargement of the blind spot. His chest was thickset. Chvostek's sign was positive but Trousseau's sign was negative. The central

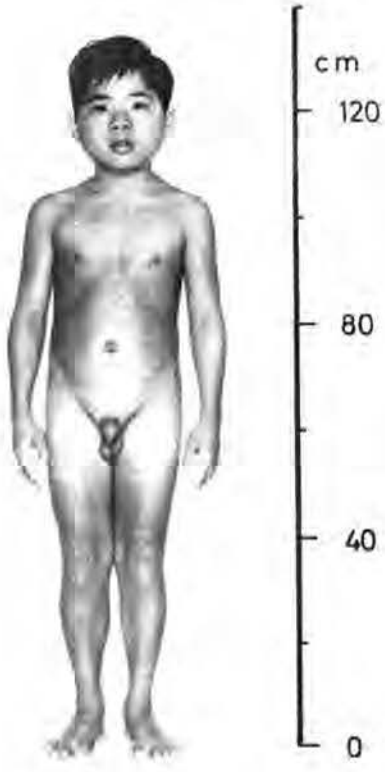

Fig. 1
Patient showing round facies and short stature.

nervous system was normal. Exostoses were noted in the lateral aspect of the sole of the left foot and between the thumb and index finger of the right hand. His dental formula was:

UJ	2	1	0	3
	2	1	0	3
LJ	2	1	0	2
	2	1	0	1

Laboratory investigations

Full blood count and urinalysis were normal. Serum calcium was low 3.6 mEq/L (normal 4.7 — 5.5 mEq/L) and inorganic phosphate high 6.2 MgP% (normal 2.2 — 4.6 MgP%). His serum magnesium was normal 1.5 mEq/L. (normal 1.4 — 2.2 mEq/L). Phosphaturia as measured by the phosphate excretion index (Nordin and Smith) was very low, minus 0.21 (normal ± 0.09). His blood urea was 20 mg%. The alkaline phosphatase and acid phosphatase were 17 KA units/100 ml. and 5.9 KA units/100 ml. respectively. The electrocardiogram showed a prolonged QTc of 0.54 seconds. His waking electroencephalogram revealed occasional paroxysmal bilateral synchronous theta activity which was also present with some spikes intermixed during hyperventilation, suggesting an epileptiform disturbance of primary subcortical origin. Sleep electroencephalogram was normal.

Radiological investigations

The hands and feet showed abnormally short metacarpals and metatarsals especially of the fourth and fifth digits (Fig. 3). Soft tissue calcification was evident in the periarticular soft tissue of the right second metacarpophalangeal joint. His teeth showed delay in eruptions of the canines on both sides of the lower jaw. In the upper jaw, three deciduous teeth was still present. The skull and chest were normal.

Family study

The patient's mother and three of the five siblings were physically examined and blood samples were taken for serum calcium and inorganic phosphate. They were all found to be normal except for one elder sister, aged 16 years. She was asymptomatic. On examination, she was noted to be obese with a round facies and short stature. Her height was 147.3 cm. Her fingers were short, especially the fourth and fifth digits. Her fundi were normal. Chvostek's and Trousseau's signs were negative. Her serum calcium was 4.7 mEq/L and inorganic phosphate 2.6 mgP%. Roentgenograms of the hand demonstrated marked shortening of the metacarpals, especially of the fourth and fifth digits. This sibling thus showed somatic features of pseudohypoparathyroidism without the biochemical features and would thus fit in the category of pseudo-pseudo- hypoparathyroidism as described by Albright, Forbes and Henneman in 1952.

Discussion

The features of pseudohypoparathyroidism have been well reviewed by Cohen and Donnell (1960) and Papaioannou (1963). The main somatic features of this syndrome include short stature, obesity, a round facies and short metacarpals and metatarsals. Mental retardation may also occur. Tetany, convulsions or combination of the two were reported in 88% of the cases. The short broad finger nails of the thumbs seen in the patient reported here is also a striking clinical feature.

Radiologically, the most common abnormalities are shortening of metacarpals and metatarsals, soft

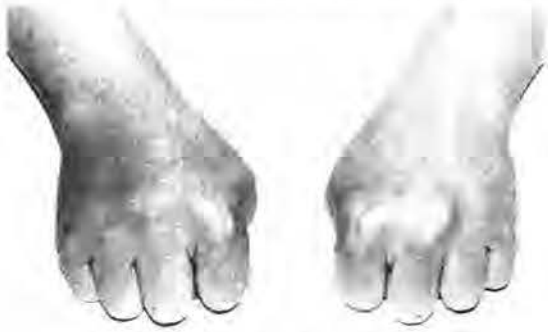

Fig. 2
Hands showing inspicuous 4th and 5th knuckles due to short 4th and 5th metacarpals.

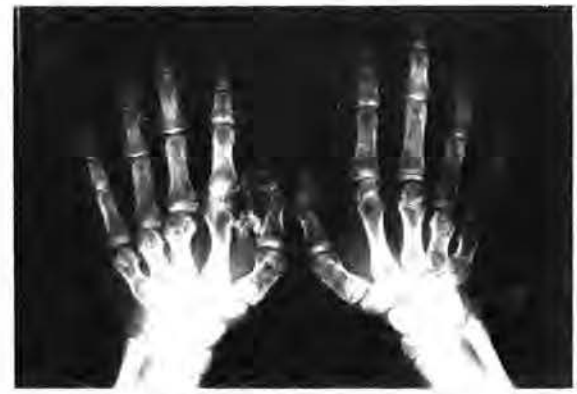

Fig. 3
Roentgenograms of the hands showing brachydactylia with short 4th and 5th metacarpals. Exostoses between thumb and index finger of left hand are also seen.

tissue calcification, cerebral calcification and abnormalities in dental development.

The most consistent biochemical abnormalities are an elevated serum inorganic phosphate, low serum calcium and low phosphaturia. The low level of phosphaturia does not usually respond to injections of parathyroid hormone (Ellsworth Howard Test) but this feature is not consistently found (Mamou and See).

The somatic, radiological and biochemical features in this patient are clearly consistent with the diagnosis of pseudohypoparathyroidism. Familiai occurrence of pseudohypoparathyroidism or the closely related syndrome of pseudo-pseudohypoparathyroidism is well recognised (Cusmano, Talbot, Lackmann). In the case reported, the patient's sister, aged 16 years, shows definite evidence of pseudo-pseudohypoparathyroidism. Inheritance is thought to be a sex-linked dominant transmission (Schwarz and Bahner).

Treatment and progress

The patient was treated with a high calcium and a low phosphate diet consisting of calcium 2mEq/Kg body weight per day and phosphorus less than 600 mg. per day. He remained free of fits on the above diet and the fundi reverted back to normal after ten weeks. However, Chvostek's sign was still positive.

Dihydrotachysterol 25,000 units per day was then added to this regime. Fourteen weeks after initiating this treatment, his serum calcium was 4.0 mEq/L and inorganic phosphate 5.9 mgP/100 ml.

Summary

A case of pseudohypoparathyroidism is reported. He presented with generalised fits and was found to have the characteristic somatic, radiological and biochemical features of pseudohypoparathyroidism. A family study showed one sister to have the characteristic somatic, radiological and biochemical features of pseudo-pseudohypoparathyroidism.

Acknowledgement

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