CASE REPORT

ALBRIGHT HEREDITARY OSTEODYSTROPHY: A CASE REPORT

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PJR July - September 2022; 32(3): 168-171

ABSTRACT

Parathyroid hormone is a vital hormone that maintains calcium and phosphorous balance in the body. It acts on the kidney through distal tubule calcium resorption, bone resorption, and increased production of 1,25 hydroxy vitamin D. Albright hereditary osteodystrophy, first described in 20th century consists of a combination of symptoms that include a round face, short stature, brachydactyly, subcutaneous calcification, and dental anomalies. It is a condition in which the body does not respond to parathyroid hormone. It is an inherited autosomal dominant disorder. We report a case of a 13- year old boy having characteristic signs of subcutaneous calcification, hypocalcemia, hyperparathyroidism, and calcifications on a brain CT scan which led to the diagnosis. The patient was prescribed calcium, calcitriol, and dietary phosphate restriction.

Introduction

Albright's hereditary osteodystrophy was first described in mid-20th century by Fuller Albright. It refers to a constellation of signs which include a round face, short stature, brachydactyly, subcutaneous ossification, and dental anomalies. Additionally, features such as macrocephaly and obesity can also be seen in patients with the disease. Albright hereditary osteodystrophy (AHO) is primarily a condition in which the body does not respond to parathyroid hormone. It is a genetic metabolic disorder that can be inherited in autosomal dominant, autosomal recessive, and also X-linked dominant forms.[1] The data about the prevalence of AHO is limited. The major related disease, pseudohypoparathyroidism is seen in 0.34 per 100000. The phenotype of AHO is mostly observed in pseudohypoparathyroidism types 1A and 1C. It occurs due to inactivating the GNAS1 gene which codes for the alpha subunit of stimulatory G protein. The initial evaluation should be targeted towards assessment for PTH resistance. Features of hypocalcemia, hypophosphatemia and renal dysfunction are all indicative of PTH resistance. Radiographs can be employed to check for short metacarpals, metatarsals, and distal phalanges of thumbs. The treatment is often done by supplementing calcium and by promoting phosphate restriction. If there are accompanying other hormonal deficits, they are all managed accordingly.

Case Presentation

A 13-year-old boy was reported to our center in the endocrinology department clinic with complaints of carpopedal spasms since 6 months of age. The physical examination and hand radiograph showed brachydactyly which was prominent on the index, thumb, and little finger (Fig.1). He also had calcinosis cutis (Fig.2) and his appearance was consistent with round facies.

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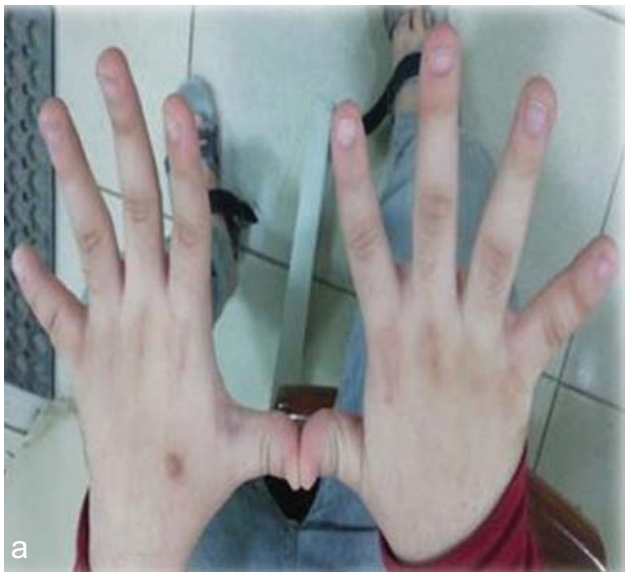
Submitted 22 July 2022, Accepted 27 August 2022



