A RARE CASE OF SEIZURE ATTACK IN A PATIENT WITH HYPOPARATHYROIDISM

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Abstract

Seizure is one of the neurological manifestations in patients with hypoparathyroidism. Hypoparathyroidism is usually associated with chronic hypocalcemia, and the occurrence of seizures is uncommon in patients with this metabolic condition. It is often overlooked as a secondary cause of epilepsy at the initial examination, which leads to delays in treatment. Extensive bilateral symmetric intracranial calcification, especially of the basal ganglia, is a rare finding in hypoparathyroidism; such findings should alert physicians to the possibility of this condition, and the patient should be examined further. We describe the case of a 50-year-old man who experienced his first episode of seizure and had extensive bilateral symmetric intracranial calcification. Investigations revealed hypocalcemia, hyperphosphatemia, and a low serum level of intact parathyroid hormone. Hypoparathyroidism-induced seizure was diagnosed and was attributed to the coexistence of extensive intracranial calcification and hypocalcemia. The seizure was brought under control with calcium and vitamin D supplements.

Key words: Hypoparathyroidism, Extensive intracranial calcification, Seizure

Introduction

Seizure is a common cause of admission to the emergency department (ED). Patients presenting with seizures or seizure-related complaints represent approximately 1% to 2% of all patients visiting the ED. The causes of seizures are idiopathic (unprovoked seizures) in the majority of patients (62%). The causes of provoked seizures are stroke (9.0%), head trauma (9.0%), alcohol (6.0%), neurodegenerative disease (4.0%), static encephalopathy (3.5%), brain tumors (3.0%), and infection (2.0%). Metabolic disturbances such as uremia, hepatic failure, hypoglycemia, and electrolyte abnormalities are relatively uncommon causes. Seizures are rare in patients with hypoparathyroidism because of the chronic nature of hypocalcemia. According to the review data on the causes of seizure, hypoparathyroidism accounts for approximately less than 1% of all causes.

Hypoparathyroidism is caused by insufficient secretion of parathyroid hormone (PTH) and, less commonly, by impaired responsiveness.
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of the target tissues to PTH. Low PTH levels and hypocalcemia are the diagnostic factors for hypoparathyroidism. Extensive bilateral symmetric intracranial calcification is a characteristic finding in patients with hypoparathyroidism.\textsuperscript{3} Calcification is more common in the basal ganglia than in other sites. In this report, we describe the case of a seizure patient presenting with hypoparathyroidism and extensive bilateral symmetric intracranial calcification.

\textbf{Case Report}

A 50-year-old man experiencing a first episode of generalized tonic-clonic seizure was admitted to our ED. He had a history of poliomyelitis in his childhood, because of which his right lower extremity was atrophic. The extremity was further shortened after he underwent surgery for intertrochanteric fracture of the right femur at the age of 47. He reported no history of neck surgery or radiation therapy and no family history of epilepsy.

The seizure had subsided by the time the patient arrived at the ED. A physical examination showed that his vital signs were stable and that he was fully conscious. The results of a neurological examination were normal. Further, Chvostek’s and Trousseau’s signs were negative. Other physical examinations showed no skin pigmentation or icteric sclera and no abnormalities in the chest, abdomen, and testes. Ophthalmologic evaluation revealed no cataract, and the Kayser-Fleischer ring was absent. Laboratory studies revealed the following results: serum total calcium level, 4.6 mg/dl (normal range, 8.8-10.6); serum free calcium level, 2.21 mg/dl (normal range, 4.48-5.28); serum phosphorus level, 5.1 mg/dl (normal range, 2.6-4.4); serum magnesium level, 1.79 mg/dl (normal range, 1.8-2.55); serum albumin level, 4.3 g/dl (normal range, 3.1-4.8); serum intact PTH level, \(<2.5 \text{ pg/ml (normal range, 14-72)}\); morning serum cortisol level, 13.9 \(\mu\text{g/dl (normal range, 4.3-22.4)}\); serum free thyroxine (T4) level, 0.887 ng/dl (normal range, 0.93-1.7); and serum thyroid-stimulating hor- mone level, 2.71 \(\mu\text{IU/ml (normal range, 0.27-4.2)}\). Electrocardiography (ECG) revealed a normal sinus rhythm and a prolonged QT interval corrected for heart rate (QTc) of 521 ms. A non-contrast computed tomography (CT) scan of the brain showed extensive calcification in the left and right dentate nuclei (Fig. 1A) and the globus pallidus (Fig. 1B) and within the white matter of the frontal, parietal, and occipital lobes (Figs. 1B & 1C). The result of electroencephalography was normal, with the posterior background activity being 8.5 Hz.

The biochemical findings indicated hypoparathyroidism. The patient was administered phenytoin and calcium gluconate intravenously at doses of 300 mg per day and 3000 mg per day, respectively. One week later, his serum total calcium level rose to 5.7 mg/dl. Excellent seizure control was achieved, and the 2 drugs were discontinued. Thereafter, the patient was administered a supplementary treatment consisting of 0.25 \(\mu\text{g calcitriol per day and 4000 mg calcium carbonate per day. At a follow-up visit 1 month later, the patient’s serum total calcium level was 6.6 mg/dl. Until 4 months after this visit, no further episode of seizure had been reported.}

\textbf{Discussion}

The causes of seizure vary with age. Our patient was 50 years old and the common causes of seizures in this age group include cerebrovascular disease, trauma, tumors, and degenerative diseases.\textsuperscript{4} Seizures rarely occur in patients with hypoparathyroidism in this age group. Hence, it is often misdiagnosed at the initial examination, because of which treatment is delayed. As the seizure control worsens over time, further investigations are performed and hypocalcemia is detected. This leads to the identification of the underlying cause, namely, hypoparathyroidism.

