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Case Report

Internal Medicine Section

Delayed Post-Surgical Hypoparathyroidism: The Forgotten Chameleon!

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ABSTRACT

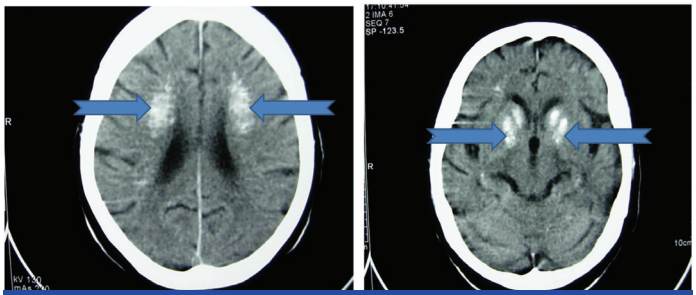
Delayed hypoparathyroidism, due to accidental gland removal or ischemia of parathyroids can present many years after thyroidectomy and symptoms may be non-specific. This condition, if not diagnosed timely, may prove fatal and have serious consequences. Hence, clinicians must have a high index of suspicion to treat this condition. All patients with a history of previous thyroid surgery, who come with vague symptoms like fatigue, muscle aches should undergo estimation of serum calcium, phosphorus and Parathyroid Hormone (PTH) due to the lack of any pathognomonic features of hypoparathyroidism. We report a rare case of delayed post-surgical hypoparathyroidism who became symptomatic 15 years after thyroid surgery and remained so for another 10 years before the final diagnosis was established.

Keywords: Hypocalcaemia, Late, Parathyroid glands, Surgery, Tetany

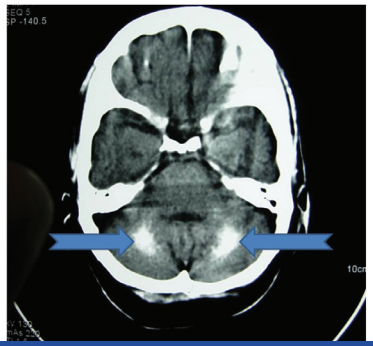
CASE REPORT

A 76-year-old female patient was admitted with two episodes of generalized seizures followed by altered sensorium for the first time, on the day of admission. She had history of recurrent calf muscle cramps and aches in the legs for past 10 years. Over last five years, she had developed progressive forgetfulness, jitteriness, difficulty in walking, getting up from squatting position and rising from the chair, tingling and numbness in the hands, toes and around the mouth. The difficulty in walking had progressed and presently patient was unable to walk and stand without support. She also had developed difficulty in speaking, breathlessness on mild exertion and occasional choking episodes especially at nights. She again had two episodes of generalized tonic, clonic seizures while in the hospital. She was on thyroxin supplement for hypothyroidism. On direct questioning, she reported to having undergone thyroidectomy 25 years back for a large goiter. She could not recollect further surgical details. Patient was well for 15 years after surgery after which, her above mentioned symptoms had started gradually. She had no addictions. She had seen various doctors from different specialties, without relief before she finally came to our hospital. There was no family history of similar symptoms.

