CASE REPORT

Pseudohypoparathyroidism: A case of hypocalcemia and hypothyroidism diagnosed during the postpartum period

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Abstract

We describe a 29-year-old Para 1 post-Emergency Lower Segment Caesarean Section (EMLSCS) for fetal distress and Preterm Rupture of the Membrane (PROM) referred by the Obstetric team for persistent bradycardia. She had the typical features of Albright's Hereditary Osteodystrophy (AHO). The laboratory investigation revealed hypocalcemia, hyperphosphatemia with a high Parathyroid hormone (PTH) level and low free Thyroxine 4 (fT4) with high Thyroid Stimulating Hormone (TSH). The patient was diagnosed with Pseudohypoparathyroidism (PHP) Type 1A associated with TSH resistance based on the somatic features of AHO present as well as biochemical and radiological abnormalities.

Introduction

Pseudohypoparathyroidism (PHP) is a heterogeneous group of disorders defined by targeted organ (kidney and bone) insensitivity to parathyroid hormone (PTH). It is characterized by hypocalcemia, hyperphosphatemia and an elevated serum concentration of parathyroid hormone (PTH).[1] PHP can be subdivided into several distinct entities (Types 1A, 1B, 1C and 2) and pseudo-pseudohypoparathyroidism (Pseudo-PHP). PHP Type 1A is caused by the loss of function of one allele of the gene encoding the stimulatory G protein alpha subunit (Gsα), which, in turn, blunts the response of urinary Cyclic Adenosine Monophosphate (cAMP) to exogenous PTH. It is associated with primary hypothyroidism and hypogonadism due to the malfunction of the G protein leading towards resistance to Thyroid Stimulating Hormone (TSH), Lutenising Hormone (LH) and Follicle Stimulating Hormone (FSH).

PHP Types 1A and 1C both have features associated with Albright's Hereditary Osteodystrophy (AHO) and are characterized by heterogeneous clinical findings, such as brachydactyly, rounded face, short stature, central obesity and subcutaneous calcifications in conjunction with variable levels of mental retardation.[2,3] PHP Type 1B can be easily differentiated clinically from PHP Types 1A and 1C through the presence of normal phenotype/somatic features. The differentiation between PHP Type 1A and PHP Type 1C requires genetic analysis of erythrocyte Gsα activity.[1] Type 2 PHP is characterized by resistance to PTH in the absence of AHO, along with resistance to other hormones, while pseudo-PHP is characterized by the presence of AHO and the absence of any hormone resistance.[1]

Case report

A 29-year-old Para 1 post- Emergency Lower Segment Caesarean Section (EMLSCS) for fetal distress and Preterm Rupture of the Membrane (PROM) was referred by the Obstetric team for persistent bradycardia. She was previously healthy and well. She booked late at the antenatal clinic at 28 weeks. She denied any hypocalcemic, hypothyroid and hypogonadal symptoms antenatally; however, bradycardia was recorded in her antenatal book. She had normal, regular menses and had planned for this pregnancy since marrying in 2015. Her family history was unremarkable. She had had learning disabilities since childhood, and she did not complete her primary school education. She is a housewife and is able to perform daily housework.

On examination, her vital signs were stable with bradycardia at 50-55 beats per minute. Anthropometry showed proportionate short stature (**Figure 1**), with a height of 114 cm and weight of 44 kg. Her body mass index (BMI) was 34 kg/m^2. She had typical features of AHO, which included round face, short stature and neck, obesity, brachydactyly with shortened metacarpals and metatarsals, and

Fig. 1 Features of AHO include short stature, disproportionate shortening of the limbs, and round, flattened face.

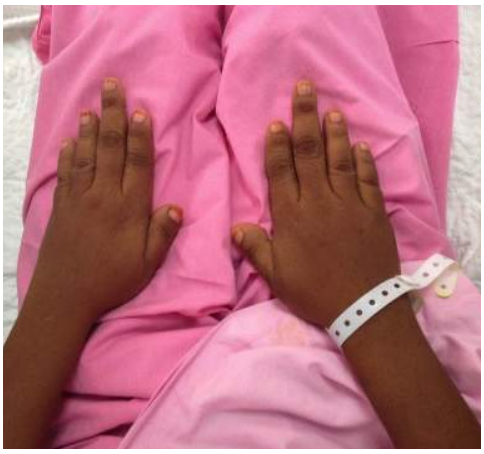

Fig. 2 Brachydactyly of both hands, with the shortened 4th and 5th fingers, the greatly foreshortened terminal 1st digit, and short, wide thumbnail (potter's thumb).

