Case Report

Pseudohypoparathyroidism Type-II with Striopallidodentate calcification with positive anti glutamic acid decarboxylase antibody and seizures

Zohair Alaseri[1], M. Owais Suriya[2], Galal H. Elnour[3]

ABSTRACT

Pseudohypoparathyroidism (PHP) is disorder characterized by biological insensitivity of parathyroid hormone (PTH) at tissue level. There are several sub types of PHP have been described with identical features of increased resistance to PTH by kidney and bone with resultant biochemical features of increased level of PTH, hypocalcemia and hyperphosphatemia.

We describe unique case of subtype of Pseudohypoparathyroidism (PHP) type II complicated by massive intracranial calcification of Striopallidentate (SPD) system resulting in seizure activity. This case is quite unique and worthwhile to report linking PHP type II and intra cranial calcification.

KEY WORDS: Striopallidentate (SPD), Pseudohypoparathyroidism (PHP), hypocalcemia, Parathyroid hormone (PTH), intracranial calcification.

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INTRODUCTION

Calcification of the Striopallidentate (SPD) system is a unique feature of symmetrical bilateral deposition of calcium involving cerebrum, basal ganglia and dentate nuclei of the cerebellum.[1,2]

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Pseudohypoparathyroidism (PHP) is a heterogeneous group of disorders characterized by target organ (bone and kidney) resistance to parathyroid hormone (PTH). In all its forms PHP is presented with hypocalcemia, hyperphosphatemia, increased serum concentration of PTH and insensitivity to the biological activity of PTH.[3]

We describe a patient who presented with epileptic seizure and subsequently was diagnosed to have type II of Pseudohypoparathyroidism which is a rare entity with Striopallidentate phenomenon of calcification along with positive Anti Glutamic Acid decarbooxylase antibody (AntiGAD).

CASE REPORT

A 14 year old male student presented to Emergency Department (ED) of our hospital brought by father with complaint of shaking movement of the left upper limb with up rolling of both eyeballs, there were two episodes in the last 24 hours of presentation. Both episodes were witnessed by family members and they explained that there was sudden shaking movement of the left arm accompanied with up rolling of both

eyes with momentary loss of consciousness for approximately two minutes. There was no history of aura or post ictal neurological deficit. He gave a history of same event a month earlier for which he did not seek any medical advice. Twenty four hours prior to presentation he experienced two episodes of fits for which he was brought to the hospital for evaluation.

The patient was not on any medical treatment and there was no history of illicit drug abuse, he had no family history of epilepsy or any other medical problem. He was a regular student of secondary level with good academic performance. His past medical history revealed tonsillectectomy and correction of deviated nasal septum at the age of seven and nine years respectively.

Physical examination revealed BMI of 24 with normal somatic features vital signs revealed Temperature 37.4 °C, Blood Pressure 100/80 mmHg, Pulse 88/min regular, respiratory rate 21/min, O_2 saturation 99% at room air. Systemic review including respiratory, cardiovascular, and abdominal examination were unremarkable. Central nervous system examination revealed positive features of hypocalcaemia in the form of Chvostek sign i.e., twitching of facial muscles after tapping the facial nerve just in front of the ear and Trousseau sign i.e., carpal spasm after maintaining an arm blood pressure cuff at 20 mm Hg above the patient's systolic blood pressure (120 mm Hg) for three minutes. Other findings including orientation, mentation, muscle's power, tone and reflexes were normal.

Laboratory studies at admission showed the following: Calcium corrected: 1.32 mmol/L, Phosphate 3.48 mmol;/L, Alkaline phosphate 555 u/l, Magnesium 0.67 mmol/L, Albumin 37g/L, Parathyroid Hormone 32.97 pmol/L. Other investigations likewise, liver enzymes, bilirubin, urea and electrolytes, complete blood count, thyroid function test and calcitonin were within normal parameters.

Computed tomography showed bilateral subcortical juxta central lesions involving frontal, temporal and parietal areas in both hemispheres, basal ganglia, dentate and lentiform nucleu. (Fig. 1-4) Although there was symmetrical calcium deposition of equal proportion in both hemispheres there was no evidence of mass effect. The skeleton survey did not reveal any somatic features of Albright Hereditary Osteodystrophy (AOH) (Fig 5-7). However, Electroencephalogra-

