

Reversible Hypercalcemic Cerebral Vasoconstriction with Seizures and Blindness: A Paradigm for Eclampsia?

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Key words

Cortical Blindness
Eclampsia
Hypercalcemia
Magnesium
Periodic Lateralized Epileptiform Discharges
Seizures

INTRODUCTION

Hypercalcemia can cause drowsiness, lethargy, weakness, confusional states and coma but rarely causes seizures.¹⁻⁴ Reversible diffuse or focal neurologic deficits can occur, often associated with electroencephalographic (EEG) correlates.⁵⁻⁸ A patient with reversible blindness due to ischemia and seizures with hypercalcemia is presented with pathophysiologic comparison to eclampsia.

Case Report

A 66-year-old woman developed hypercalcemia from multiple myeloma and ingestion of calcium-containing antacids. Serum calcium was 13.6 mg/dL, total protein 10.9 mg/dL; albumin 3.4 mg/dL; magnesium 2.2 mg/dL; and ionized calcium 1.80 mg/dL. On neurological examination she appeared awake, but was having auditory and visual hallucinations despite being oriented to time, place and person. She had conjugate gaze, full extraocular movements, reactive pupils, normal fundi, and visual fields that were full to examination by confrontation. Strength, tone, sensation and reflexes were intact with down-going plantar responses.

Despite hydration and treatment with pamidronate (a calcium-lowering agent), serum calcium remained elevated between 11.5-12.5 mg/dL. Following a generalized tonic-clonic seizure, computerized head tomography (CT), and cerebrospinal fluid studies showed no abnormality; the patient was given intravenous phenytoin with a level of 11.0 µg per ml. The next day she was confused, and examination still showed full extraocular movements, reactive pupils and normal fundi, but there was no reaction to visual threat, sight for objects or movement. Repeat head CT scan again showed no abnormality, but EEG revealed an occipital high-voltage spike-and-slow-wave complex seen approximately every 1½ - 2 seconds throughout the recording (Figure 1). Pattern-reversal visual evoked poten-

tial studies showed no responses bilaterally. Single Photon Emission Computerized Tomography (SPECT) showed multiple perfusion defects in the right occipital, left parietal and frontal regions (Figure 2). With the further lowering of serum calcium to 6.4 mg/dL, hallucinations resolved, and the patient had no further seizures.

By hospital day 21 she was alert and oriented, and her vision had returned although with a residual right hemianopsia. Magnetic Resonance Imaging (MRI) showed an increased T₂ signal in the occipital lobes consistent with cerebral infarction.