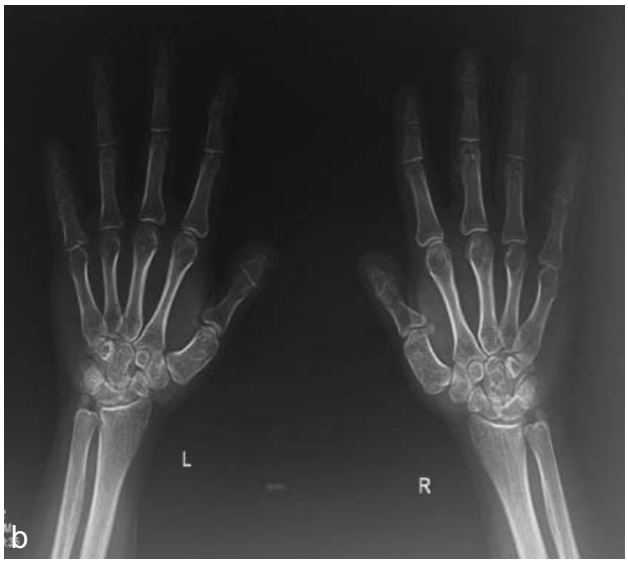
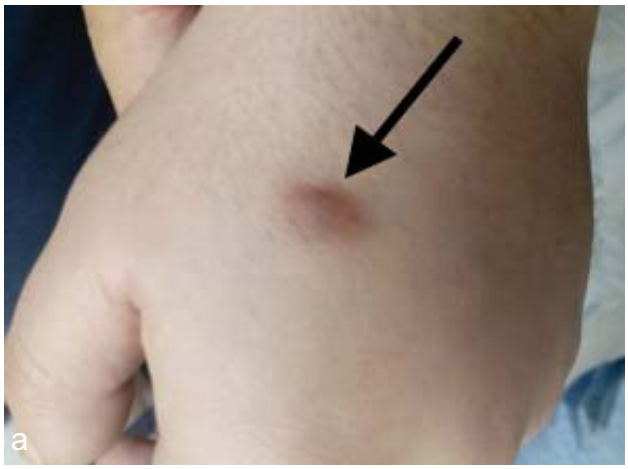


Figure 1a,b: Brachydactyly prominent on index, thumb and little finger



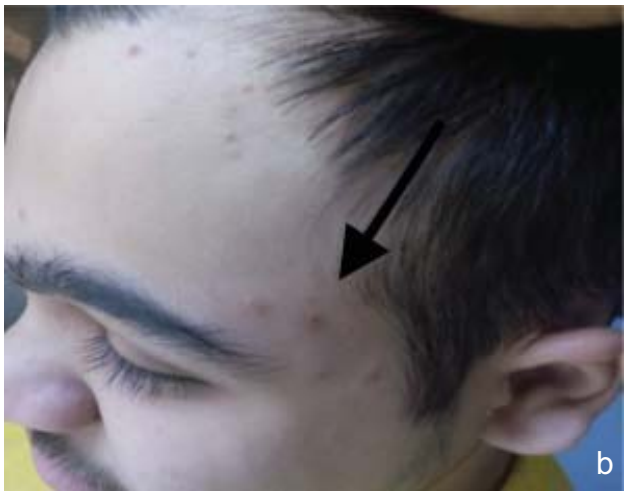
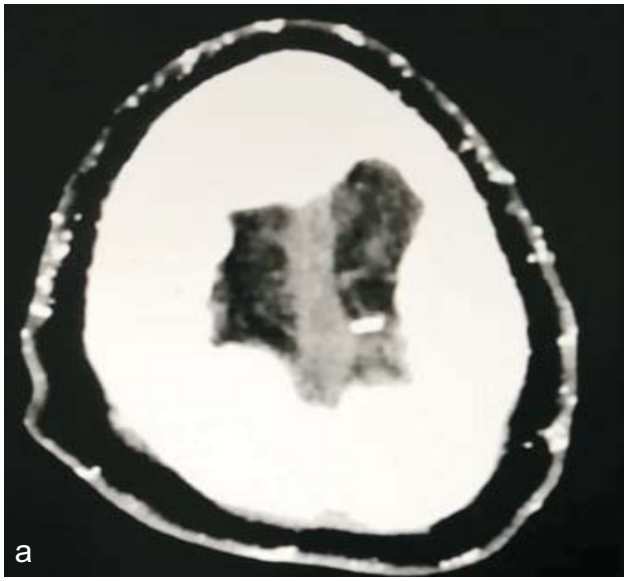
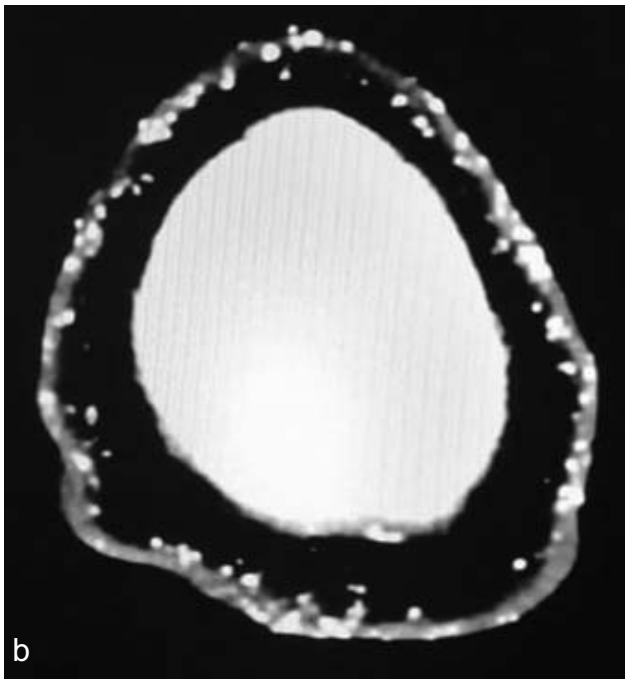


