



Clinical Analysis of a Case of Pseudohypoparathyroidism

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Abstract: Objective — To investigate the clinical treatment effect of pseudoparathyroidism. Methods — A case of pseudoparathyroidism admitted to our hospital was clinically diagnosed and treated, and analyzed. Results — The patient received standard treatment in our hospital, and the clinical symptoms were significantly improved. Conclusion — Timely and correct diagnosis and symptomatic supportive treatment are of great significance to improve the prognosis of pseudohypoparathyroidism patients.

Keywords: pseudohypoparathyroidism, parathyroid hormone, low blood calcium, high blood phosphorus

Pseudoparathyroidism is a rare clinical genetic disorder, which is related to GNAS1 gene defect encoding Gs protein α subunit, and is the earliest discovered hormone resistance syndrome. Normally, parathyroid hormone acts on receptors in target cells, setting off a cascade of reactions that achieve the biological effects of parathyroid hormone. Pseudo patients with parathyroid function disorder, the role of parathyroid hormone target cell's response to parathyroid hormone will complete loss or loss in a certain extent, show low blood calcium and high elevated blood phosphorus, parathyroid hormone by blood, urinary calcium and phosphorus decrease urine etc. Phenomenon, at the same time, associated with multiple endocrine defects and congenital dysplasia ^[1]. Pseudo-hypoparathyroidism can be divided into three different subtypes based on the response of the target organ to parathyroid hormone, namely, bone and renal resistance, kidney resistant bone response (also known as hyperparathyroidism), and kidney responsive bone resistance. Pseudohypoparathyroidism is classified as type I and TYPE II, based on the fact that the target cell does not respond to PARathyroid hormone before or after cyclic adenosine phosphate production. Type I is more common than type II. Type I can be divided into three subtypes: Ia, Ib and Ic, which are caused by defects of parathyroid hormone receptors on the membranes of target organs ^[2]. Type II with no clear genetics and family history, is caused by defects in parathyroid hormone receptors, parathyroid hormone resistance as the main characteristics, without genetic osteodystrophy Albright, pseudo parathyroid function disorder the clinical manifestations of diversity, much to tetany, and hair as starting symptoms epilepsy samples, It is easily misdiagnosed as epilepsy ^[3]. In this study, a retrospective analysis was conducted on the clinical diagnosis and treatment of a patient with pseudoparathyroidism admitted to our hospital, in order to improve the clinical understanding of this disease, reduce the misdiagnosis rate, and avoid missing the best treatment opportunity.

1. Clinical data

Patients were male, 30 years old, married, in January 2015, discontinuous hiccups and a half hours, suffocating in patients with intention to alleviate symptoms of hiccups, but in the process of breath in the whole body twitch, syncope down, no continue to twitch after syncope, faint patients after losing consciousness, should not call, about 20 s in apnea, whole body stiff, facial, hand turned purple, his hands were curled up state, The pupil was dilated, and the patient began to gasp for breath at about 30 minutes after fainting. The whole process lasted for about 40-60 minutes, and then normal breathing and consciousness gradually returned. During the course of the disease, the patient did not foam at the mouth or incontinence. She went to Anning County People's Hospital for treatment. After completing relevant examinations, she was diagnosed as hypoparathyroidism, and was given symptomatic treatment of calcium carbonate D3. On January 29, 2021, the patient suffered from syncope again without obvious causes and received head CT examination in Anning County People's Hospital, which showed bilateral cerebellar dentate nucleus area, basal ganglia nucleus area, symmetrical calcification foci in lateral ventricle and hypoparathyroidism. Fahr 's disease? Multiple patchy ground glass shadows in the upper and lower lobes of both lungs, accompanied by scattered thickening of interlobular septa, considering inflammatory lesions and viral pneumonia cannot be excluded.

Cervical plain scan showed no obvious abnormality. On March 3, he went to Kunming Yan 'an Hospital and received relevant examinations. The results showed that PTH567.37pg/ mL, alkaline phosphatase 160U/L, calcium 1.52mmol/ L, phosphorus 1.97mmol/ L and magnesium 0.82mmol/ L, and there were no obvious thyroid abnormalities. The diagnosis was

considered as hypoparathyroidism, and symptomatic supportive treatment was given. On March 9th, he came to our hospital for further diagnosis and treatment, and was admitted to our department as pseudohypoparathyroidism. During the course of the disease, the patient was in good mental state, had good diet, had poor sleep, had normal urine and stool, and had no significant change in body weight.

Previous history: The patient had always been in good health, and denied the history of cardiovascular, cerebrovascular, lung, kidney, endocrine and other important organ diseases and infectious diseases. The history of vaccination was unknown, and the specific content of allergy history was not recorded. The patient denied the history of trauma, surgery, and blood transfusion.