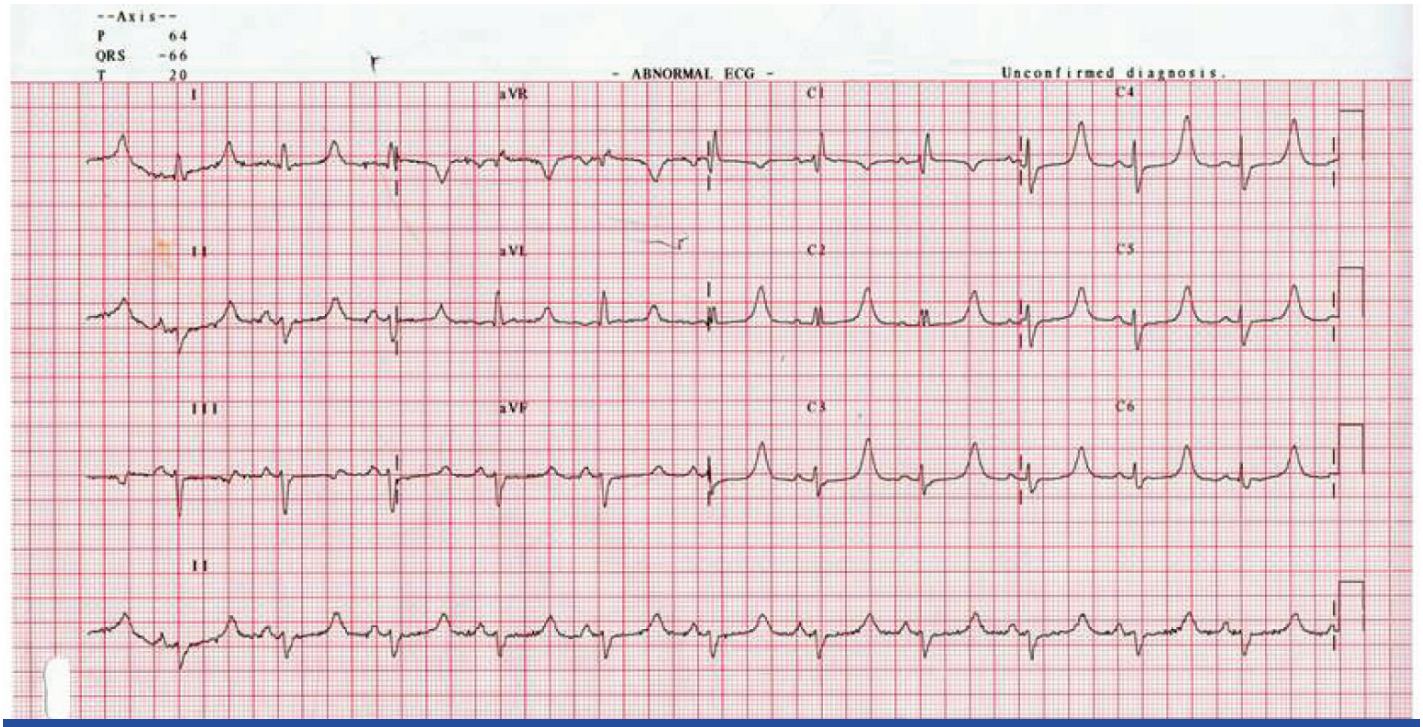
On examination, she was average build and had mild pallor. On close inspection, she had healed surgical scar in the neck which blended with the skin crease. Her pulse was 72/minute, regular, blood pressure 130/70 mm Hg. Examination of Central Nervous System (CNS) revealed an alert person, oriented to person, time but not place. She had poverty of ideas with loss of recent memory. Fluency of speech was lost but naming and comprehension was preserved. Her speech was of low intensity and was monotonous. There was no papilloedema. There was hypotonia in all groups of muscles. Muscle power was 3+/5 across all joints of upper and lower limbs. Deep tendon reflexes were grade 2. There were no abnormal movements at rest. Plantars were flexors. She was grossly ataxic on standing and had broad based gait. There was no truncal ataxia but there was dysdiadochokinesia and knee-heel incoordination. Trousseau's sign and Chovstek's sign were positive. Her laboratory tests showed hemoglobin 9.8g/dl, total leucocyte count 7,400 with 66% neutrophils and 30% lymphocytes, serum creatinine 1.3 mg/dl, serum sodium 138 mmol/L, potassium 3.9 mmol/L, serum total calcium 4.5 mg/dl (normal range 9 to 11 mg/dl), ionized calcium 0.21 mg/dl (normal 1.19-1.57), (pH of arterial blood-7.42), serum phosphorus–8.5 mg/dl. Her total serum proteins were 7.2 g/dl and serum albumin was 4.2 gm/dl. Her serum Alkaline Phosphatase (ALP) was 146 KA. Rest of the liver function tests were within normal limits. Her serum intact Parathyroid Hormone (PTH) level was 3.3 ng/ml (normal range 9.5–75 pg/ml), thyroid stimulating hormone (TSH) - 2.99 mIU/ml, and serum 25- hydroxyvitamin D (vitamin D3) level was - 27 ng/ml. Chest X-Ray was normal. Ultrasound of abdomen did not show any nephrolithiasis. Computerized Tomography (CT) brain revealed multiple calcifications in basal ganglia, [Table/Fig-1], junction of grey and white matter, thalamic