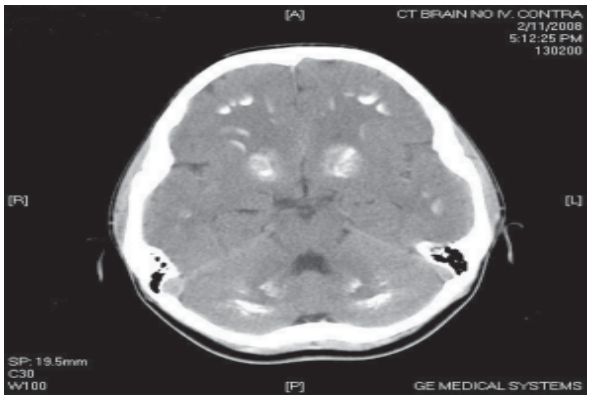

Fig-1

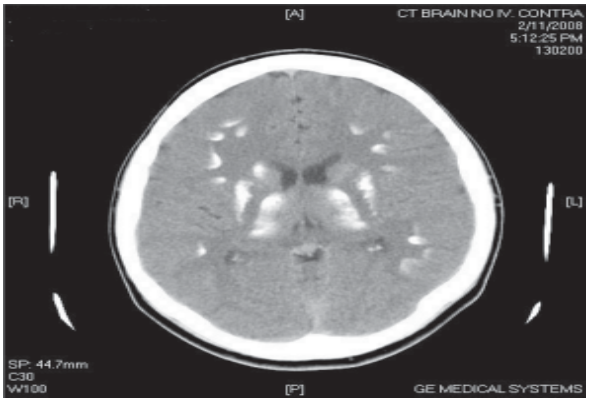

Fig-2

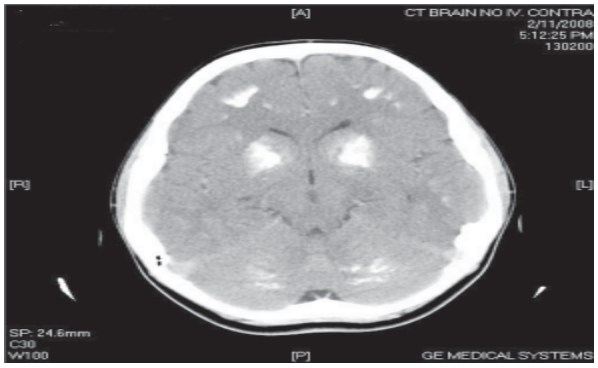

Fig-3

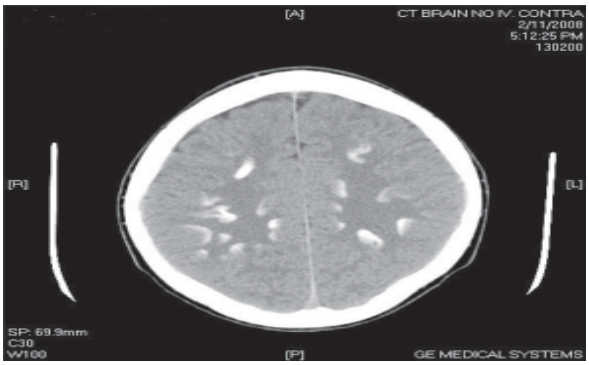

Fig-4

Fig 1-4: Extensive calcification of brain showing in CT brain at different levels

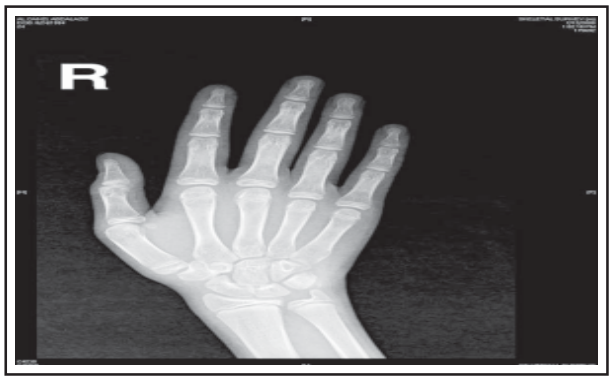

Fig-5: X-Ray right hand.

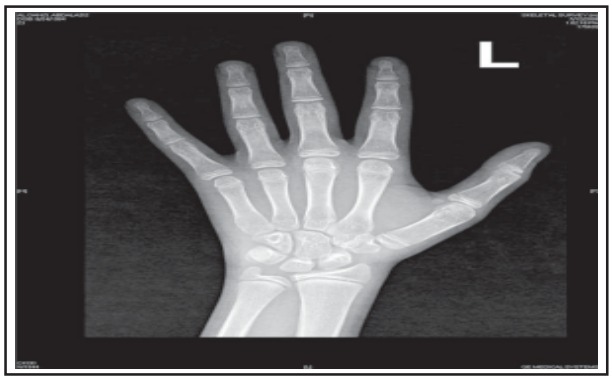

Fig-6: X-Rray left hand.

phy showed potentially epileptogenic activity over the right temporal head region in addition to mild degree of diffuse non specific slow wave abnormalities were noted. Electrocardiography revealed normal sinus rhythm with corrected QT interval of 494 msec.

On the basis of above laboratory parameters he was treated for correction of hypocalcemia and upon institution of parathyroid hormone (PTH 1-34) by using standard procedure and using the diagnostic criteria of the Ellsworth-Howard test[4] he was diagnosed finally as Pseudohypoparathyroidism (PHP) type II. He remained seizure free during hospitalization and discharged on oral 1 alpha calcidiol 0.50 microgram, calcium carbonate 600 mg three times a day and levetiracetam 250 mg two times a day. He was followed at the neurology and endocrinology clinic with normal laboratory parameters and stable condition.

