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Case Report

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# ALBRIGHT HEREDITARY OSTEODYSTROPHY: A CASE REPORT

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## ABSTRACT

Albright hereditary osteodystrophy (AHO) is a syndrome characterized by short stature, obesity and brachydactyly especially of 4th and 5th digits, which are the phenotypic features of genetic mutation with features of pseudohypoparathyroidism (PHP) like hypocalcemia, hyperphosphatemia, increased Intact PTH (parathyroid hormone) and calcification in brain because of inability of the body to respond appropriately to parathormone. AHO when seen in association with resistance to parathormone (PTH), it is called PHP. Here is a case report of 15-year-old male patient presented with recurrent generalised tonic clonic seizure (GTCS) with classical features of AHO.

**KEYWORDS:** Albright hereditary osteodystrophy (AHO), Brachydactyly, Pseudohypoparathyroidism.

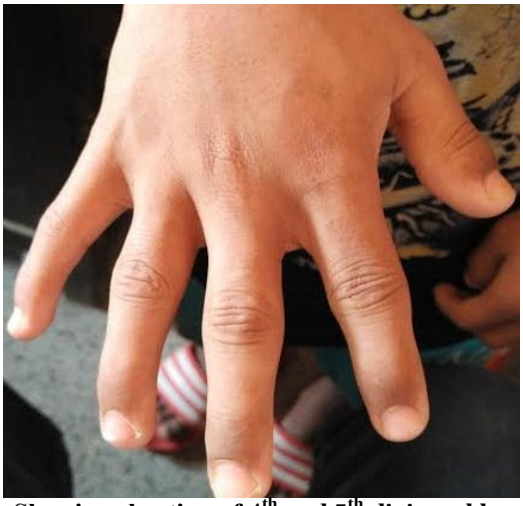
## INTRODUCTION

In 1942, Fuller Albright first introduced the term pseudohypoparathyroidism to describe patients who presented with PTH-resistant hypocalcemia and hyperphosphatemia along with an unusual constellation of developmental and skeletal defects, collectively termed as Albright hereditary osteodystrophy (AHO).[1] In 1998, a nationwide epidemiologic survey of pseudohypoparathyroidism (PHP) was conducted in Japan based on hospital visits in 1997; the period prevalence was 3.4 cases per 1 million people.[2] No information is available regarding the prevalence of PHP in the rest of the world. PHP occurs approximately twice as frequently in females as in males. Several variants of PHP have been identified. The molecular defects in the gene (GNAS1) encoding the alpha subunit of the stimulatory G protein (Gsa) contribute to at least 3 different forms of the disease: PHP type 1a, PHP type 1b, and pseudopseudohypoparathyroidism (pseudo-PHP). PHP type 1a is the best understood form of the disease.[3] Albright's hereditary osteodystrophy is a syndrome with a wide range of manifestations including short stature, obesity, round face, subcutaneous (under the skin) ossifications (gradual replacement of cartilage by bone) and characteristic shortening and widening of the bones in the hands and feet (brachydactyly). The features of Albright's hereditary osteodystrophy are associated with resistance to parathyroid hormone (pseudohypoparathyroidism) and to other hormones (thyroid-stimulation hormone, in particular). This autosomal dominant inherited condition is caused by mutations in the GNAS gene.[4] The goals of therapy are to maintain serum total and ionized calcium levels within the reference range to avoid hypercalciuria and to suppress PTH levels to normal. Treatment consists of calcium and vitamin D supplements.[5]

## CASE REPORT

A 15-year-old male patient was referred to the Tertiary Health Care Center of North-East, India from district hospital for repeated episodes of generalized tonic clonic seizure for last 2 years and not responded to one antiepileptic drug. Family history reveals no consanguineous marriage of his parents. His father gives history of hypertension. Mother was healthy and normal. The younger sibling of the patient was normal. General physical examination revealed short stature, round face, short neck, low set ears, depressed nasal bridge, hypertelorism (Fig. 1,2), B.P was 146/90 mmHg. Patient Body Mass Index (BMI) calculated as 20.6 for a height of 134 cm weighing 37 kg. The other prominent feature presented in the case was evident brachydactyly of bilateral $4^{th}$ and $5^{th}$ finger with loss of knuckle prominence (Fig. 3).