[Table/Fig-1]: CECT brain showing bilateral basal ganglion calcification. **[Table/Fig-2]:** CECT brain showing bilateral thalami calcification.



[Table/Fig-3]: CECT brain showing bilateral cerebellar calcification.



[Table/Fig-4]: ECG showing tall T waves and prolonged QTc interval.

nuclei [Table/Fig-2] and dendate nucleus of cerebellum [Table/Fig-3]. ECG showed sinus bradycardia, prolonged QTc interval (0.503 sec) and tall T waves [Table/Fig-4]. Echocardiography revealed grade 2 diastolic dysfunction. Osteoporosis was detected in X-Ray of lumbosacral spine. A diagnosis of hypocalcaemia due to post surgical hypoparathyroidism with hypothyroidism was made. There was no evidence of any other factor contributing to the hypocalcaemia. Patient was treated initially with intravenous calcium gluconate (200 mg calcium in 100 mL 5% dextrose, for 5-10 min) and magnesium sulfate (1g tid intravenously), later by oral 500 mg of calcium carbonate four times a day (3g/day) along with 0.5mcg of 1,25 dihydroxy vitamin D3 (alfacalcidol) and thyroxine supplement 150 mcg/day. In addition, the patient was scheduled to receive bisphosphonate therapy once her calcium level returned to normal. Her neuromuscular and biochemical abnormalities slowly responded to calcium and vitamin D supplementation over two weeks. The QTc interval was decreased to 0.41s. She left the hospital against the medical advice after 2 weeks. Her serum calcium had increased to 7.0 mg/dl and symptomatically was much better at discharge.

DISCUSSION

Hypoparathyroidism is caused as result of congenital disorders, iatrogenic causes (e.g., removal or injury of the parathyroid glands during thyroid or parathyroid surgery, radiation), infiltration of the parathyroid glands (e.g., metastatic carcinoma, Wilson's disease, sarcoidosis), suppression of parathyroid function such as in hypomagnesaemia, HIV/AIDS, or idiopathic mechanisms [1]. The most common cause of hypoparathyroidism is inadvertent accidental removal of or damage to the parathyroid glands or their vascular supply during thyroidectomy and haematoma formation [2].

The incidence of postoperative permanent hypoparathyroidism varies widely in literature from 1.7% to 68% [3-6]. The various risk factors found were large volume goiter, total thyroidectomy, retrosternal extension, malignancy, hyperthyroidism, and experience of the operating surgeon [7]. Hypocalcaemia persisting 6 months after surgery in the presence of low or inappropriately normal PTH levels is defined as permanent hypoparathyroidism [3,5,6] and needs lifelong oral calcium and vitamin D supplementation. Hence, patients should undergo long term follow up to ensure that this complication does not present at a later date.

Hypoparathyroidism is biochemically characterized by hypocalcaemia, hyperphosphatemia, and a very low or undetectable PTH level. Low PTH levels result in excessive urinary calcium losses, decreased bone remodeling, and reduced intestinal calcium absorption, thus causing hypocalcaemia. Growth impairment, mental retardation, hearing loss or other congenital abnormalities suggest the presence of a genetic cause [1]. On physical examination, one must look for neck scarring, for evidence of neck surgery as patients might not recall remote neck surgery. Chvostek and Trousseau signs should be elicited in patients with hypocalcaemia. Patients who gradually develop hypocalcaemia are more likely to be asymptomatic. Our patient presented with classical symptoms of hypocalcaemia which include paresthesia, muscle spasms, cramps, main d'accoucheur, tetany, circumoral numbness, laryngospasm, neuromuscular irritability, cognitive impairment, personality disturbances, dementia, seizures, and Parkinsonism. ECG changes include prolongation of QT interval via prolongation of the plateau phase of the cardiac action potential making them prone for ventricular arrhythmias [8]. The tall T waves seen in our patient was probably due to associated hypomagnesaemia. QT interval was narrowed once the hypocalemia got partially corrected.