DISCUSSION

Pseudohypoparathyroidism was first described by the Fuller Albright in 1942 in the report of several patients who apparently had biochemical hypoparathyroidism with hormonal resistance by the target tissues. Earlier, Fuller Albright described biochemical hypoparathyroidism as tissue resistance for PTH with somatic abnormalities that includes stocky or obese body habitus, moon shaped face, hypoplasia of dental enamel, joint deformities (genu valgum, coxa vara, cabitus valgus, and anomalies of the hands and feet particularly, short metacarpal and metatarsal of the fourth and fifth digits with impaired mentation. This clinical syndrome was termed as Albright Hereditary Osteodystrophy (AHO).[3] With further clinical experience, it became evident that not all PHP patients have the AHO phenotype and some AHO phenotype patients do not have PHP. Furthermore, by time, despite having apparent common serum biochemical features, some distinct types have been classified on the basis of different pathophysiological mechanisms which made these confusing description comprehensible. Therefore, current revised classification of PHP gave five distinct forms on the basis of clinical appearance, biochemical parameters and underlying molecular mechanism of hormone resistance.

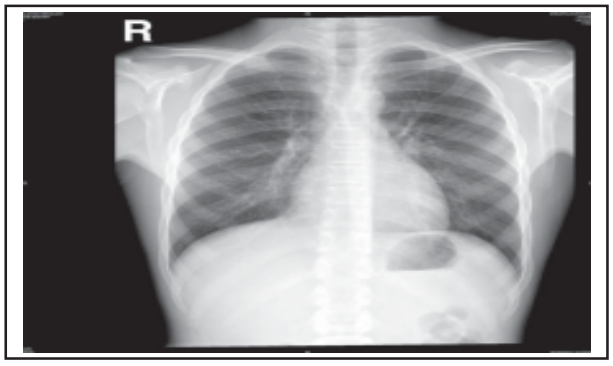

Fig-7: X-Ray chest.

Type Ia is the most common type which is an autosomal dominant condition it has phenotypic features of AHO with hormone resistance and decreased nephrogenic cAMP response to PTH and GNSA 1 mutation as well. GNAS1defects encode a subunit of guanine necucleotide binding protein which is key to transducing signals in a variety of hormones target tissues explaining the involvement of other hormones, the defect has been found in chromosome 20q 13.11.[5] Whereas, classical AHO pseudo-PHP carry no hormone resistance and normal nephrogenic response to cAMP on PTH, type Ic appears uncommonly and despite positive phenotypic features, resistance to other hormones and decreased response of nephrogenic cAMP, it does not possess GNSA 1 mutation. Considering type Ib, which is the second most common form of PHP, it can either be familial or sporadic. In this type, gene mutation does not exist rather it has regulation defect of PTH receptor as well as decreased nephrogenic c AMP response without other hormonal resistance and somatic features of AHO.[6,7]

Type II PHP is characterized by increased PTH, hypocalcemia, hyperphosphatemia and absolute lack of physical somatic features of AHO, further unique differentiating features is a normal cAMP response to PTH infusion but a deficient phosphaturic response indicating a defect distal to c AMP generation in renal cells and normal GNAS1 activity.[8-11]

Our case at presentation was diagnosed as PHP on the basis of common features of PHP which are increased PTH, hyperphosphatemia and hypocalcemia. For further distinction, our patient was given exogenous PTH using standard protocol.[4] Response was noted as increased cAMP response and a deficient phosphateuric response. This unique characteristic of type II PHP has been described as a defect of cAMP generation in renal cells and distinct it from type I PHP.[12]

Furthermore, vitamin D deficiency in our patient even in the presence of increased alkaline phosphate and low vitamin D level was excluded due to hyperphosphatemia. In our case computed tomography scan showed extensive brain calcification which has been described earlier in several reports of other types of PHP.[13-16] Including one case report on PHP type II mentioning its biochemical features with basal ganglia calcification without seizure or any other problem.[17] Whereas our case presented with seizures and extensive Striopallidodentate calcification. There are postulates which describe possible reason behind the calcification of brain tissue that include hyperphosphatemia promoting this phenomenon and presence of parathyroid hormone receptor type II in the brain as well as increase activity of mitochondrial superoxide in PHP.[18]

Another striking finding in our case was the presence of Anti Glutamic Acid decarboxylase antibody which is never described in conjunction with PHP. However, anti GAD antibodies has been found positive in few studies in relation to therapy resistant forms of epilepsy.[19,20] But in conjunction with PHP type II, it is not reported yet and workup is needed to define correlation between them.

CONCLUSION

To the best of our knowledge this is the first case of type II PHP manifested with Striopallidodentate calcification and positive anti GAD. The coexistence of the two phenomenon redundant or it could suggest a new mutation that links the disease.

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