Original article

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Hypocalcemic generalised seizures as a manifestation of iatrogenic hypoparathyroidism months to years after thyroid surgery

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ABSTRACT – Hypoparathyroidism is a relatively common side effect of a thyroidectomy and leads to hypocalcemia. Carpopedal spasm and tetany are typical manifestations and usually occur within weeks after surgery. The first signs can be less typical and include movement disorders such as chorea, as well as symptoms of increased intracranial pressure or epileptic seizures. We describe two cases with generalised tonic-clonic seizures as the first manifestation of postoperative hypoparathyroidism, appearing months and years after thyroidectomy. Iatrogenic hypoparathyroidism needs to be considered in the differential diagnosis of adult-onset, generalised, tonic-clonic seizures even if the thyroidectomy was performed years earlier.

KEY WORDS: adult-onset, generalised, tonic-clonic seizure; hypocalcemia; hypoparathyroidism, thyroidectomy.

Hypoparathyroidism results in an insufficient or non-existent secretion of parathyroid hormone (PTH). It can be iatrogenic (following thyroidectomy), idiopathic, hereditary, and can occur in association with autoimmune diseases, with pancreas insufficiency or with hypomagnesemia [1-4]. The resultant hypocalcemia can be divided into different degrees of severity depending on the plasma levels of calcium and phosphate [5].

Patients with iatrogenic hypoparathyroidism usually present with tetany within weeks of the thyroidectomy. However, the clinical presentation of hypoparathyroidism can be less obvious and much delayed. The first manifestation may be a movement disorder such as chorea, symptoms of an increased intracranial pressure or epileptic seizures [6-8].

We describe two cases with generalised tonic-clonic seizures, accompanied by generalised spike and wave complexes in one case, as the initial manifestation of postoperative hypoparathyroidism months to years after thyroidectomy.

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Case reports

Case 1

A 42-year-old woman was admitted because of a first generalised of tonic-clonic seizure. On admission, the postictal drowsiness had subsided. The neurological examination showed a right lateral tongue bite and enuresis, but no others abnormalities. Past medical history revealed a subtotal thyroidectomy performed nine month earlier. Since the operation the patient had been on 25µgL-thyroxine once a day. There was no family history of epilepsy and no history of alcohol abuse. The initial laboratory findings showed a low serum calcium level (1.5 mmol/L; normal value 2.2-2.6 mmol/L). Thyroxin levels were normal. The EEG revealed intermittent slowing and generalised spike-wave-complexes, *(figure 1)*. The tentative diagnosis of hypoparathyroidism was confirmed by the following laboratory tests: parathyroid hormone was low (3 pg/mL; normal value 15-70 pg/mL) and urinary excretion of both calcium (0.6 mmol/d; normal value 2.5-7.5 mmol/d) and phosphate (7.2 mmol/d; normal value 10-33 mmol/d) were subnormal. Cranial CT and MRI were both normal. Treatment with cholecalciferol and calcium was initiated and resulted in normalised serum calcium level and EEG. The patient was discharged without anticonvulsants but with oral calcium and Vitamin D. She did not experience any further seizures during the 12-month follow-up.

