Primary hyperthyroidism due to a parathyroid adenoma with subsequent myasthenia gravis

Sir,

There are two cases in the world literature reporting an association between myasthenia gravis with thymoma and hyperparathyroidism.\(^1\) In the first, the hyperparathyroidism was due to a parathyroid adenoma,\(^1\) while in the second it was due to nodular hyperplasia.\(^2\) Subsequently, a case with no myasthenia gravis but with a thymoma and hyperparathyroidism due to a parathyroid adenoma has been published.\(^3\)

We report a case of myasthenia gravis and hyperparathyroidism due to a parathyroid adenoma with no thymoma detected. We also raise the possibility that the myasthenia gravis was precipitated by the use of intravenous pamidronate.

A 67-year-old lady, previously treated for thyrotoxicosis with radiiodine, presented to the urologists with renal colic. Laboratory investigation revealed hypercalcaemia (3.13 mmol/l; normal range 2–2.6 mmol/l) and a high PTH level (320 ng/l; normal range 12–72 ng/l). At this time, the patient reported no other symptoms. TSH was within the laboratory reference range with the patient taking thyroxine 100 mcg daily.

Initial treatment of the hypercalcaemia was given with intravenous pamidronate (60 mg in 250 ml 0.9% normal saline over 4 h). Serum calcium fell from 3.13 mmol/l to 2.56 mmol/l over the next week. However, the patient reported that an influenza-like illness occurred on the day following the infusion, which is a recognized side-effect of pamidronate. This was followed by ‘difficulty using legs’ and ‘difficulty taking the top off toothpaste and jars.’ Subsequently, a speech problem was reported, with the voice becoming ‘higher in pitch’ with inability ‘to get the words out—as though choking in throat.’ A strange sensation in the tongue whilst talking was also described.

When the patient attended for preoperative assessment prior to parathyroidectomy, dysarthria was noted. Surgery followed with a parathyroid adenoma being successfully removed. Whilst some facial tingling was noted post-operatively, no hypocalcaemia was evident, with 1-alpha-calcidol being given perioperatively, although rebound hypercalcaemia (3.53 mmol/l) had occurred prior to surgery. During routine post-operative follow-up, reports of occasional double vision and difficulty swallowing were made. A diagnosis of myasthenia gravis was made, with high levels of acetylcholine receptor antibodies being detected (>10 nmol/l; normal range 0–0.5 nmol/l). A tension test was also positive, with fatigability of speech being used to assess response since no proximal muscle fatigability or reproducible ocular muscle plasies were present.

Our patient was initially treated with pyridostigmine 30 mg qds with good response, although a relapse of her myasthenia gravis followed. Her pyridostigmine was increased to 120 mg qds, and prednisolone commenced. At the time of writing she is symptom-free and her dose of prednisolone is being reduced.

Further investigation failed to show the presence of a thymoma with a normal chest radiograph and
a thoracic CT scan, although antibodies to striated muscle were detected.

Our patient developed symptoms that were first reported following treatment of hypercalcaemia with pamidronate and a subsequent fall in the serum calcium. The symptoms did not improve following removal of the parathyroid adenoma. Therapeutic drugs are well known to exacerbate myasthenia gravis, to cause a reversible myasthenic syndrome or even to precipitate myasthenia gravis. Examples of drugs associated with these effects include aminoglycosides, penicillamine, beta-blockers and chloroquine. It is possible that intravenous pamidronate precipitated myasthenia gravis in our patient, although this is the first reported potential association.

The coexistence of myasthenia gravis with autoimmune disease is well-recognized. One such association is Graves’ disease as seen in our patient. It is recognized that a thymoma is present in 10–15% of cases of myasthenia gravis, especially in patients developing the condition in middle age. This appears to correlate with the presence of antibodies against striated muscle, but the presence of these antibodies is not diagnostic. Thymectomy may lead to an improvement in the symptoms of myasthenia gravis. This appears to vary depending on the duration of symptoms and is most marked in women and the young. Removal of a thymoma, although necessary to exclude malignant disease, is less commonly associated with an improvement in symptoms. Both cases of hyperparathyroidism and myasthenia gravis reported to date were associated with a thymoma. No thymoma has been detected to date in our patient.

Our patient presented with hyperparathyroidism, the signs of which may be striking and may suggest a primary neuromuscular disorder, although this is not thought to be a common occurrence. However, in hyperparathyroidism, it is recognized that symptoms of neuromuscular disease resolve or at least improve when the parathyroid adenoma is removed and the serum calcium levels fall. In the first case reported, an increase in strength was observed following removal of the parathyroid adenoma without a change having been made to the patient’s medication for myasthenia gravis. The thymoma was removed prior to the detection of hyperparathyroidism. The situation is less clear in the second case, since the thymoma and three and a half of the parathyroid glands were removed at the same operation. An improvement in the patient’s symptoms was seen post-operatively, with a reduction in patient’s medication for myasthenia gravis becoming possible.

In conclusion, we report the third case associating myasthenia gravis with hyperparathyroidism, but also raise the possibility that the syndrome was precipitated by administration of pamidronate.

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References