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Pseudopseudohypoparathyroidism With Pseudo Seizure .

Medical Science

KEYWORDS : PHP,Pseudo PHP,PNEA/ pseudoseizure,short metacarpals.

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ABSTRACT

Pseudohypoparathyroidism (PHP) pertain to a diverse group of disorders concerning parathyroid hormone (PTH) resistance. PHP is an unusual sporadic or inherited genetic disorder subdivided into different distinct entities. In 1952, Albright, Forbes, and Henneman reported a case of pseudo-hypoparathyroidism in which all the usual anatomical stigmata of hypoparathyroidism were present, but serum calcium and phosphorous levels were normal and the patient exhibited no clinical evidence of hypoparathyroidism. They called this new syndrome "pseudopseudohypoparathyroidism"(pseudo PHP). Seizures are not known to occur in pseudo PHP while they have been described in PHP.We report a 17 years old female, who presented with involuntary jerky movements of all four limbs and on further evaluation was diagnosed to have the syndrome 'Pseudo PHP'.

Summary: Seizures have been reported in patients with PHP but are not known occur in PPHP.Our patient on evaluation,turned out to be having PNEA(pseudo seizures).The case is being reported for the rare combination of pseudoPHP with pseudoseizure(PNEA).

Introduction:

Albright, Burnett, Smith and Parson [1942] (Ref-1)investigated a female patient of 28 years who had suffered from idiopathic epilepsy since the age of 12. Because the patient's skull bones were unusually dense, hypoparathyroidism was suspected. The diagnosis was made when it was found that her chvosket's sign was positive and that her serum calcium was 6.4mg/100ml and phosphorous was 6.0mg/100ml.In addition the authors described certain developmental anomalies that served to delineate it from hypoparathyroidism, i.e small stature, round face and shortness of all fingers except the index finger, due to short metacarpals. They named the syndrome 'pseudo-hypoparathyroidism'. Ten years later in 1952, Albright, Forbes and Henneman(Ref-3) reported a case of PHP, in which all the usual anatomical stigmata were present, but serum calcium and phosphorous levels were normal and the patient exhibited no clinical evidence of hypoparathyroidism. They called this new syndrome 'pseudo-pseudohypoparathyroidism'.

Case Report:

A 17 years old female presented with 3 episodes of supposedly involuntary jerking of all four limbs, preceding which she had headache and movement of the head towards either side, with uprolling of eyes.She did not have tonguebite, bowel or bladder incontinence or loss of consciousness. She was fully aware of the surrounding . History of hyperventilation was present during the episodes. She had similar episodes in childhood(about 10 years of age) for which she was given antiepileptics which she discontinued after two years. Birth history was normal, she was born to non-consanguinous parents.

On examination, she was short statured [height of 146cms], [weight 42kgs] with a body mass index (BMI) of 19.7 kg/m2.Her BP was 120/80 mmHg and PR-76/min.She had a round face, short hands, wide finger nails, short fourth and fifth metacarpal bones(Fig.1&2) short neck and no subcutaneous calcifications. The metacarpophalangeal line of the clenched fist was concave in the medial part. Neurological examination showed no abnormality. Ophthalmology examination showed a normal fundus and no cataract. Cardiovascular, respiratory and abdominal examination was normal. Her complete blood count, renal function test, liver function test, thyroid function tests were done and found to be normal. Serum calcium was 9.4mg/dl [8.5-10.5] magnesium-2.1mg/dl, phosphorous-4.3mg/dl [3.5-5.5], ESR-32mm/hr, parathormone-39pg/ml[12-65]. Serum prolactin was found to be high-93mcg/L[2.3-29]. Routine examination of urine was normal. MRI -Brain was suggested to rule out any prolactin secreting adenomas but it was normal.A video EEG was done which showed a normal EEG when she had the jerky movements of limbs. Hence a diagnosis of PNEA(paroxysmal non epileptic attacks) was made. Radiographs of the hands showed shortening of the fourth and fifth metacarpals on both sides(Fig.3)Her father also had short fourth and fifth metacarpals(Fig.4a&b). Therefore "pseudopseudohypoparathyroidism" was suspected as there is phenotypic variation but biochemical evaluation was normal.

Discussion:

In pseudo-hypoparathyroidism, there are recognised subtypes which include:Type 1 -Type 1a [Albright hereditary osteodystrophy (AHO)] (Ref-2)which has characteristic phenotype features and Type 1b- which lacks phenotypical features and Type 2:normal CAMP response to PTH stimulation.