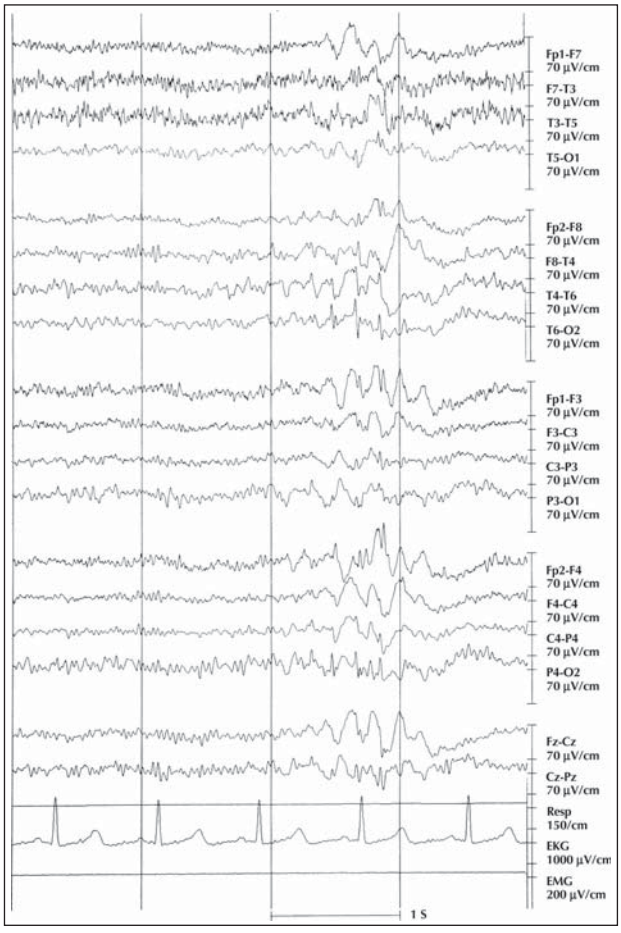

Figure 1. *The EEG on the day of admission shows irregular spike and wave complexes, generalised, maximum bifrontal.*

Case 2

A 53-year-old woman was admitted after a first episode of generalised tonic-clonic seizure. She had a right lateral tongue bite, enuresis and demonstrated a positive Chvostek sign. Past medical history revealed a subtotal thyroidectomy two years earlier. There was no family history of epilepsy. Both serum calcium (1.0 mmol/L; normal value 2.2-2.6 mmol/L) and PTH (5.5 pg/mL, normal value 15-70pg/mL) were clearly subnormal. The EEG showed an intermittent generalised slowing, without spike-wave-complexes or focal abnormalities. The patient was discharged on oral calcium and Vitamin D and without anticonvulsant therapy. As the patient did not return to the hospital during the next 12 months, no follow-up was possible.

Discussion

We report on two patients with generalised seizures as the first symptom of iatrogenic hypoparathyroidism and hypocalcemia several months to years after thyroid surgery. Carpopedal spasm and tetany are common effects of hypocalcemia following a thyroidectomy if the parathyroid glands are accidentally removed. Seizures are less common. Fonseca and Calverley described 42 patients with hypoparathyroidism, 30 of which had tetany and 12 with seizures [7]. Dimich and co-workers observed epileptic seizures in nine out of 34 patients with hypoparathyroidism, with tetany occurring in 29 patients [8]. Seizures were more common in idiopathic as compared to postsurgical hypoparathyroidism, and there was no positive family history of epilepsy in such patients [7, 8].

Tetany usually appears within the first month after surgery. In contrast, the time after which seizures develop varies considerably. In the study of Basser, 32 out of 36 patients with postsurgical hypoparathyroidism developed tetany within the first four weeks after surgery, only five patients had seizures in the first twelve month, and in six patients seizures appeared later 4-15 years [9]. Intervals from surgery to the first seizure of up to 61 years have been reported in single cases [10-12]. In our patients, there was a latency of nine month and two years between surgery and the seizures as the initial clinical presentation of hypoparathyroidism.

In our case one, an adult-onset idiopathic generalised epilepsy was considered as the diagnosis because of the generalised spike and wave complexes recorded in the

EEG [13]. Loiseau *et al.* reported adult-onset idiopathic epilepsy to be rare and more frequent in women than in men [14]. They suggested a genetic predisposition for epilepsy as the aetiology. Basser and co-workers reported that the EEG showed diffuse slow-wave abnormalities in 12 out of 41 patients with hypoparathyroidism [9]. No correlation was found between calcium levels and EEG changes, suggesting that constitutional factors may have an influence on the risk of developing seizures. On the other hand, the lack of a positive family history for epilepsy in our case one and the cases reported so far argues against a strong involvement of a genetic predisposition [7, 8].

There was also no indication of vitamin D deficiency as a possible differential diagnosis for the hypocalcemia [15, 16].

In the second case, there was no history of any clinical signs of hypocalcemia, but in the medical examination there was a positive Chvostek sign, indicating hyperexcitability as result of hypocalcemia. The EEG showed only non-specific generalised changes without spike-wave-complexes or focal EEG findings similar to the findings reported by Basser and co-workers [9].

These case reports demonstrate a rare but important differential diagnosis in generalised tonic-clonic seizures of adult onset. Generalised tonic-clonic seizures as initial clinical presentation of hypoparathyroidism tend to occur with a relatively long latency after thyroidectomy. This underlines the necessity of taking a careful medical history and measuring the electrolytes in patients admitted with first epileptic seizures.

In summary, iatrogenic hypoparathyroidism is an important differential diagnosis in adult patients presenting with a first generalised tonic clonic seizure. The EEG may show generalised spike-wave complexes in this setting. □

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