Hypoparathyroidism can be congenital or acquired. Congenital hypoparathyroidism is caused by developmental defects in the parathyroid glands. It can occur as an isolated entity or in association
Acquired hypoparathyroidism is most often the result of inadvertent removal of the parathyroid gland during neck surgery. Other causes include radiotherapy-induced damage, hemochromatosis, Wilson disease, metastatic neoplasia, autoimmune polyendocrine syndrome type 1, and infectious diseases. In our patient, there was no evidence of secondary causes, and the results of the examinations indicated primary hypoparathyroidism with extensive bilateral symmetric intracranial calcification. The patient had a history of poliomyelitis, but no definite relationship between poliovirus and hypoparathyroidism has been determined to date. To the best of our knowledge, there has been no case report describing the pathogenesis of this condition. In addition, congenital hypoparathyroidism cannot be excluded, and gene sequencing may be required to confirm this.

Hypoparathyroidism leads to hypocalcemia, and its clinical manifestation depends on the duration, severity, and the rate of development of hypocalcemia. Rapid development of hypocalcemia may result in paresthesias, muscle spasms, confusion, irritability, seizures, heart failure, and respiratory failure. In chronic hypoparathyroidism, hypocalcemia develops gradually and is usually asymptomatic. While patients may present with extrapyramidal signs, cerebellar signs, reduced intelligence quotient, and cognitive impairment, such instances have rarely been reported. Moreover, it is likely that QTc prolongation will be revealed on ECG and that Chvostek’s and Trousseau’s signs will be positive. Other complications include premature cataracts, pseudotumor cerebri, and extensive intracranial calcification.

Intracranial calcification commonly occurs in physiological processes, tumors, aneurysms, atherosclerosis, and infectious diseases. Extensive bilateral symmetric intracranial calcification is the characteristic observation in hypoparathyroidism. Calcification has been reported to occur in the dentate nuclei of the cerebellum, cerebrum (particularly the white matter of the frontal lobes), and the basal ganglia, which is the most common with other endocrine abnormalities.

Fig. 1. Noncontrast computed tomography of head revealed extensive symmetric intracranial calcification in the bilateral dentate nuclei of the cerebellum (A), globus pallidus (B), and the white matter of the frontal (B, C), parietal, and occipital lobes (C).
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The mechanism of calcification is still unclear and may be related to the chronic abnormal intra- and extracellular concentrations of calcium and phosphate. The intracranial calcification associated with chronic hypoparathyroidism primarily affects small deep vessels and occurs in vascular and perivascular regions. The extrapyramidal signs, cerebellar signs, and reduced intelligence quotient may be related to calcification of the basal ganglia, cerebellum, and cerebrum respectively. In our patient, seizure may have been secondary to cerebral calcification, and hypocalcemia may have been the precipitating factor.

Seizure control in patients with hypoparathyroidism is often difficult with anti-epileptic drugs alone. The therapy should be targeted at treating the underlying cause-hypoparathyroidism. Hypoparathyroidism can be treated with calcium salts, vitamin D or vitamin D analogues, and thiazide diuretics. After the serum calcium level is restored, the neurological manifestations disappear. In our patient, the seizures were brought under excellent control by administering calcium and vitamin D supplements. After 1 month of therapy, the patient’s serum total calcium level increased substantially but was still below the normal range. However, the patient did not have any further symptoms. Intracranial calcification may be inhibited with early treatment. However, progressive cerebral calcification has been observed even in cases where normocalcemia is maintained. Hence, the correction of hypocalcemia alone may not be sufficient to prevent cerebral calcification in our patient in the future.

Secondary causes of epilepsy are usually overlooked in patients presenting with seizure. Hypoparathyroidism should be considered in the diagnosis of such patients irrespective of their age. The serum calcium level should be evaluated in the case of new-onset seizures, especially when the CT scans of the brain show extensive bilateral symmetric intracranial calcification. After calcium supplement therapy has been initiated, the serum calcium level should be measured frequently and maintained at a low normal level in order to prevent side effects such as hypercalciuria and nephrolithiasis.

References

一個副甲狀腺功能低下症病人併發罕見的癲癇發作

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摘要

癲癇是副甲狀腺功能低下症病人的其中一種神經學症狀。副甲狀腺功能低下症通常呈現慢性的低血鈣，而且癲癇在這些病人裡面並不常見。作爲一個癲癇的次發性原因，它常在一開始的檢查中被遺漏，因而延誤治療。廣泛性顱內鈣化，特別是發生在基底核這個部位，是副甲狀腺功能低下症一個很罕見的影像學發現，同時也提醒臨床醫師進一步評估病人。我們報告一位五十歲男性，以初次癲癇發作及廣泛性顱內鈣化為表現。檢查結果發現低血鈣、高血磷及低副甲狀腺素。之後被診斷為副甲狀腺功能低下症誘發的癲癇，這是因爲同時合併廣泛性顱內鈣化及低血鈣。這個病人的癲癇症狀在鈣補充劑及維生素D的治療下，獲得良好的控制。

關鍵詞：副甲狀腺功能低下症，廣泛性顱內鈣化，癲癇

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