

Hypoparathyroidism and Pseudotumor Cerebri: An Infrequent Clinical Association

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ABSTRACT: We report a patient with chronic, untreated idiopathic hypoparathyroidism who presented with papilledema and progressive deterioration of visual function. The papilledema resolved with treatment of the hypocalcemia. Visual acuity progressively improved as the serum calcium rose during treatment with vitamin D and calcium supplements. Lumbar puncture may also have contributed to the normalization of cerebrospinal fluid pressure and recovery of vision in this patient. The association of hypoparathyroidism and pseudotumor cerebri is rare, and a retrospective review of 41 patients with hypoparathyroidism admitted to two local general hospitals revealed no other cases.

RÉSUMÉ: Hypoparathyroïdie et syndrome d'hypertension intracrânienne bénigne: une association clinique rare. Nous rapportons la cas d'un patient porteur d'une hypoparathyroïdie idiopathique chronique non traitée, qui s'est présenté avec un oedème papillaire et une détérioration progressive de la vision. L'oedème papillaire s'est résorbé avec le traitement de l'hypocalcémie. L'acuité visuelle s'est améliorée progressivement à mesure que le taux du calcium sérique s'élevait au cours du traitement par la vitamine D et les suppléments calciques. La ponction lombaire pratiquée chez ce patient peut aussi avoir contribué à la normalisation de la pression du liquide céphalo-rachidien et à l'amélioration de la vision. L'association d'hypoparathyroïdie et d'un syndrome d'hypertension intracrânienne bénigne est rare et une revue rétrospective de 41 cas d'hypoparathyroïdie admis dans deux hôpitaux généraux locaux n'a révélé l'existence d'aucun autre cas ayant présenté cette association.

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The syndrome of pseudotumor cerebri is characterized by raised intracranial pressure greater than 200 mm of water, no radiologic evidence of intracranial mass lesion or hydrocephalus, and normal cerebrospinal fluid (CSF). If symptoms or signs are present, they must be explained by raised intracranial pressure alone.¹ Patients commonly present with headache, papilledema and visual loss. In a recent review, Ahlskog and O'Neil¹ documented eleven conditions thought to be associated with pseudotumor, one of which was hypoparathyroidism. We report here a patient with idiopathic hypoparathyroidism who presented with pseudotumor cerebri.

CASE REPORT

A 29 year old male presented to his ophthalmologist in July 1983 complaining of reduced clarity of vision in the left eye which was progressive in nature. There was no headache or eye pain. Visual acuity measurements (corrected) showed the right eye to be unchanged from previous examinations (20/25+) while visual acuity in the left eye had decreased to 20/30+ from 20/20 measured six months previously. Intraocular pressures were normal at 15 mm Hg in both eyes. Increased fullness of both optic nerve heads was noted, with slight blurring of the

nasal margins. Within three weeks his vision had decreased further to OD 20/400 and OS 20/40. There was increased blurring of both optic nerve heads, and retinal veins were slightly engorged. There were no visible cells within the vitreous body immediately anterior to the optic nerve head as one would see with papillitis. A diagnosis of early papilledema was made, and confirmed by fluorescein angiography (Figure 1). The angiogram showed no evidence of macular edema.

Past history included chronic dental enamel defects, severe long-standing sensori-neural hearing loss, duodenal ulcer, chronic fungal paronychia, and chronic muscle cramps. He had developed tonic clonic seizures at age 23, and had undergone surgery for cataracts with bilateral posterior chamber lens implants in 1982. Medications included phenytoin and phenobarbital.

Physical examination revealed a thin, well appearing young man with no focal neurological deficits or meningismus. Chvostek's sign was positive. He had poor dentition and paronychia were present. Examination of optic fundi revealed bilateral papilledema with flame hemorrhages and right macular edema. He had a large inferior field defect to confrontation in the left eye and visual acuity OD 20/800 and OS 20/40.