Hypoparathyroidism from any cause, causes pathological calcification most often symmetrically in bilateral basal ganglia. The most common site of ectopic calcification is the globus pallidus. However, intracranial calcifications have also been described at other sites like in the cerebellum, sub cortical white matter, corona radiata and the thalamus [9]. The mechanism of intracranial calcification in hypoparathyroidism is probably due to hyperphosphatemia which promotes ectopic calcification in the brain tissue. Intracerebral calcium deposition also occurs in many conditions like familial idiopathic cerebral calcification (Fahr's syndrome), infections like cerebral toxoplasmosis, lead and carbon monoxide poisoning, radiotherapy, mitochondrial cytopathies or may be physiological (age-related) in about 0.3-1.5% of normal people [9]. In addition, calcifications may also be found in skull, soft tissues and premature closure of epiphysis may occur [10]. The clinical presentations of basal ganglia calcification are diverse, the most common being seizures, psychosis, papilloedema, mental deterioration and disorders of cerebellar or extra-pyramidal function. Adequate treatment of hypoparathyroidism can lead to clinical improvement in neurological disorders (except Parkinsonism) [11]. Hence, it is

essential to determine the serum calcium, phosphorus, and parathyroid hormone in all individuals with calcification of the basal ganglia to rule out hypoparathyroidism so as to treat these patients early, and prevent irreversible damage.

This case reminds us of one of the late complications of thyroid surgery. Although hypocalcaemia usually occurs soon after surgery, progressive atrophy of the parathyroid glands results in late presentation. In our case the correct diagnosis was not established until 10 years after the onset of symptoms, though she had later developed florid manifestations. Although some patients may tolerate low calcium for many years as in our case, those reported by Bellamy [12], Cox [13], and Blanchard [14] illustrate that it may potentially be life-threatening due to seizures and fatal laryngeal spasm.

Only few cases of hypoparathyroidism diagnosed several years after surgery have been reported. Bellamy et al., described a patient of unrecognized hypocalcaemia 36 years after total thyroidectomy for papillary carcinoma [12]. Arpaci et al., reported a case of hypocalcaemia related generalised seizure 20 years after sub-total thyroidectomy [6]. Halperin et al., reviewed four patients with delayed postoperative hypoparathyroidism presenting five to 23 years after thyroid surgery [15]. Agarwal R et al., described a rare case of iatrogenic hypoparathyroidism after total thyroidectomy done 10 years earlier with features of Parkinsonism, cerebellar symptoms and seizures. CT brain showed extensive intracranical calcifications like in our case [16]. This case is presented in view of its rarity of occurrence and to create awareness about this potential complication in post thyroidectomy patients.

CONCLUSION

Late-onset hypoparathyroidism which occurs several years after total thyroidectomy is rare. Symptoms of hypocalcaemia such as weakness, tiredness, irritability and depression are non-specific and may be mistaken for other diseases like anxiety neurosis. Although hypocalcaemia typically occurs in the immediate postoperative period, progressive atrophy of the parathyroid glands, leading to its insufficiency can occur years after thyroid surgery, resulting in late hypocalcaemia. As these patients may not be on regular follow up, the diagnosis is easily missed. Hence, serum calcium, phosphorus and PTH assay must always be done in patients who have undergone thyroidectomy irrespective of the timing of surgery to identify and treat these patients early as delay in treatment can lead to life-threatening complications and irreversible damage. Besides, history of thyroid surgery may not be forthcoming in every case and hence the need to always look for a thyroidectomy scar.

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