Hypocalcemia and Fahr syndrome in a patient with Graves'disease: Difficult etiological diagnosis

Sir,

Graves' disease is an autoimmune disorder typically characterized by the presence of circulating autoantibodies that tie to and stimulate the thyroid hormone receptor, resulting in hyperthyroidism, and goiter.[1] Hyperthyroidism is known to cause a relatively mild hypercalcemia secondary to an increase in bone turnover and mobilization of calcium from bone into the circulation.[2]

Fahr syndrome is a rare inherited or sporadic neurological disorder characterized by the presence of bilateral intracranial calcifications with predilection for the basal ganglia and dentate nuclei.[3] It is commonly associated with endocrine disorders, particularly parathyroid and Vitamin D disturbances.

A 29-year-old male was referred to our department with a malignant Graves' ophthalmopathy. One year ago, he was diagnosed with Graves' disease and treated with benzylthiouracil. While thyrotoxicosis symptoms showed improvement, the proptosis deteriorated following the initiation of antithyroid drug.

On examination, he had a body weight of 48 kg, a body mass index of 17 kg/m^2, a blood pressure of 120/80 mmHg, and a regular pulse of 80 beats/min and diffusely enlarged thyroid gland. He had a bilateral and asymmetric proptosis with conjunctive edema, hyperemia, and vertical diplopia. No typical findings of Albright's hereditary osteodystrophy were observed. Moreover, Trousseau and Chvostek signs were negative. The rest of clinical examination and the electrocardiograph were normal.

Laboratory investigations revealed normal thyroid tests, normal renal function, hypocalcemia of 1.77 mmol/L (normal range: 2.1–2.55), hyperphosphatemia of 1.8 mmol/L (normal range: 0.74–1.52), calciuria of 1.2 mmol/24 h, serum magnesium of 0.86 mmol/L (normal range: 0.66–1.07), serum alkaline phosphatase of 94 U/L (normal range: 40–150 U/L), serum albumin of 50.3 g/L (normal range: 38–56), a low 25 OH Vitamin D level (9.3 μg/L, normal range: 30–80 μg/L), and elevated parathormone

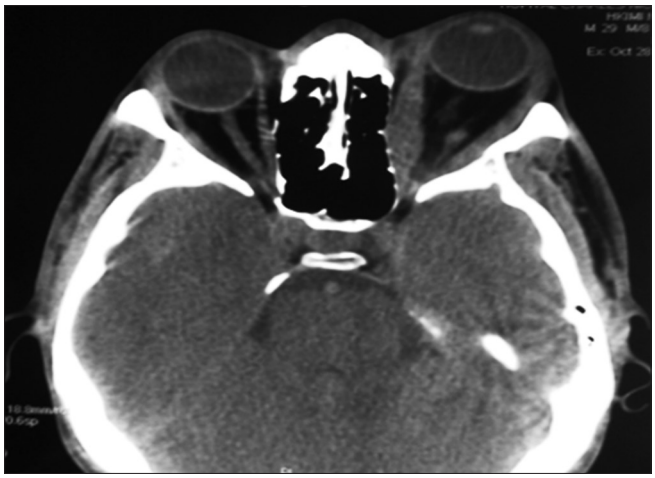

Figure 1: Orbital computed tomography showed Grade III left proptosis

level of 203.3 pg/ml (normal range: 15–68.3). Urinary cyclic adenosine monophosphate level and Gsα subunit assay were not available.

Ultrasound of the neck showed enlarged thyroid gland with an intense vascularity; no nodules were identified. Orbital computed tomography showed Grade III left proptosis [Figure 1].

Computed tomography scan of the brain revealed Fahr syndrome with a bilateral and symmetric striatopallidal calcifications [Figure 2]. The bone mineral density showed osteopenia.

The patient was prescribed Vitamin D supplementation, calcium gluconate, and corticosteroids.

After 3 months, serum calcium level was found to be 2.07 mmol/L, and phosphatemia was found to be 1.5 mmol/L. The serum parathyroid hormone (PTH) was persistently high (163.8 pg/ml).

Hypocalcemic disorders with a normal to elevated serum phosphate level can be subdivided into hypoparathyroidism and pseudohypoparathyroidism (PHP) in the absence of chronic renal failure. In our patient, the diagnosis of hypoparathyroidism was ruled out according to the high PTH level.

In this case, low 25 OH Vitamin D level was consistent with the diagnosis of secondary hyperparathyroidism due to Vitamin D deficiency. Typically, Vitamin D deficiency is associated with normal or decreased serum phosphorus levels. However, in some patients, marked hypocalcemia is accompanied by normo- or hyperphosphatemia.[4]

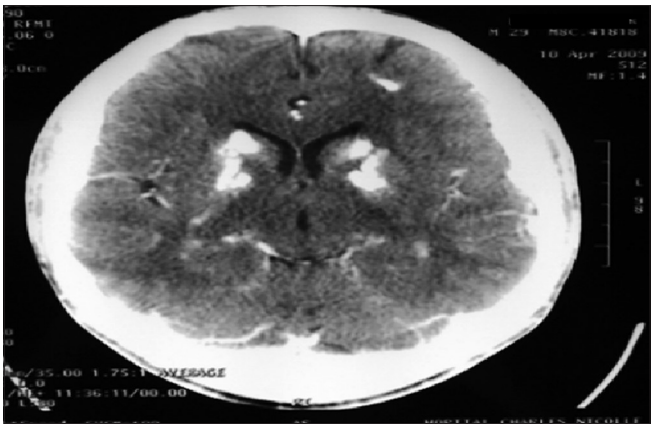

Figure 2: Computed tomography-scan of the brain revealed Fahr syndrome with a bilateral and symmetric striatopallidal calcifications

PHP has been reported as a cause of Fahr syndrome. It constitutes a very rare group of heterogeneous disorders characterized by hypocalcemia, hyperphosphatemia, normal or increased PTH secretion, and target tissue resistance to the actions of PTH.[5] Most reported cases of PHP Type II are preceded by or simultaneously present with autoimmune disorders, such as Sjogren's syndrome, Hashimoto's thyroiditis, or Graves' disease.[5]

According to the biochemical similarities between Vitamin D deficiency and PHP, differential diagnosis based on routine biochemistry can be difficult.[6]

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Conflicts of interest
There are no conflicts of interest.

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