**"Fig. 1"**



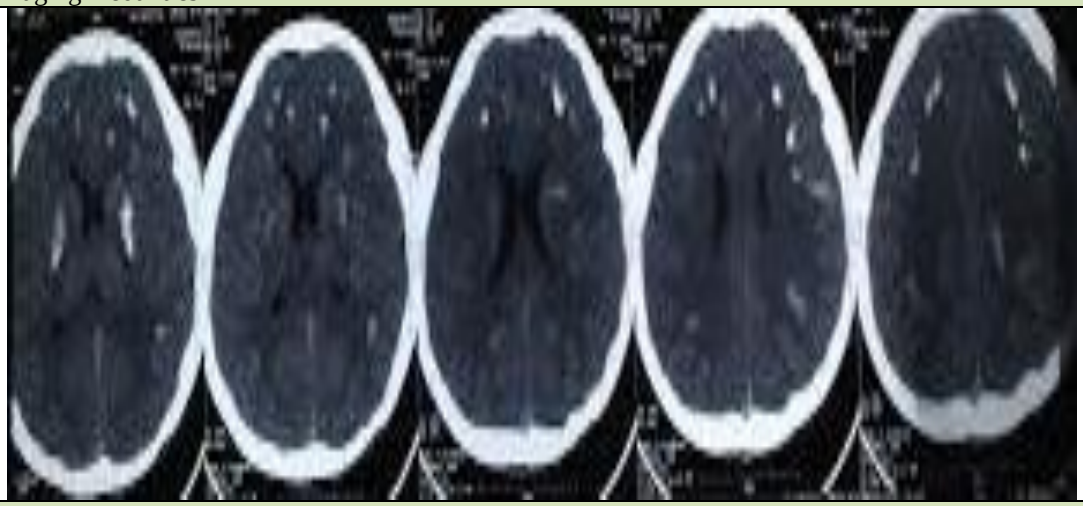
**"Fig. 3": Showing shorting of 4th and 5th digit and loss of knuckle prominence of 4th and 5th finger.**

**"Fig. 2"**

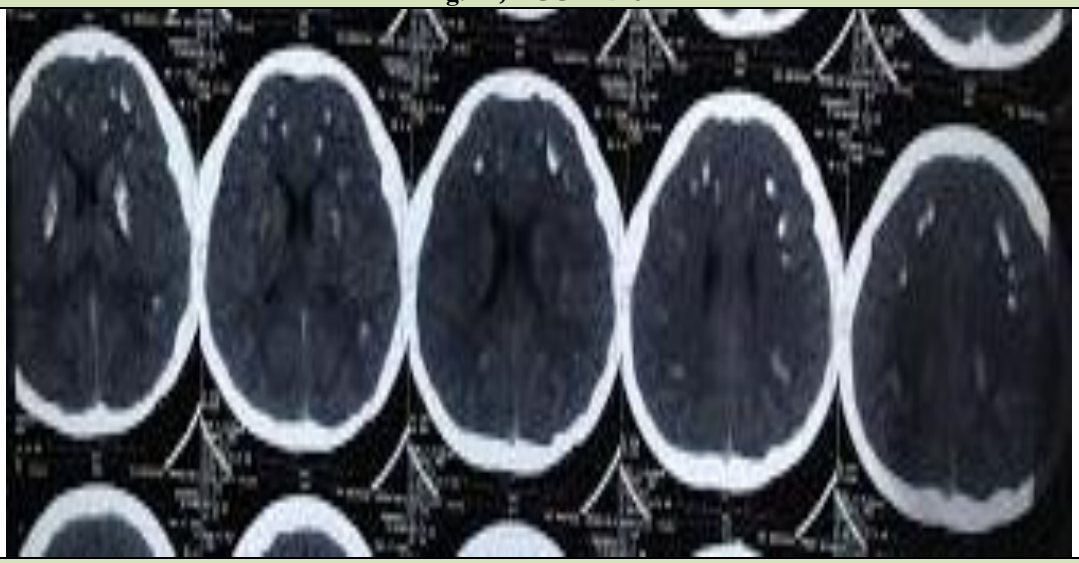
**Laboratory investigations**

| CBC | | KFT and S.E | |
|---|---|---|---|
| Haemoglobin | 10.6 gm/dl | Sr. Urea | 19 mg/dl |
| T. RBC | 3.53 Cells/L | Sr. Creatinine | 0.5 mg/dl |
| TLC | 8000 Cells/L | $Na^+$ | 137 mmol/L |
| Platelet count | 250 Cells/L | $K^+$ | 4 mmol/L |
| ESR | 15 mm/1st hr | $Cl^-$ | 95 mmol/L |
| Peripheral smear | Normocytic Normochromic | **RBS** | 76 mg/dl |
| **LFT** | | **THYROID PROFILE** | |
| Total bilirubin | 2 mg/dl | T3 | 1.44 ng/dl |
| Conjugated/ Unconjugated bilirubin | 0.6/1.4 | T4 | 8.52 microgm/dl |
| SGOT/SGPT | 33/20 | TSH | 4.57 microIU/Ml |
| Sr. Albumin/ globulin | 4.7/2.6 | Corrected Sr. $Ca^{+2}$ | 5.5 mg/dl |
| Sr. Alkaline Phosphatase | 417 U/L | Sr. Phosphorus | 7.6 mg/dl |
| GGT= | 12 U/L | Intact PTH | 186 pg/ml |
| Sr. Growth Hormone | 0.26 ng/mL | Sr. Vitamin D | 25.8 ng/ml |
| ECG | Normal | R-Ab | Non-reactive |
| Echocardiography | Situs solitus with levocardia | HBsAg | Negative |
| | Normal cardiac chamber | Anti-HCV-Ab | Negative |
| | No septal defect | | |
| | LVEF = 77.37 % | | |

