Pseudopseudohypoparathyroidism: A case report

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Introduction:

Idiopathic hypoparathyroidism is due to a deficiency of parathyroid hormone with elevation of serum phosphorus and depression of serum calcium levels resulting in tetany. However administration of parathormone results in a six to ten fold increase in inorganic phosphate excretion (Ellsworth-Howard Test.)[1]

In 1942, Albright et al.[2] described a group of patients with biochemical findings of hypoparathyroidism together with a short and stocky stature, round face, short metacarpal and metatarsal bones, mental deficiency, calcification in the basal ganglia and subcutaneous tissues. There was no increased phosphaturic response to the administration of parathormone, which suggested an 'end organ defect'. Albright et al. called this pseudohypoparathyroidism. Pseudohypoparathyroidism was alluded to in the original communication as an example of the "Seabright Bantam Syndrome" after a species of cockerel in which the male bird developed female plumage despite a normal level of circulating male hormones.

Then, in 1952, Albright et al.[4] reported a syndrome with the somatic and radiological features of pseudohypoparathyroidism but without hypocalcaemia and hyperphosphataemia which was named pseudopseudohypoparathyroidism.

Wong[5] reported a case of pseudohpoparathyroidism, and pseudopseudohypoparathyroidism in the patient's elder sister. This paper reports yet another case of pseudopseudohypoparathyroidism which may well be the second in Malaysia medical literature.

History:

T.C.J., a 13 year old Chinese female was seen on 18th March 1974 at the General Hospital, Penang with a history of itchiness, generalized fits "since birth" and mental deficiency. On direct questioning her parents were not able to give the age of onset of fits. The fits were usually precipitated by fever. She had not experienced any fits for the past five years. She was delivered by forceps after a normal full term pregnancy. Milestones were all delayed. She spent only 3 years at school as she had persistently performed badly, and was in a Home for retarded children for 1 month. She was second in a family of four. There were no similar complaints nor similar physical abnormalities in other members of the family.

Physical Examination:

The patient was of stocky build. The height was 4' 6" and the weight 82 lb. The face was round. There were widespread pigmented lesions secondary to recurrent impetigo. The skull showed frontal bossing, scaphocephaly and facial asymmetry. The uvula was *bifid*. The thyroid was not enlarged. The 4th and 5th metacarpals were short in both hands and there was deformity of the (L) 4th toe due to shortening of the (L) 4th metatarsal. Chvostek's and Trousseau's signs were negative. She was mentally subnormal. Examination of the other systems did not reveal any abnormalities.

Laboratory Investigations:

Serum Calcium was 9.7 mg per 100 ml. Inorganic phosphate was 3.8 mg per 100 ml. Exami-

nation of the urine did not reveal any abnormal findings.

Radiological Investigations:

Radiographs of hands showed shortened 4th and 5th metacarpals of both hands and of (L) 4th metatarsal.

A Skull Radiograph showed scaphocephaly and exaggeration of the convolutional markings. There were no intracranial calcifications. Radiographs of the chest and pelvis did not reveal any abnormalities.

Discussion:

This girl had the clinical and biochemical features consistent with the diagnosis of pseudo-pseudohypoparathyroidism, namely a shocky build, round face, short metacarpals and metatarsal, mental deficiency, normal serum calcium and inorganic phosphate. The history of fits was significant too, as it is a recognised associated symptom in cases of both pseudo and pseudopseudohypoparathyroidism. Whether tetany was a contributory factor in the aetiology of the fits could not be ascertained. Apart from the usual clinical findings of this syn-