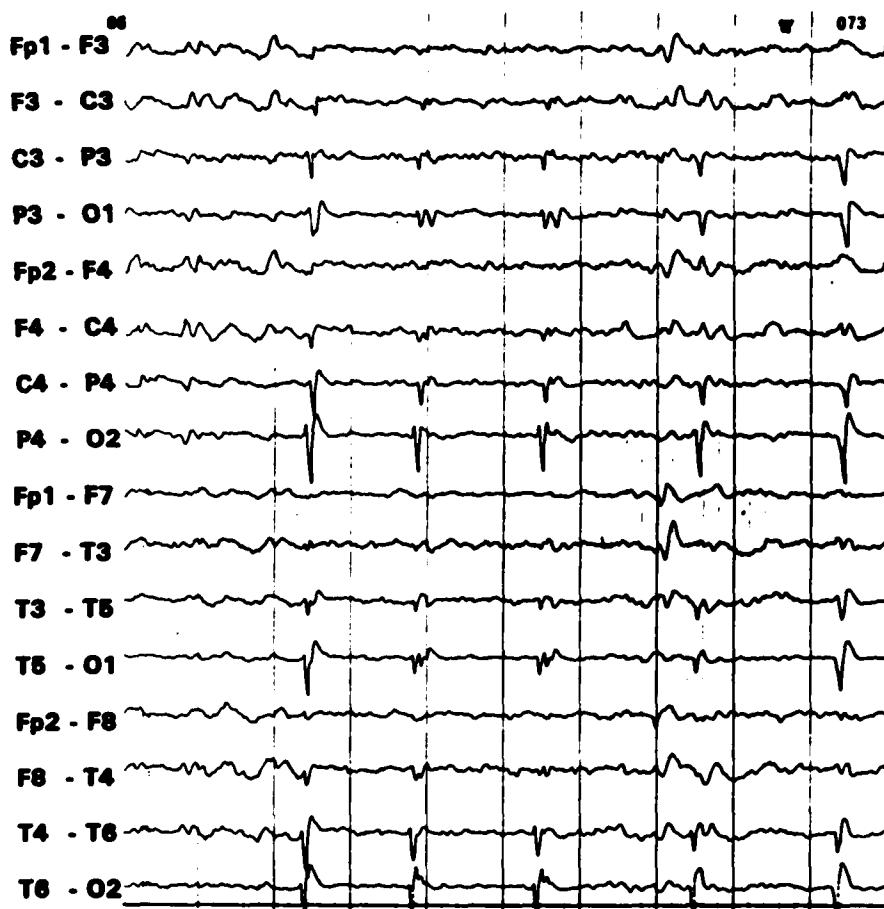
DISCUSSION

This patient presented with marked hypercalcemia, confusion, hallucinosis, and a tonic-clonic seizure. Her clinical state evolved, and she became cortically blind with occipital spike-slow-wave complexes on EEG, and evidence of occipital hypoperfusion on SPECT despite a normal head CT scan. Following a marked reduction in serum calcium, occipital spike-slow-wave activity stopped and vision returned. This is the first well-documented case of hypercalcemic reversible ischemia with bioccipital epileptiform discharges and cortical blindness. In one previous case, hypercalcemia without seizures resulted in cerebral vasospasm and infarction of both the right parietal parasagittal cortex and the occipital region.⁹

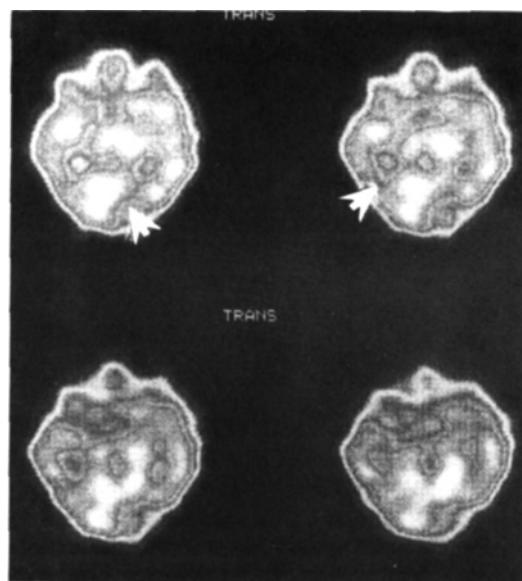
Differentiating cause and effect in a patient with visual loss, occipital epileptiform activity and hypercalcemia may be difficult. Many mechanisms can be involved in producing this association: a) hypercalcemia may produce cerebral vasospasm resulting in cerebral infarction⁹; b) hypercalcemia may cause focal or generalized seizures with encephalopathy⁹⁻¹³; c) hypercalcemia may produce hypertensive encephalopathy¹⁴, with raised intracerebral pressure and cerebral ischemia. To complicate matters, there may also be interplay between these pathophysiological mechanisms: For example, vasospasm may itself produce reversible⁹ or permanent ischemia which, in turn,

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**Figure 1.**

EEG showing bioccipital periodic epileptiform discharges, more marked on the right in a patient with hypercalcemia and occipital blindness. The focus is congruent with the occipital region of hypoperfusion seen on SPECT.