In the former days,the diagnosis of PHP was established by administering bovine or synthetic PTH(Ref-10).This test helped to differentiate patients with PHP types1 [characterised by a decreased urinary CAMP and phosphate excretion] from patients with PHP type 2 [characterised by abnormal urinary CAMP excretion and a decreased phosphate excretion].The subtypes are caused as a result of "MUTATION" or "IMPRINTING" abnormalities in the stimulatory G protein (Gs)(Ref-7,8).The alpha-subunit of the Gs [Gs alpha] is a signalling protein essential for the actions of PTH and other hormones. Patients with type '1a' PHP show only 50% activity of GS alpha subunit.

Genetics:

GNAS gene encodes the alpha-chain of the heterotrimeric G-protein Gs, (Ref-7)which couples receptors for many hormones and neurotransmitters to activate G protein and adenylyl cyclase which generate intacellular c-AMP for the action(physiological effects) of the hormones.In pseudo PHP there is an autosomal dominant inheritance. The gene is found on chromosome 20. It is usually inherited from the father "genomic imprinting".

Pseudopseudohypoparathyroididsm [pseudo PHP] is an inherited disorder. It has a phenotypic appearance similar to pseudohyparathyroidism PHP type 1a, but it is biochemically normal. It is sometimes considered as a variant of Albright hereditary osteodystrophy(Ref9)

In pseudo-PHP there is short fourth and fifth metacarpal bones and therefore when the patient make a fist, the knuckles will have dimples at the fourth and fifth positions, hence it is called

as ARCHIBALD'S SIGN, (Ref11)"KNUCKLE KNUCKLE DIMPLE DIMPLE" .This is as opposed to Turner and Albright syndromes where only the fourth metacarpal is short and is called as "KNUCKLE KNUCKLE DIMPLE KNUCKLE" sign, and in Down's syndrome which is characterised by a hypoplastic middle phalanx.

PNEA: Paroxysmal nonepileptic seizures or pseudoseizures are episodes which are often misdiagnosed as epileptic seizures. PNEA can be either organic or psychogenic.Syncope,migraine and transient ischemic attacks(TIA'S) are examples of organic nonepileptic paroxysmal symptoms.Bydefinition,PNEA is a paroxysmal disorder,(Ref-5)more specifically a psychiatric disorder which falls under the diagnostic category of somatic symptom disorders in the Diagnostic and Statistical Manual of Mental Disorders,Fifth Edition(DSM-V).According to the DSM-V classification,neurological symptoms that are found,after appropriate neurological assessment,to be incompatible with neurological pathophysiology can be considered under conversion disorder,factitiousdisorder,or malingering.Paroxysmal nonepileptic seizures often present as a prolonged episode with generalised,atypical-appearing motor activity and a prompt return of consciousness.During psychogenic nonepileptic seizures,(Ref-6)patients often close their eyes tightly and resist their opening.Incontrast,patients having a generalised epileptic convulsion typically have their eyes open.Nonepileptic seizures are best distinguished from true seizures by capture of an event on video-electroencephalogram(EEG) monitoring.

FIGURES:

Figure 1.Patient's hands.

Figure2.Short fourth and fifth metacarpals

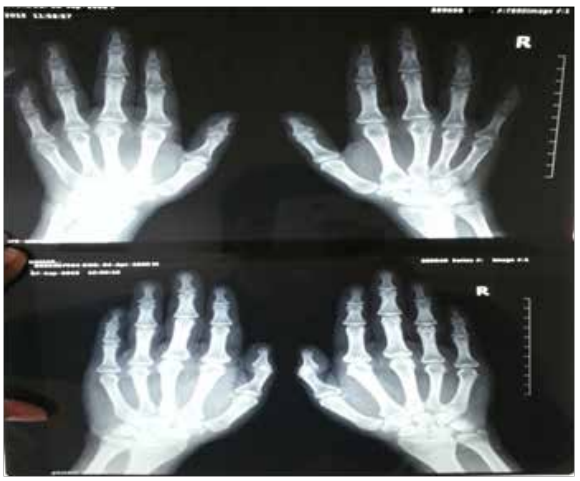

Figure.3- X-Ray of both hands

Figure.4-Patient father's hand.

Figure.5-Patient's and her father's hand.

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