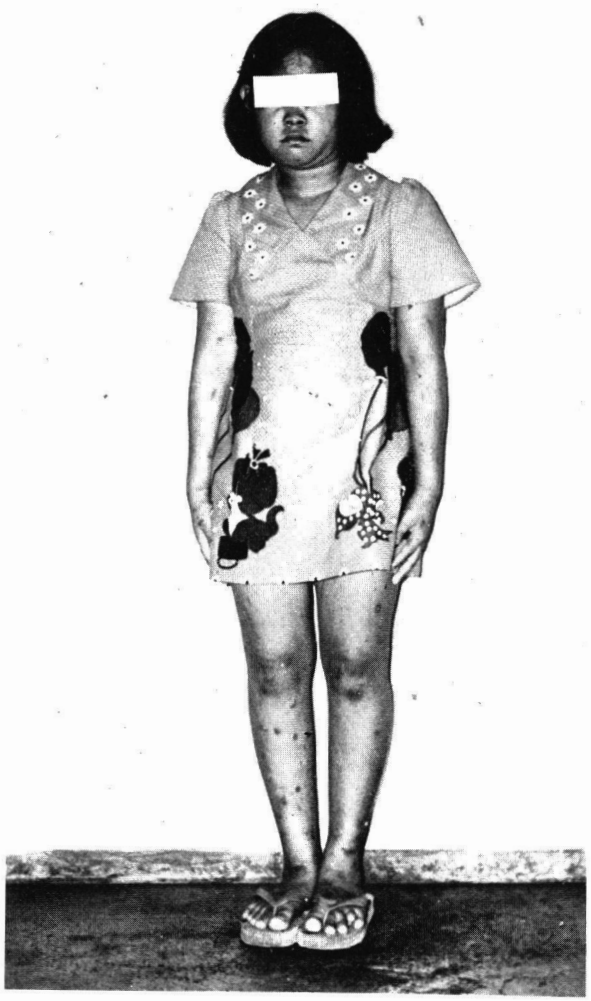

Fig. 1. Patient with Round Face and Stocky Build.

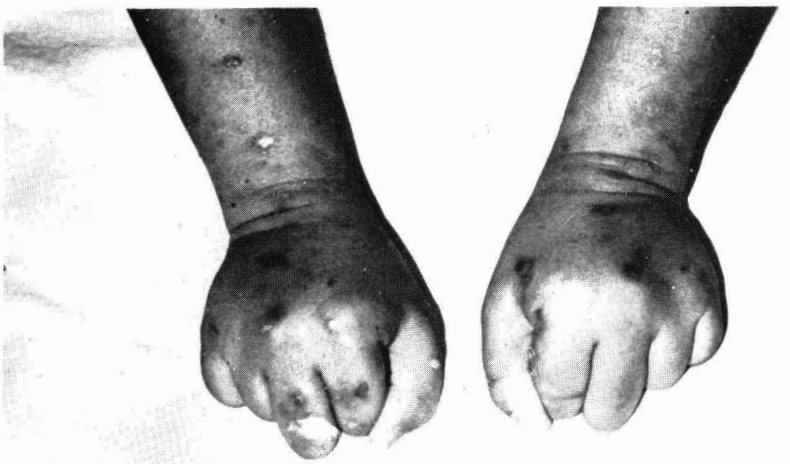

Fig. II. Both Hands showing Absence of the 4th & 5th Knuckles due to shortening of 4th and 5th Metacarpals.

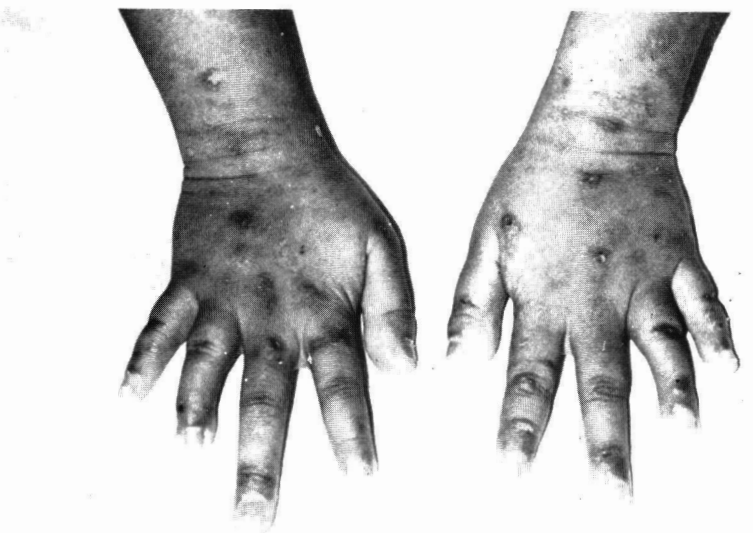

Fig. III. Short 4th and 5th Fingers of Both Hands.

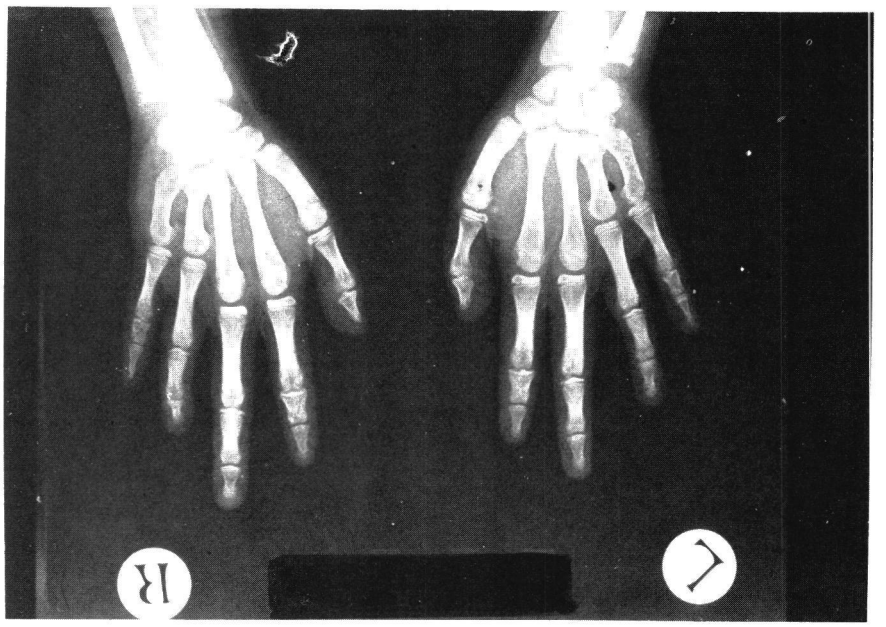

Fig. IV. Radiograph Showing Short 4th and 5th Metacarpals of Both Hands.