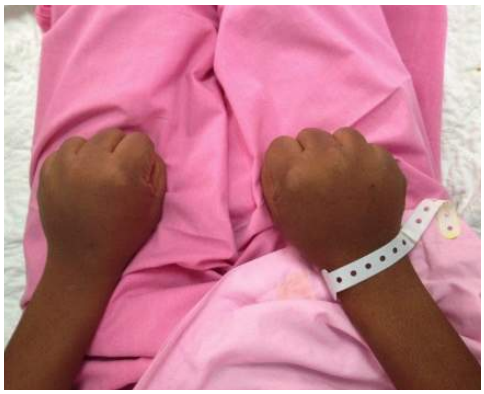

Fig. 3 Fist with the characteristic 'dimples' over the 4th and 5th digits replacing the knuckles formed by the distal head of normally-sized metacarpal bones (Archibald sign).

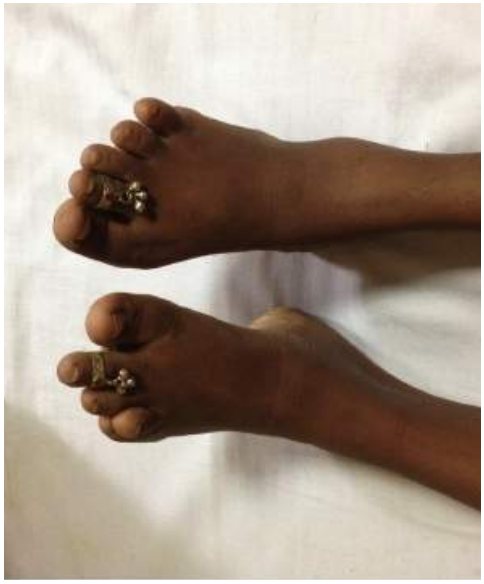

Fig. 4 Brachydactyly of the feet, with the short 4th and 5th toes.

a slight learning disability (**Figure 1-4**). No goitre was present, and her deep tendon reflexes were normal. Chvostek and Trousseau's signs were negative. Her cardiovascular, respiratory and abdominal examinations were unremarkable.

The laboratory results were as follows:

corrected Calcium	1.87 mmol/L (Normal Range (NR) 2.1-2.6)
Phosphate	1.81 mmol/L (NR 0.87-1.5)
PTH	18.1 pmol/L (NR 1.6-6.9)
Creatinine	63 mmol/L (NR 53-106)
fT4	10.62 mIU/L (NR 11.8-23.2)
TSH	17.3 mIU/L (NR 0.35-5.5)
Antithyroid Peroxidase	Negative

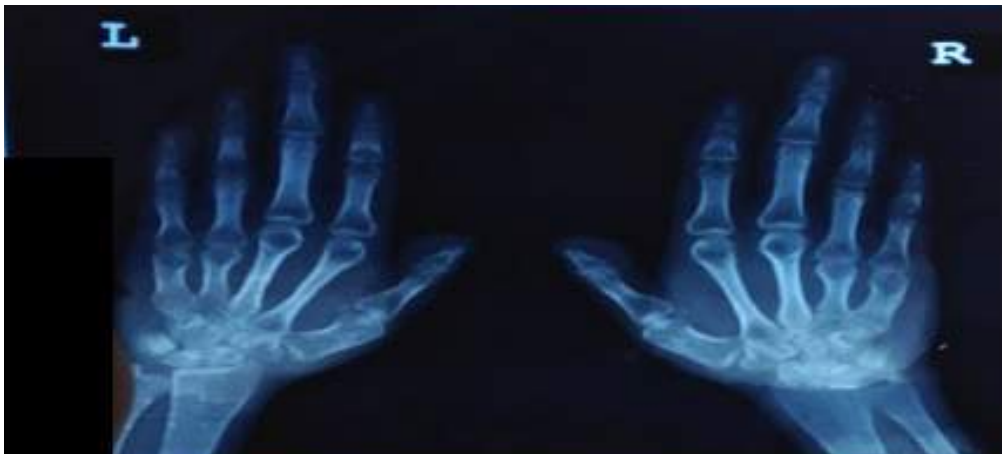

Fig. 5 Hand radiography showed bilateral shortening of fourth and fifth metacarpal bones.

