

# Basal ganglia calcification in idiopathic hypoparathyroidism

Two case reports show how hypocalcemia due to a deficiency of parathyroid hormone can cause neuromuscular dysfunction.

**ABSTRACT:** Hypoparathyroidism refers to a group of disorders in which extracellular calcium levels cannot be maintained within the normal range due to relative or absolute deficiency of parathyroid hormone. Clinically, hypoparathyroidism manifests predominantly as neuromuscular dysfunction caused by hypocalcemia. Basal ganglia calcification in particular is associated with hypoparathyroidism. Two different presentations of basal ganglia calcification associated with idiopathic hypoparathyroidism illustrate common features and clinical findings of this condition.

## Case 1 data

In January 2007, a 62-year-old male was involved in a motor vehicle collision secondary to a sudden loss of consciousness following a witnessed generalized tonic-clonic seizure. Investigations found low levels of serum parathyroid hormone levels at 1.4 pmol/L (reference range 1.2 to 8.4 pmol/L), low serum total calcium (Ca) at 1.48 mmol/L (2.10 to 2.55 mmol/L), low ionized calcium (iCa) at 0.91 mmol/L (1.17 to 1.29 mmol/L), and low albumin at 26 g/L (35 to 51 g/L). Levels were within the reference range for phosphate at 0.91 mmol/L (0.81 to 1.45 mmol/L), magnesium at 0.78 mmol/L (0.70 to 1.00 mmol/L), and creatinine at 101 µmol/L (71 to 133 µmol/L). A CT scan of the head showed prominent basal ganglia calcification (BGC), especially in the lentiform nuclei bilaterally (**Figure**). Findings from an EEG were normal, and full neurological and cardiac assessment found no apparent cause for the loss of consciousness. The seizure was presumed to be secondary to hypocalcemia due to primary hypoparathyroidism. The patient was

started on vitamin D (50 000 units daily) and calcium carbonate (3000 mg daily). On discharge, the patient's serum calcium level had increased to 2.15 mmol/L, and his serum phosphate had increased to 1.37 mmol/L. In retrospect, he described a history of cramping of the thumbs bilaterally, sweeping across the hands and fingers, but no other symptoms of hypocalcemia. His medical history was unremarkable otherwise, and he was not taking any medications prior to the motor vehicle collision.

## Case 2 data

In 2008, a 27-year-old female presented with a 14-year history of headaches and a 1-year history of hand cramps. Investigations found low levels of both total serum calcium at 1.28 mmol/L and ionized calcium at 0.6 mmol/L, and a very low level of PTH. The patient's serum creatinine level was normal and her medical his-

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*This article has been peer reviewed.*



**Figure.** CT image of Case 1 patient showing calcification of the basal ganglia.

tory was unremarkable. After a CT scan of the head found calcification of the basal ganglia she was diagnosed with primary hypoparathyroidism and started on alfacalcidol and calcium supplementation. Follow-up investigations in 2011 revealed low serum calcium at 1.64 mmol/L, elevated phosphate at 1.7 mmol/L, and low 24-hour urinary calcium excre-

tion at 0.4 mmol (reference range 1.0 to 7.0 mmol). The patient's dose of alfacalcidol was increased from 0.5 µg daily to 0.75 µg daily and she was continued on calcium carbonate at 3000 mg daily.

### Discussion

Basal ganglia calcification is a non-specific finding in 1% of all CT head

scans.<sup>1</sup> It is divided into two broad categories: physiological and pathological. Physiological BGC is an incidental asymptomatic finding on CT, most commonly seen in elderly patients. Conversely, pathological BGC presents with clinical manifestations and should be suspected in patients under age 30.<sup>1</sup> The most common causes of pathological BGC are

hypoparathyroidism and pseudo-hypoparathyroidism.<sup>2</sup> Other causes include hypoxia at birth, exposure to toxins (lead, carbon monoxide, chemotherapeutic agents), radiation therapy, infections (TORCH infections, HIV, tuberculosis), infiltrative diseases (malignancy, sarcoidosis), and inherited neurodegenerative disorders. Familial idiopathic BGC,

Other areas affected by BCG include the thalamus, dentate nuclei, cerebral cortex, gray-white junctions, and the cerebellum.<sup>4,6</sup> Such intracranial calcification occurs in 0.3% to 1.5% of patients with hypoparathyroidism, and is often detected incidentally.<sup>7,8</sup>

As a result of calcification and hypocalcemia, various neurological symptoms may arise. Most common-

the calcium-sensing receptors regulating PTH can also occur, secondary to genetic mutations. Some patients have idiopathic hypoparathyroidism, and in these cases, it may be useful to investigate for an attenuated form of DiGeorge syndrome with a 22q11.2 deletion on chromosome 22.<sup>11</sup>