Figure 2a,b: Calcinosis cutis

The body weight was 63.5 kg, height 149 cm, and a BMI of 28.8 which was consistent with obese body habitus. His past medical history was significant for bilateral adenoidectomy and tonsillectomy at age 6 years due to multiple repeated oral and tonsillar infections, myringotomy and radical mastoidectomy at age 8 years, a biopsy for cholesteatoma at 9 years, and a unilateral orchidopexy and orchidectomy at 9 years. The laboratory tests were significant for hypocalcemia (7.4 mg/dl), increased alkaline phosphatase (294 U/L), increased phosphorus (7.8 mg/dl), and increased PTH (547 pg/ml). On brain CT with contrast, it was revealed that he had calcific foci of different sizes in the parietal lobe bilaterally (Fig.3), few specks of calcification in basal ganglia, and loss of pneuma-





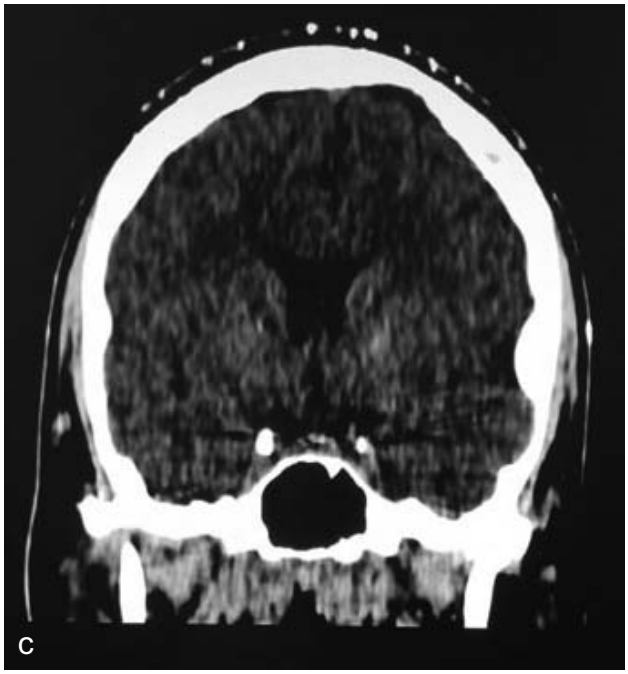


Figure 3a,b,c: Unenhanced CT brain: Multiple calcific foci in subcutaneous soft tissues of scalp and bilateral basal ganglia

tization in left mastoid air cells (Fig.4). An ultrasound KUB was also obtained which was completely normal and unremarkable. These findings along with laboratory results were suggestive of Albright hereditary osteodystrophy. The patient was then prescribed oral calcium supplementation, calcitriol, and dietary phosphate restriction. Sex steroid replacement was also offered for the management of hypogonadism.