Personal history: Never been to endemic or infectious diseases, no smoking history, no drinking history, no exposure to toxic substances, dust or radioactive substances, no genetic history, no infectious history, physical examination results show: Body temperature 36.1 degrees Celsius, pulse 95 times /min, respiration 23 times /min, blood pressure 116/70mmHg, height 168cm, weight 55kg, BMI19.49kg/m², waist circumference 85cm, hip circumference 81cm, waist-hip ratio 0.93, general condition ok, no special face, good nutrition, clear, answer to the question, The heart rate was 95 times /min, and there was no pathological murmur in the auscultation area of each valve. The abdomen was soft, no tenderness or rebound pain. The liver and spleen were not reached, and there was no percussion pain in the liver area. There was no pigmentation, edema, rash, redness and ulceration in the lower limbs. The dorsalis pulses normally.

Physiological reflex was present, but pathological reflex was not elicited. Beam arm compression test was positive, facial nerve buckle sign was negative, muscle strength and tension of limbs were normal. Auxiliary examination results showed that CT examination showed symmetrical calcification of bilateral cerebellar dentate nuclei, basal ganglia nuclei, lateral paraventricular lesions, hypoparathyroidism. Fahr's disease? Multiple patchy ground glass shadows in the upper and lower lobes of both lungs, accompanied by scattered thickening of interlobular septa, considering inflammatory lesions and viral pneumonia cannot be excluded. Cervical plain scan showed no obvious abnormality. On March 3, he went to Kunming Yan 'an Hospital and received relevant examinations. The results showed that PTH567.37pg/ mL, alkaline phosphatase 160U/L, calcium 1.52mmol/ L, phosphorus 1.97mmol/ L and magnesium 0.82mmol/ L, and there were no obvious thyroid abnormalities. Blood glucose was 6.1mmol/ L at random upon admission. Electroencephalogram showed no obvious abnormality, parathyroid imaging showed no obvious MIBI affinity lesion in parathyroid region, and no obvious abnormality in thyroid density and radioactivity distribution. Ion six detection: calcium 1.58mmol/L, inorganic phosphorus 1.81mmol/L, otorhinolaryngology department to improve the hearing examination without abnormality. The diagnosis was pseudohypoparathyroidism.

2. Treatment measures

Generally, the general treatment principle of this disease is to limit the intake of high-phosphorus foods such as milk, meat and soy products, and increase the intake of high-calcium foods.

For patients in the acute stage, convulsions should be actively controlled. For those with mild symptoms, 10% calcium gluconate should be given 10-20ml intravenously, which can be repeated every 4-6 days according to the reaction. For moderate and severe patients, 10% calcium gluconate should be given 20-40ml intravenously. Diazepam 5-10mg can be injected intramuscularly or intravenously. For patients with uncontrollable convulsions or frequent seizures in a short period, 10% calcium gluconate 10-20ml can be injected intravenously with fluid at a slow infusion rate of 4mg/h. For patients with hypomagnemia, 25% magnesium sulfate 10-20ml can be given intravenously. Increase the sensitivity of target organs to parathyroid hormone, thus improving the symptoms of hypocalcaemia^[4-5].

For the treatment of the acute phase, in the treatment, in order to prevent acute and prevent the progress of the disease, at the same time in order to prevent vitamin D deficiency and hypocalcemia, also in order to prevent vitamin D intoxication and hypercalcemia caused by urinary tract stones, and ectopic calcification is aggravating, in the process of treatment, can oral calcium, calcium gluconate, for patients with moderately severe, Active vitamin D preparations such as rocitrol (calcitriol, 1,25- (OH) 2D3) should be added, starting at 0.25ug/ D and gradually increasing to 2ug/ D. And can be combined with aluminum hydroxide gel to inhibit the absorption of intestinal phosphorus, thereby promoting the elevation of blood calcium level. In this study, after completing relevant examinations in this patient, the results showed that pTH567.37pg/mL, alkaline phosphatase 160U/L, calcium 1.52mmol/ L, phosphorus 1.97mmol/ L and magnesium 0.82mmol/ L, and no obvious thyroid abnormalities were observed. Blood glucose was 6.1mmol/ L at random upon admission. Electroencephalogram showed no obvious abnormality, parathyroid imaging showed no obvious MIBI affinity lesion in parathyroid region, and no obvious abnormality in thyroid density and radioactivity distribution. Six ion tests: calcium 1.58mmol/L, inorganic phosphorus 1.81mmol/L, diagnosis of pseudohypoparathyroidism, calcitriol 0.5ug bid, calcium carbonate D31.2g Qd

symptomatic support treatment. In the course of treatment, blood magnesium, blood calcium, blood phosphorus levels and urinary calcium excretion should be measured regularly to control blood calcium level within the normal low limit of 2.0-2.2mmol/L. Patients with hypercalciuria can be treated with oral thiazide diuretics. If patients develop hypomagnesemia, they should be treated with magnesium to increase the sensitivity of the target organ to parathyroid hormone and ameliorate the problem of hypocalcemia.