Basal ganglia calcification in idiopathic hypoparathyroidism is a progressive disorder and has been observed to worsen despite maintenance of normal calcium levels.<sup>5</sup> A recent prospective study found that increased risk of BGC progression—defined as new sites of calcification or increased volume of calcification detected on CT—is significantly associated with a low calcium to phosphorus ratio (119% vs 151%;  $P < 0.001$ ), hyperphosphatemia (2.1 mmol/L vs 1.7 mmol/L;  $P < 0.01$ ), and a history of seizure (71.4% vs 28.6%;  $P = 0.01$ ). Interestingly, 25(OH)D (calcifediol) or 1,25(OH)2D (calcitriol) levels were not significantly associated with progression. Furthermore, the researchers found that for every 1% increase in the calcium to phosphorus ratio, progression of basal ganglia calcification decreased by 5%.<sup>5</sup> These findings suggest that early diagnosis and strict control of phosphorus is another crucial component in treating and preventing progression of BGC.<sup>5</sup>

In a prospective study, Aggarwal and colleagues found there was a significant association between cognitive dysfunction and the duration of hypocalcemia, serum calcium levels, and calcium-phosphorus complex formation, but no association with serum 25(OH)D levels, serum PTH levels, or the volume or site of basal ganglia calcification.<sup>12</sup>

Despite some uncertainty about the exact pathogenesis of BGC, treatment is known to prevent progression. Thus, clinicians are advised to:

1. Investigate for hypoparathyroidism

### **Presently, treatment consists of calcium supplementation and the use of vitamin D analogs, but PTH replacement is under investigation.**

known as Fahr disease, is a rare disorder that can be sporadic or inherited in an autosomal dominant pattern. It is diagnosed when infectious, toxic, and traumatic causes have been ruled out.<sup>3</sup>

BGC was first described in association with chronic hypoparathyroidism by Eaton in 1939.<sup>4</sup> Pathogenesis is unknown, but its occurrence with hypocalcemia suggests that increased calcium-phosphorus complex formation plays a role. Radiological studies have found that calcification surrounding cerebral blood vessels most frequently occurs in the lentiform (putamen and globus pallidus) and the caudate nuclei of the basal ganglia; however, the factors that predispose individuals to basal ganglia calcification have not been identified.<sup>5</sup>

ly, seizures and tetany occur. Extrapyramidal symptoms such as parkinsonism and cerebellar dysfunction are also seen.<sup>9</sup> Other complications are known to result from hypocalcemia, including increased risk of fractures, but generally the lack of large long-term prospective studies means the natural history of idiopathic hypoparathyroidism and related complications are not well understood.<sup>10</sup>

There are various causes of hypoparathyroidism. These include postsurgical effects from thyroid, parathyroid, or radical neck surgery for head and neck cancer, and autoimmune, radiation-induced, infiltrative, and infectious destruction of the parathyroid glands. Abnormal development of the parathyroid gland, abnormal production of PTH, or abnormal function of

in the presence of basal ganglia calcification.

2. Identify any manifestations of basal ganglia calcification and hypoparathyroidism, including cognitive dysfunction, neuromuscular dysfunction, and seizure.
3. Treat hypoparathyroidism with calcium and vitamin D.
4. Treat to obtain a target serum calcium level in the low normal range (~ 2.00 to 2.13 mmol/L).
5. Monitor for a target 24-hour urinary calcium excretion rate of 2.5 to 3.75 mmol daily.

Clinicians should remain aware that treatment with calcium supplements and vitamin D analogs increases the risk of hypercalciuria, which in turn can lead to nephrolithiasis, nephrocalcinosis, and decreased renal function.<sup>10</sup>

Recombinant parathyroid hormone replacement has been studied but not yet approved for hypoparathyroidism. Although some studies have shown that subcutaneous administration of parathyroid hormone can decrease hypercalciuria and decrease skeletal complications when compared with administration of calcitriol, the long-term safety of this therapy has not been established.<sup>13-16</sup>

### Summary

The two cases described here show that idiopathic hypoparathyroidism associated with basal ganglia calcification can present in different ways. Various neuromuscular manifestations secondary to basal ganglia calcification, hypoparathyroidism, and hypocalcemia commonly occur. Presently, treatment consists of calcium supplementation and the use of vitamin D analogs, but PTH replacement is under investigation. Treatment is important to prevent progression of BGC.

### Competing interests

None declared.

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