| NCCT- Brain |
|---|
| Symmetrical coarse calcification in B/L basal ganglia and deep white matter in fronto- parietal region.<br>F/S/O= Pseudohypoparathyroidism "Fig. 4" |
| CECT- Brain |
| Multiple coarse calcifications in B/L basal ganglia and deep cerebral white matter.<br>F/S/O= Pseudohypoparathyroidism "Fig. 5" |
| Imaging modalities |



**"Fig. 4", NCCT- Brain**



**"Fig. 5", CECT- Brain**

Treatment plan included medication with Phenobarbitone 60mg orally once daily, 3 gms of Calcium supplements orally, 60 mcg vitamin D3 daily was started as initial phase of treatment. Patient was recalled after three weeks where in hematological investigations were carried out. There was a considerable increase in serum calcium level to 7.8mg%, serum phosphate recorded was 3.7mg% which was reduced compared to initial values and PTH levels were 32.5pg/ml which showed considerable reduction from the aforementioned values.

## DISCUSSION

Genetic studies done to know the aetiology of AHO has revealed mutation of GNAS1 gene located on 20q13-11 as the culprit gene.[6] In literature, AHO has been reported with characteristic features like short stature, round face, flat, wide and low nasal bridge, obesity, short neck, flat occiput, mental retardation, brachydactyly of 4th and 5th digits, knuckle dimples in the clenched fists, short broad nails, osteoporosis, cataract, dementia, epileptic seizures, ankylosis of temporomandibular joint (TMJ), rheumatoid arthritis of hand and foot joints, cone shaped epiphysis, thickened calvaria, basal ganglia calcification and subcutaneous ossification.[4,7,8,9] The present case does not give a familial history of AHO which is in agreement to studies done by Gomes M et al but is contrary to series of erratic cases reported in literature.[7,8] Cases documented previously show preponderance of AHO in female individuals, stating that AHO occurs twice frequently in females than males. But the present case contradicts and presents itself in a male patient. In accord with female preponderance are studies

done by Ecsel E et al.[9] The characteristics typical of AHO piled in literature are round faces, short stature, brachydactyly of 4th and 5th digit, hypocalcemia and mental deficiency, also described in the present case, in concurrence with string of reports on AHO by Ambika L & Vaishali K, Gomes M et al, Kapoor K et al. [7,8,10] TMJ ankylosis has been reported in case reports by Ambika L & Vaishali K but the presenting case shows no ankylosis of TMJ.[7] Basal ganglia calcification seen in Computed Tomography (CT) has also been reported by Ambika L & Vaishali K.[7] The reason for the focal accumulation of calcium in basal ganglia can be due to local factors and disturbance of calcium metabolism. Dementia, seizures and Parkinsonism are seen associated with basal ganglia calcification.[9] Oral manifestations in AHO patients include aplasia, thin enamel with enlarged pulp chamber, hypoplasia, hypodontia, pulp calcification, multiple carious teeth, multiple unerupted teeth, crowded anterior teeth, anterior open bite, gingival hyperplasia, gingivitis with spontaneous bleeding and pain.[7,10]

## CONCLUSION

In Albright Hereditary Osteodystrophy, Hypocalcemia due to pseudohypoparathyroidism may occur in the context of a vague or misleading history and in the absence of typical physical stigmata. Our patient presented with H/O multiple episodes of GTCS with Phenotypic character of short stature, round face, hypertelorism, low set ears, depressed nasal bridge, brachydactyly and laboratory tests reveals significant decrease in corrected serum $Ca^{+2}$ (5.5 mg/dl), increase in serum phosphorus (7.6 mg/dl), increase of PTH (186 pg/ml), decrease in Vit-D (25.8 ng/ml) and decrease in serum Growth hormone (0.26 ng/ml) with Brain calcifications on imaging. Classical presentation of AHO may not be present. So multidisciplinary approach is required among medical and dental professionals for precise diagnosis.

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