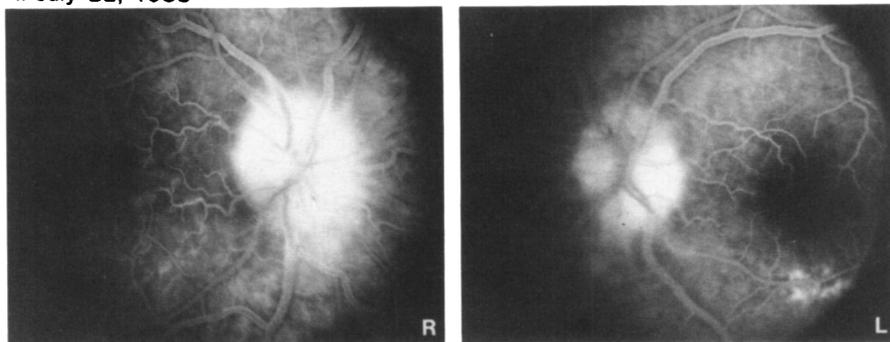
Complete blood count, electrolytes and brain CT scan were normal. Lumbar puncture showed an opening pressure of 230 mm CSF with normal protein and glucose, no white blood cells, and sterile cultures. His serum calcium was 1.06 mM/L, phosphorus 2.59 mM/L, magnesium 0.54 mM/L, and albumin 4.6 grams/dL. Subsequent laboratory examination revealed a low 24 hour urine cyclic AMP excretion of

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A. July 22, 1983



B. Nov. 15, 1983

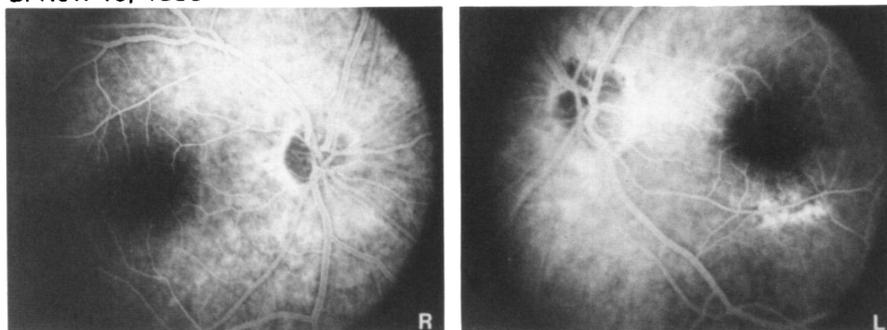


Figure 1 — Fluorescein angiography was done prior to treatment (A) and after almost four months of therapy for hypoparathyroidism (B). Angiograms for right and left eye are indicated by R and L respectively. Typical findings of papilledema were present prior to treatment. The second study shows no evidence of papilledema.

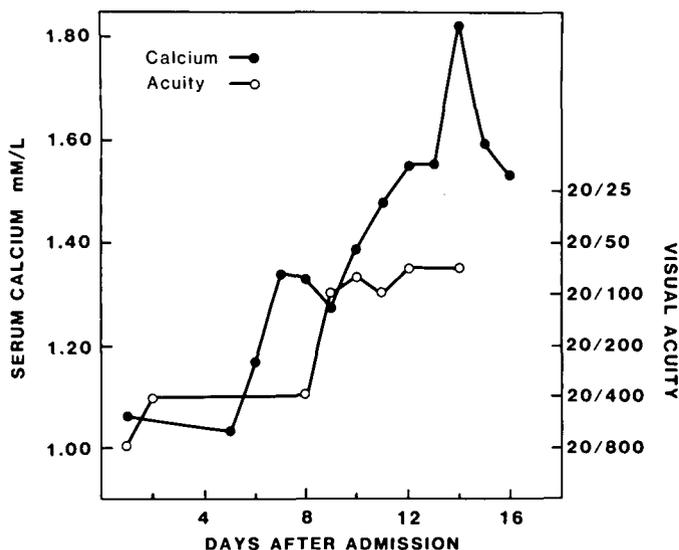


Figure 2 — Changes in visual acuity for the right eye and changes in serum calcium are shown during our patient's hospitalization. Treatment with calcitriol and oral calcium supplements was started on day four. Rapid improvement in visual acuity was seen as the serum calcium rose in response to therapy. Repeat lumbar puncture revealed a normal opening pressure on day eleven.

2.73 nm/100 ml creatinine clearance, and a low normal serum 25-hydroxy vitamin D of 12 ng/ml (normal 10-55 ng/ml). Serum PTH was undetectable by radioimmunoassay in the laboratory of one of the authors.²

After initiation of treatment with 2 grams of elemental calcium p.o. per day and 1,25-dihydroxy vitamin D 0.25 ug p.o. B.I.D., his serum calcium began to rise. His visual acuity improved as his serum calcium increased (Figure 2). A second lumbar puncture one week after starting treatment for hypoparathyroidism revealed a normal opening pressure

of 130 mm CSF. Visual acuity gradually improved to OD 20/80, OS 20/20 by September 1983. Intraocular pressures remained normal at 15 mmHg bilaterally. All ophthalmoscopic signs of papilledema had disappeared by October 1983 and this was confirmed by fluorescein angiography in November 1983 (Figure 1). Goldman visual fields done in December 1983 showed a persisting visual field defect in the inferior half field of the left eye, most dense in the inferior nasal quadrant. The right eye showed a small centrocecal scotoma. Goldman visual fields done in November 1984 were unchanged from December 1983.