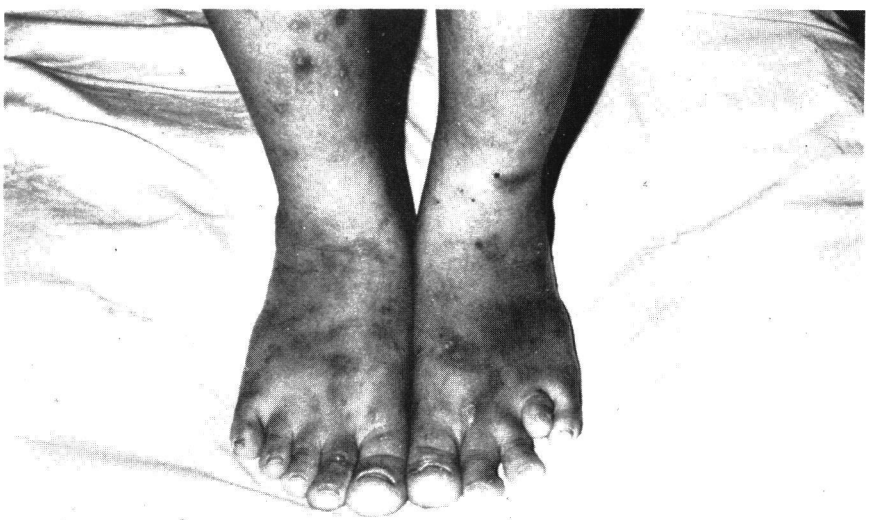

Fig. V. Deformity of Left 4th Toe due to Shortening of Left 4th Metatarsal.

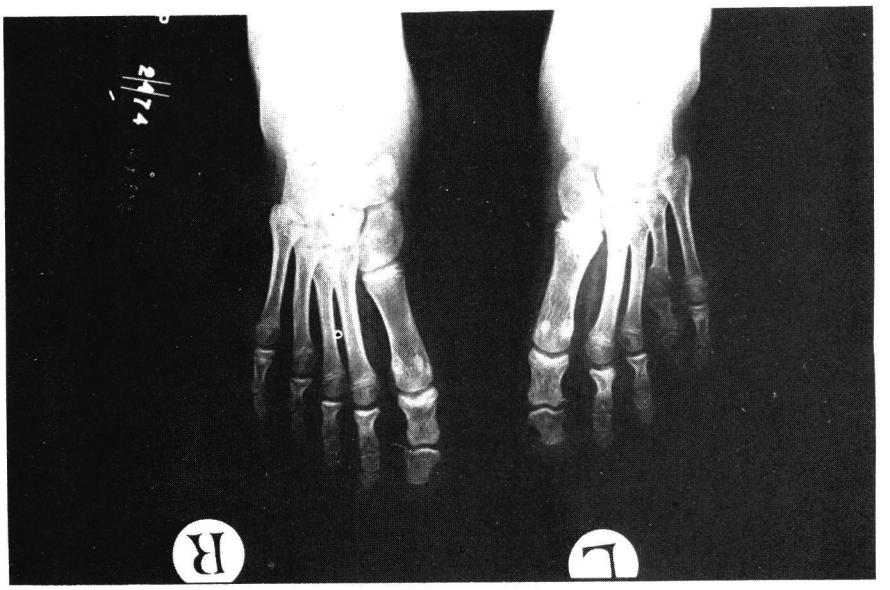

Fig. VI. Radiograph Showing Shortening of Left 4th Metatarsal.