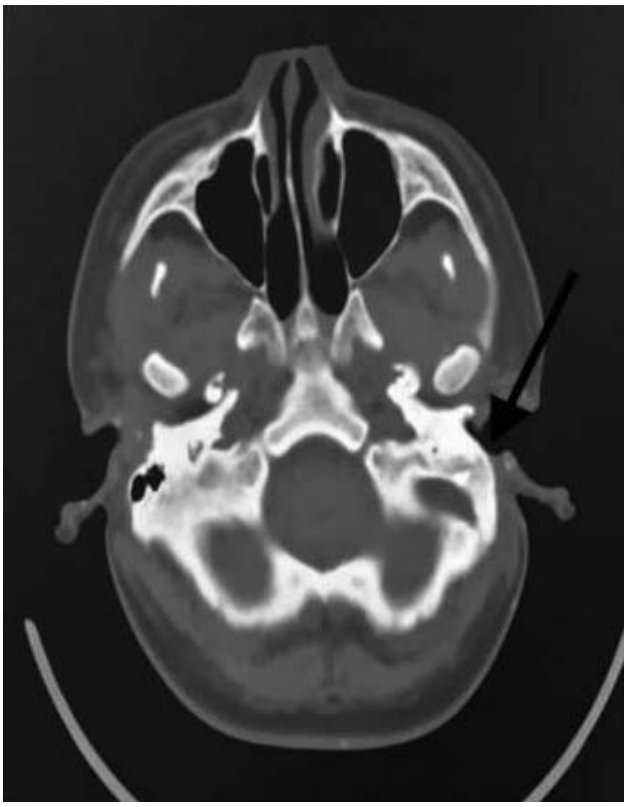


Figure 4: Loss of pneumatization in left mastoid air cells

Discussion

In 1942, Fuller Albright and his colleagues introduced the term pseudohypoparathyroidism to describe resistance to PTH in 3 patients with a constellation of symptoms such as obesity, short stature, round faces, brachydactyly with heterotropic calcification also known as Albright hereditary osteodystrophy. The term PHP is broadly applied to heterogeneous disorders which have PTH resistance as a theme common in all of them. Despite having a normal renal function PHP has abnormalities in calcium and phosphate levels.

Parathyroid hormone is an essential hormone to maintain calcium and phosphorous homeostasis in the body. The function of parathyroid hormone includes distal tubule calcium resorption, bone resorption, and increased production of 1,25 hydroxy vitamin D. Pseudohypoparathyroidism was the first hormone resistance state to be recognized in humans.[2] Pseudohypoparathyroidism is a condition that includes

resistance to parathyroid hormone with normal levels of it in the body. Patients have symptoms such as hypocalcemia, and hyperphosphatemia which are consistent with hormone deficiency. Despite having low calcium, patients with PHP rarely present with symptomatic hypocalcemia at an early age due to reasons that are not well elucidated. Patients with AHO have characteristic signs and symptoms such as short stature, round face, flat nasal bridge, brachydactyly of mainly 4th and 5th digit metacarpals present as dimpling over knuckles also known as Archibald sign . When the fourth metacarpal is short, it forms a knuckle, knuckle, dimple, dimple sign.[3]

PTH performs its functions by stimulating the intracellular adenylyl cyclase which produces cyclic AMP from adenosine triphosphate. Patients suffering from PHP and AHO are frequently found to have hypothyroidism which is secondary to thyroid stimulating hormone resistance and with some degree of hypogonadism though the patients remain fertile. This hormonal resistance diverts the attention towards investigating the activity of Gs and alpha subunits which have a reduction of about 50% when compared to control groups.[4]

As soon as the final diagnosis is made, patients should be treated with calcium. Oral calcium along with alpha hydroxylated vitamin D remains the treatment of choice along with close observation of calcium levels. Growth hormone is also recommended for patients with low hormone levels, levothyroxine is also replaced in patients with low thyroid hormone.

Conclusion

Albright hereditary osteodystrophy is a rare disorder that was first described in mid 20th century. The patients have clusters of symptoms such as a round face, short stature, brachydactyly, and subcutaneous ossifications. Additional features such as macrocephaly and obesity are also seen. It is primarily a condition where the body does not respond to parathyroid hormone due to underlying resistance. Despite having low calcium, symptomatic hypocalcemia is absent. The management is targeted toward hormone deficiencies. Calcium and vitamin D supplementation is the mainstay of the treatment. Levothyroxine and growth hormone supplementation could also be given if there is accompanied thyroid and growth hormone deficiency.

Conflict of Interest: None

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