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Diplopia Associated with Hyperparathyroidism: Report of a Case

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A patient with hypercalcemia due to primary hyperparathyroidism presented with diplopia that resolved with surgical removal of his parathyroid adenoma and normalization of his serum calcium values. No previous report of this feature of hyperparathyroidism has been reported.

CASE REPORT

A 60 year old male with a history of calcium-containing renal stones and arthralgia, presented to his primary care physician for evaluation of a one-month history of mild memory loss and fatigue. Laboratory testing revealed a serum calcium level of 12.5 mg/dl (normal range: 8.4-10.2) and an inorganic phosphorus level of 2.1 mg/dl (normal range: 2.2–4.5). On further questioning, he reported mild blurring of his vision. He was being treated for hypertension with terazosin and had benign prostatic hypertrophy treated with finasteride. He was seen by an endocrinologist, and further testing showed a normal alkaline phosphatase level of 99 IU (normal range: 30–130), an elevated ionized calcium level of 7.4 mg/dl (normal range: 4.6–5.4), normal magnesium level of 1.7 meq/l (normal range: 1.3–2.1) and "C–terminal" parathyroid hormone level of 2,954 pg/ml (normal range: 50–330). A repeat serum calcium determination was 13.4 mg/dl with an "intact" parathyroid hormone level of 268 pg/ml (normal range: 10–65). Spot urinary cyclic-AMP determination was 6.69 nmol/mg creatinine (normal: less than 3.82). Review of previous laboratory tests showed a normal calcium level of 10.2 mg/dl in January 1994 and 9.3 mg.dl in November 1992.

One year earlier, a complete routine ophthalmologic examination had been normal. Five weeks prior to presentation, examination showed each eye corrected to 20/20 at distance and its near equivalent. No tropies (manifest strabismus) were elicited, but he noted vague problems with night-time distance vision and depth perception. At presentation to the endocrinologist, deep tendon reflexes were decreased and peripheral nerve testing to pain and vibration were normal. There was no band keratopathy or proximal muscle weakness. Because he complained about diplopia and worsening eye symptoms, he was immediately referred back to his ophthalmologist who then noted intact fusion at distance but diplopia at near. Using a Maddox Rod, four diopters of right hyperphoria and two diopters of esophoria were measured at distance. At near, three diopters of right hyperphoria and sixdiopters of exophoria were measured. He could no longer read the newspaper unless one eye was patched. To further investigate his diplopia, computed axial tomography of his brain and orbits was performed but was unremarkable. Extra-ocular muscles were of normal size. Random post-prandial glucose levels and a glycohemoglobin were normal. There was no clinical or laboratory evidence for a transient ischemic attack, stroke or other neurologic disease, collagen vascular disease or diabetes.

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The diagnosis of primary hyperparathyroidism was made, and the patient was begun on oral furosemide 20 mg/day and oral phosphate 250 mg, three times daily in an attempt to lower his calcium until parathyroidectomy could be performed. On January 3, 1995, a neck exploration was performed at the Hospital of St. Raphael. His immediate preoperative calcium level was 11.2 mg/dl. Three normal parathyroid glands were identified, and a 1.424 gram parathyroid adenoma was removed without difficulty.

Twelve hours post-operatively, his calcium level was 9.3 mg.dl, at 36 hours it was 8.0 mg/dl and at 72 hours it was 7.6 mg/dl. Inorganic phosphorous values remained below 3.0 mg/dl. There was synchronous improvement in his diplopia and strabismus. The patient noted that he could now read the newspaper and no longer had to patch one eye. The patient was discharged on supplemental calcium tablets. Ten days after surgery, his calcium was 8.5 mg/dl and inorganic phosphorus 2.9 mg/dl. Formal ophthalmologic examination seven days after surgery showed no diplopia in any cardinal position by red lens testing. Maddox Rod testing revealed, at distance, no hyperphoria and only 0.50 diopters of esophoria. At near, there were one diopter of left hyperphoria and seven diopters of exophoria. One month later, he was no longer taking supplemental calcium and had normal serum calcium and phosphorous levels.

DISCUSSION

This patient clearly had many signs and symptoms of hyperparathyroidism including fatigue, anorexia, arthralgia, and perhaps his hypertension, and renal calculi as well. However, the finding of significant diplopia was further investigated with a CAT scan of his brain to rule out intra-cranial pathology, as none of his treating or consulting physicians were aware of cranial nerve or eye muscle abnormalities as possible consequences of hyperparathyroidism. A complete review of the literature failed to identify such an occurrence. Patten's review of 16 patients with primary hyperparathyroidism showed 14 to have neuromuscular abnormalities with altered electromyograms and muscle atrophy of both type I and type II fibers on biopsy [1]. However, none of the patients had eye findings. The review by Turken et al. [2] fifteen years later failed to demonstrate any muscular involvement in 42 patients with mild hyperparathyroidism (average calcium levels 10.8-11.3 mg/dl), although 22 patients complained of paresthesias or muscle cramps and 12 patients showed signs of neuropathy with loss of vibratory sense, diminished reflexes or stocking-glove loss of pain sensation. Turken suggests that the "features of the disease have changed," and believes that a primary neuronal event leads to secondary muscular weakness. This conclusion is supported by data from Kaplan et al. using single fiber electromyography which showed abnormalities involving intramuscular neural branches [3, 4].

As our patient's eye muscle abnormalities reversed quite quickly and coincident with the fall in his blood calcium level, it would appear that the hypercalcemia itself caused a readily reversible alteration in muscle strength or nerve function and not muscle atrophy.

There are several explanations for Turken's belief that the presentation of patients with primary hyperparathyroidism has changed, with the most likely being the routine measurement of serum calcium as part of multi-channel autoanalyzer techniques. Therefore, patients with hypercalcemia are diagnosed much earlier when they are asymptomatic, before the classic symptoms of "bones, groans and moans" develop. However, our patient had documented normocalcemia 11 months prior to presentation, as well as a normal eye exam five weeks earlier. His hypercalcemia, however, was severe and he became symptomatic quite quickly.

Bhalla [5], on the other hand, relates the severity of the muscle symptoms to the duration of the disease and not to the level of calcium, phosphorous or magnesium. It appeared unique for this patient's most significant abnormal physical finding to have been diplopia especially as eye muscle involvement has not previously been reported. Moreover, the lack

of significant proximal muscle weakness, paresthesia, loss of sensation or vibratory sense, with preserved deep tendon reflexes while hypercalcemic, is unusual as well.

SUMMARY

We report that strabismus resulting in diplopia due to eye muscle weakness was a prominent feature in a patient with hypercalcemia due to hyperparathyroidism. Although It remains unproven that this patient's diplopia was caused by the hyperparathyroidism, the rapid reversal of the muscle weakness upon return to the normocalcemic state suggests a physiologic effect of the hypercalcemia rather than pathologic damage or atrophy of nerves or muscles.

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