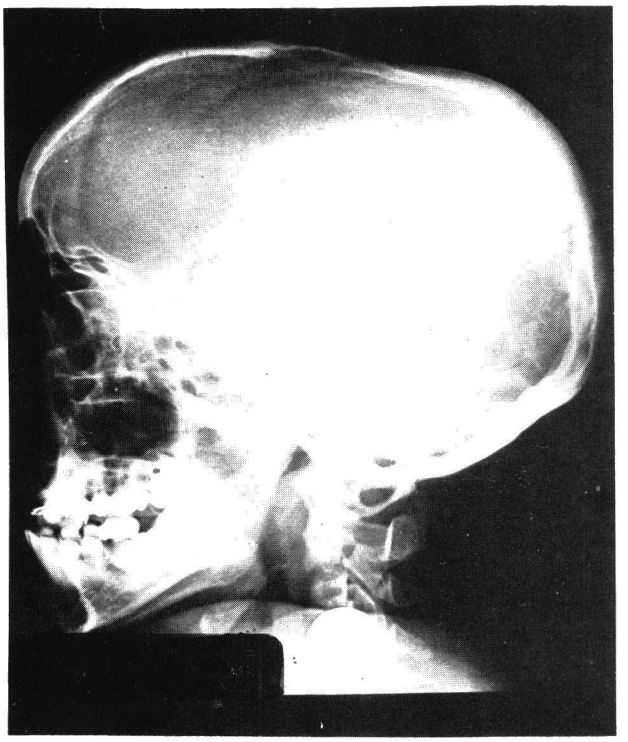

Fig. VII. Radiograph of Skull showing Scaphocephaly and Exaggeration of Convolutional Markings.

drome, this patient had in addition, a bifid uvula, scaphocephaly and exaggeration of the convolutional markings of the skull, both the latter features being suggestive of *craniostenosis.* Craniostenosis could have been significant in the causation of mental retardation and convulsions in this patient.

Cohen et al.[3] summarized the clinical features of pseudohypoparathyroidism as:-

1) Clinical & laboratory evidence of parathyroid insufficiency without evidence of renal diseases, steatorrhea or generalized osteomalacia and with little or no response to parathormone.
2) Shortening of the metacarpal and metatarsal bones.
3) Short, thick set appearance, round facies and mental retardation.
4) Soft tissue calcifications in subcutaneous areas and in the basal ganglia.

Other features include dental aplasia, delayed dentition and lenticular calcification. Diffuse electroencephalographic abnormalities may also occur (Miles et al.)[9]

Cusmano et al.[6] summarized the radiological features of pseudohypoparathyroidism which include shortening of metacarpals and metatarsals, calcification of basal ganglia, soft tissue calcifications, thickening of the calvarium with widening of the diploe space and miscellaneous findings such as bowing of extremities, osteoporosis, exostoses and accelerated osseous maturation. Other findings include osteosclerosis, coarse bony trabeculation and severe genu valgum. Clinical features of both pseudohypoparathyroidism and pseudopseudohypoparathyroidism have also been summarized by Mann et al.[7] and Papaioannou et al.[8] It is of interest to note that the features of bifid uvula and craniostenosis have not been reported in any of the earlier reviews of the condition[3,6,7,8].

The genetics of the complete syndrome of pseudohypoparathyroidism is currently explained by a sex linked dominant mode of inheritance and the incomplete syndrome of pseudopseudohypoparathyroidism is the incomplete expression of this mode of inheritance (Mann et al.)[7] The variability of the expression of the syndrome was documented by Gershberg et al.[10] who described a patient with the complete syndrome of pseudohypoparathyroidism at the age of 14, the severity of which diminished subsequently with normal serum calcium and inorganic phosphate, and had not required treatment until she was pregnant at the age of 20 when she was hypocalcaemic. Ray et al.[11] reported a case of pseudopseudohypoparathyroidism in a 7½ year old child with elevated serum phosphate but normal serum calcium. The patient later developed significant hypocalcaemia. The original diagnosis was later changed to be pseudohypoparathyroidism. Gershberg and Weseley[10] thus suggested that the two conditions were different forms of the same disease with pseudohypoparathyroidism being the more severe form, and pseudopseudohypoparathyroidism being the form in which hypocalcacima and tetany appeared only during periods of increased calcium demand such as growth and pregnancy. The sex distribution in both forms is 2:1 in favour of females. Differential diagnosis includes hereditary multiple exostoses, myositis ossoficans progressiva, multiple epiphyseal dysplasia, familial calcification of the basal ganglia and Turner's syndrome[7,12,13]. Pseudohypoparathyroidism has to be treated with dietary calcium and dihydrotachysterol while pseudopseudohypoparathyroidism needs no treatment.

Summary:

A 13 year old female having the features of pseudopseudohypoparathyroidism with craniostenosis and bifid uvula, is reported together with a brief review of the literature regarding clinical features, mode of inheritance and differential diagnosis of pseudohypoparathyroidism and pseudopseudohypoparathyroidism.

Acknowledgements:

I wish to thank the Director-General of Medical and Health Services, Malaysia, Tan Sri Datuk (Dr.) Haji Abdul Majid Ismail and Dr. V. Rudralingam, Consultant Physician, Medical Unit II, General Hospital, Penang for permission to publish this paper, and Dr. G. S. Dhillon, Consultant Radiologist, General Hospital, Penang for assistance in reading the radiographs.

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