Hand radiography showed bilateral shortening of the fourth and fifth metacarpal bones (**Fig. 5**). The patient was diagnosed with PHP Type 1A associated with TSH resistance on the basis of the somatic features of AHO and biochemical abnormalities.

She was treated with levothyroxine, a calcium supplement and activated Vitamin D. Family screening was planned, and her newborn was referred to a pediatrician for screening.

Discussion

PHP is a heterogeneous disorder with a variety of manifestations. The prevalence of the disorder is about 0.79 per 100,000.[1] In 1942, Fuller Albright first introduced the term pseudohypoparathyrodism to describe patients with hypocalcemia and hyperphosphatemia with normal renal function who had no calcemic and phosphaturic response to bovine parathyroid extract as compared to hypoparathyroid patients.[4]

PHP1A is characterized by parathyroid hormone resistance (elevated PTH in spite of the hypocalcemia and hyperphosphatemia; poor cAMP and phosphaturic response to exogenous PTH administration) along with the features of AHO described above.[1] The elevated serum concentration of PTH in a patient with hypocalcemia, hyperphosphatemia, and normal renal function excludes hypoparathyroidism and is suggestive of PHP. Often a definitive diagnosis requires careful examination of radiographs of the hands and feet.

PHP Type 1A is also associated with primary hypothyroidism and hypogonadism due to the malfunction of the G protein, leading towards resistance to TSH, LH and FSH.[5-6] Typically, the patients do not have goiters and the antithyroid antibodies are negative. The Serum fT4 level may be low or low-normal with elevated TSH.[4] Hypothyroidism may occur early in life prior to the development of hypocalcemia. Reproductive dysfunction occurs commonly in subjects with PHP Type 1A. Unlike this patient, women may exhibit delayed puberty, oligomenorrhoea, and infertility. Features of hypogonadism may be less obvious in men, but fertility appears to be decreased, as well.[5]

The long-term treatment of hypocalcemia in patients with hypoparathyroidism involves the administration of oral calcium and activated vitamin D. Treatment of PHP and pseudo-PHP is similar to that of hypoparathyroidism, except that the doses of vitamin D and calcium are usually lower than those required in true hypoparathyroidism.[7] The goals of therapy are to maintain normal thyroid function and serum calcium and phosphate concentration.

Hypothyroidism has been associated with an increased risk of several complications in pregnancy, including low birth weight, preeclampsia, gestational hypertension, preterm delivery, increased rate of cesarean section, postpartum hemorrhage, perinatal morbidity and mortality as well as neuropsychological and cognitive impairment in the child.[8-9] On the other hand, a recent meta-analysis of 12 studies found that routine calcium supplementation during pregnancy may reduce the risk of pre-eclampsia and maternal mortality. The effect was more marked in women at high risk of calcium deficiency.[10]

The patient was asymptomatic for hypothyroidism and hypocalcemia throughout her childhood and pregnancy, resulting in no

earlier attention. Furthermore, she was able to conceive despite the possible gonadotropic resistance associated with PHP Type 1A. However, she did present with asymptomatic bradycardia during antenatal follow up. Early diagnosis could not only have led to prompt treatment for this patient, but it can also reduce obstetric risks and complications of hypothyroidism as well as hypocalcemia for both the mother and her fetus.

Conclusion

Early recognition of PHP is essential to prevent delay of the diagnosis and treatment, further reducing the risks of obstetric complications.

Conflict of interest

The authors declare that there is no conflict of interest.

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How does this paper make a difference to general practice?

- It creates awareness among clinicians regarding pseudohypoparathyroidism (PHP) as a rare disease involving hypocalcemia and hypothyroidism.
- It highlights the implications of undiagnosed hypocalcemia and hypothyroidism for a pregnant mother and her fetus.
- It shows that a thorough history taking and physical examination, including heart rate monitoring, would have led to further investigation in this particular case.
- An early high index of recognition of PHP can prevent delay of the diagnosis and treatment.
- It also emphasizes the importance of family and genetic screening in patients with PHP.

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