**Figure 2.**

HMPAO-SPECT scan 10 mCi given IV in the patient with eyes closed. Data were reconstructed from 64 images obtained over 20 seconds using a GE Star 3000 computer. The four images represent transaxial views obtained in a cephalo-caudal progression from the upper left to right starting in the upper left corner. The images reveal right-occipital and left parietal hypoperfusion.

may act as a trigger for focal epileptiform discharges. Alternatively, parieto-occipital seizures themselves may result in permanent neurologic sequelae and induce cortical blindness.¹⁰ From a different perspective, up to 20% of patients with occipital EEG epileptiform foci may have visual field deficits.¹¹

In this patient, a likely sequence of events was a rise in serum calcium resulting in a confusional state, superimposed on occipital ischemia which resulted in visual hallucinations. A combination of this ischemia (as documented by SPECT scanning and subsequent MRI changes in the occipital lobes) in concert with hypercalcemia resulted in bioccipital foci in the form of periodic epileptiform discharges (*vide infra*).

The mechanism of vasospasm involves a hypercalcemic-induced actin-myosin coupling with activation of vascular smooth muscle in the arteriolar circulation.^{9,15,16} Cerebral vasospasm may then produce patchy ischemia but it favors watershed zones, typically in the parieto-occipital regions, resulting in cortical blindness.⁹ The vasospastic cause of the ischemia allows for potentially reversible deficits.

Structural abnormalities such as strokes or ischemic zones when associated with a seizure are known to result in periodic lateralized epileptiform discharges (PLEDs) on EEG. In this case, the occipital regions are those most affected and in the face of a tonic-clonic seizure, these posterior regions may engender irritative zones producing bioccipital epileptiform discharges, possibly with reversible ictal functional impairment. Cortical blindness with permanent visual loss has clearly been documented following seizures,¹⁰ although other causes include migraine, hypertensive encephalopathy and eclampsia, all of which may be reversible.

Hypercalcemia has been reported to selectively induce seizures originating in the occipital lobes¹² and to induce cerebral hypertension.⁹ Eclampsia also typically affects the parieto-occipital region, causes cerebral hypertension, reversible occipital ischemia and seizures. There is evi-

dence to suggest that cortical damage in eclampsia is produced by vasospasm,^{17,18} which is reversed by intravenous magnesium sulfate infusion. In subarachnoid hemorrhage, calcium channel blockers such as nimodipine have been used to minimize vasospasm, and the effect of magnesium sulfate might therefore be as a calcium antagonist, preventing cerebral vasoconstriction¹⁷ and subsequent epileptogenic cortical injury. One can speculate that one component of the cerebrovascular pathology of eclampsia represents an increased vascular sensitivity or reactivity of watershed zones to local calcium ions that can be counteracted in eclampsia with magnesium infusion. There are data to suggest that magnesium ions block N-methyl-D-aspartate channels that mediate calcium entry into cells.^{19,20} This case may therefore provide some parallels and insight into the interplay of calcium and magnesium cations, vasospasm in parieto-occipital watershed zones with the onset of seizures. There are few other parallels in humans to eclampsia.

SUMMARY

Although hypercalcemia may cause drowsiness, lethargy, weakness, confusion and coma it rarely causes seizures or cerebral infarction. The patient presented had a clinical evolution from hallucinosis to a generalized tonic-clonic seizure, and subsequent cortical blindness with occipital cerebral ischemia as evidenced by SPECT and MRI scans. EEG revealed occipital PLEDs. With reversal of hypercalcemia, there was a return of vision, resolution of EEG epileptiform activity, although with some residual occipital infarction. This case, in concert with a literature review of hypercalcemia, reveals examples of occipital and watershed ischemia, blindness, seizures and hypertension, a pattern markedly similar to that of eclampsia. Furthermore, medications such as magnesium sulfate, believed to reverse cerebrovasospasm responsible for the eclamptic neurologic findings, may counter the effects of hypercalcemia at a cellular level, lending support to a calcium-mediated injury in eclampsia.

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