Patients with this disease do not need special treatment if there are only physical changes but no biochemical changes. If patients only need oral vitamin D to maintain normal blood calcium and phosphorus levels, there is no need to take calcium orally. In the course of treatment, vitamin D dose should be strictly controlled to avoid vitamin D overdose. Toxic manifestations of excessive vitamin D include hypercalcemia, renal calcium deposition, hypertension and kidney damage ^[6]. If necessary, the parathyroid hormone can be controlled within the normal range to effectively prevent the occurrence of hyperparathyroidism bone disease. Inadequate suppression of parathyroid hormone levels may lead to tertiary hyperparathyroidism and fibrocystic osteitis. Some studies ^[7] have found that the application of calcium agent Sinacase in patients who failed to respond to conventional treatment has achieved good efficacy. Sinacase is commonly prescribed for hyperparathyroidism or secondary hyperparathyroidism due to renal failure. Its use suppresses the secretion of parathyroid hormone levels by activating calcium-sensitive receptors.

Patients with hypothyroidism can be given thyroxine replacement therapy, and patients with delayed sexual development and reduced menstrual volume can be given sex hormone replacement therapy. Short stature in pseudoparathyroidism is associated with premature closure of epiphysis, in addition to an accident related to GH deficiency due to GHRH resistance. Therefore, GH stimulation tests should be given as soon as possible to find evidence of this, and GH therapy should be given as soon as necessary. In this case, the patient was already an adult at the time of the initial onset and missed the best opportunity for treatment. However, timely symptomatic treatment is of great significance for improving the clinical symptoms of the patient. The lack of pseudo parathyroid function impairment of GH Ia patients, using recombinant GH treatment, for children patients, can significantly improve children height problem, improve physical and psychological symptoms in patients with all ages, such as physiological aspects of obesity, hyperlipidemia, renal function impairment, osteoporosis, etc., such as psychological fatigue, depression, etc. Recent studies ^[8] have found that obese patients with hypoparathyroidism are more likely to develop sleep apnea than obese patients, with an incidence of 45% in the former and only 1% to 5% in the latter. GH can promote fat metabolism, alleviate obesity to a certain extent, and reduce the incidence of apnea. If necessary, biphasic positive airway pressure auxiliary ventilation can be used before GH. In a small number of patients, ectopic calcification, which is bulky and affects appearance or function in specific areas such as subcutaneous connective tissue or near joints, can be treated surgically.

3. Discussion

Pseudoparathyroidism, also known as pseudoparathyroidism, is very similar to parathyroidism and is characterized by low blood calcium and high blood phosphorus levels. The disease is caused by abnormalities in the GNAS gene. GNAS gene is located in the long arm of human chromosome 20 (20Q13.3). Gs α is the most abundant gene product and also the most characteristic gene product. At the same time, it also produces four other transcripts including As, NESP55, XL α S and A/B. Exists in some renal proximal tubule, thyroid gland and gonads, pituitary, different areas of the central nervous system, and brown fat tissue, under normal circumstances, parathyroid hormone ACTS on the target cell receptor, the receptor with Gs alpha, activation of adenylate cyclase, and further activation of protein kinase A, subsequent cascade, realize the biological effect of hormone, In pseudohypoparathyroidism, the expression of Gs α is decreased, the biological activity is decreased, the response is decreased, the parathyroid gland appears compensatory hyperplasia and hypertrophy, and the parathyroid hormone secretion is increased ^[9]. In clinical practice, the clinical manifestations of pseudoparathyroidism vary depending on the target organ involved, such as epilepsy, ectopic calcification, juvenile dementia, etc. Laboratory examination of these patients showed elevated or normal PTH level, with low blood calcium, high blood phosphorus, low urinary calcium, urinary phosphorus, etc. Imaging examination showed that CT of the brain showed frequent calcification in the basal ganglia area, calcification foci in the cerebral cortex and other parts, and thickening of the skull plate, which was characterized by typical inverted figural calcification in the putamen and symmetrical spark calcification in the subcortical area ^[10-11]. Lens examination showed cataract, lens opacity, eeg showed diffuse lesions, epileptic waves, ECG showed frequent q-T interval prolongation and ST-segment specific changes.

At present, typical clinical symptoms and biochemical tests are the most reliable for the diagnosis of pseudoparathyroidism. When hypocalcemia occurs in children, serum parathyroid hormone and biochemical tests should be performed to diagnose or rule out pseudohypoparathyroidism. Molecular genetics research is a hot spot of current research, which can detect and

determine the type of pseudoparathyroidism according to gene mutation. If the patient does not show typical symptoms or biochemical changes in the early stage, the diagnosis of pseudoparathyroidism is difficult, and GNAS1 sequencing can be carried out. Some patients can also be identified by Gsα bioactivity testing and the Ellsworth-Howard test. To have fertility requirements of pseudo parathyroid function decline, should actively make prenatal gene diagnosis, several studies have found that GNAS1 gene expression and regulation mechanism and the function has been clear, all sorts of new pathogenic gene discovery also further deepen the understanding of the disease, has been clear about the pathogenic gene mutation genetic way, provides a convenient for prenatal counseling.

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