DISCUSSION

With papilledema, raised intracranial pressure, a normal brain CT scan, and normal CSF our patient satisfied the criteria for pseudotumor cerebri (benign intracranial hypertension).¹ In addition, he also most likely had idiopathic hypoparathyroidism dating from early childhood, manifested by chronic enamel defects, cataracts at a young age, tonic clonic seizures, hypocalcemia, hyperphosphatemia, and undetectable parathyroid hormone levels.

The association of pseudotumor cerebri and hypoparathyroidism is unusual. None of 387 cases of pseudotumor cerebri documented in five major reviews of pseudotumor cerebri since 1955,³⁻⁷ was found to have hypoparathyroidism.

An important issue is whether our patient's papilledema was the result of raised intracranial pressure, or due to optic neuritis. Optic neuritis has occasionally been reported in association with hypoparathyroidism, but cases have been poorly documented, or unilateral.⁸ Our patient had markedly reduced visual acuity, a finding more commonly associated with optic neuritis than pseudotumor cerebri, but Johnston and Paterson⁵ found that 17% of 110 patients with pseudotumor cerebri had a marked reduction in visual acuity at the time of clinical presentation.

Our patient showed a persistent visual field deficit in the left eye which involved the lower half of the visual field and was most dense in the inferior nasal quadrant. While "altitudinal"

field defects involving either the superior or inferior visual half-fields are commonly seen as a result of vascular lesions, both retinal artery occlusions and segmental optic nerve head infarctions,⁹ unilateral and bilateral inferior nasal quadrantanopsia has been reported in pseudotumor.^{4,7,10} These visual field defects in pseudotumor might result from ischemia in the swollen optic disc. While most patients with papilledema do not show major visual loss, patients with chronic papilledema may show irregular peripheral visual field contractions and nerve fibre bundle defects with preferential involvement of inferior nasal areas.⁹ We feel that the visual changes in our patient resulted from pseudotumor cerebri because an elevation of CSF pressure was present, and because his visual acuity improved with treatment of the hypoparathyroidism and normalization of CSF pressure. The absence of headache in our patient might be taken as a point against pseudotumor cerebri, but in the series reported by Rush,⁴ headache was absent in approximately 25% of patients. In our patient, papilledema as a result of ocular hypotony secondary to cataract surgery was ruled out by repeatedly normal intraocular pressure measurements both immediately before and after his hospitalization.

It is difficult to determine the prevalence of papilledema in hypoparathyroid patients from the literature, as the unusual combination of pseudotumor cerebri and hypoparathyroidism is more likely to be reported than hypoparathyroidism alone. In fifty reported cases of hypoparathyroidism reviewed by Bronsky et al¹¹ in 1958, nine showed papilledema. In a later review, Bajandas and Smith⁸ found a total of 39 reported cases of papilledema in association with hypoparathyroidism in the literature, including the cases previously reviewed by Bronsky et al.¹¹ Raised intracranial pressure was documented in only seventeen of them. Ten of these patients had CSF opening pressures between 200 and 300 mm CSF, similar to our patient.

We reviewed the clinical records of 41 patients who were admitted to the Calgary General or Foothills Hospitals since 1977 with a diagnosis of hypoparathyroidism. Of these, eleven had idiopathic (probably autoimmune) hypoparathyroidism while the rest had post-surgical hypoparathyroidism. Many had been followed for ten years or more. In none of these patients was papilledema noted, confirming that in unselected cases of hypoparathyroidism, papilledema is rare. Although most of our patients had post-surgical hypoparathyroidism, this alone cannot explain our low incidence of papilledema. In the 39 patients with papilledema and hypoparathyroidism reported by Bajandas and Smith,⁸ 24 had idiopathic hypoparathyroidism, 12 had post-thyroidectomy hypoparathyroidism, and 3 had pseudo-hypoparathyroidism. The severity of hypocalcemia and its duration may both be important in the generation of pseudotumor cerebri, in that our patient had probably been hypoparathyroid for at least twenty years, and presented with an extremely low serum calcium. The visual impairment improved with an increase in serum calcium up to a level which would still be regarded as severe hypocalcemia.

Because the association of pseudotumor cerebri and hypoparathyroidism is so rare it might be fortuitous. However, four patients with hypoparathyroidism have been reported^{12,13} in whom papilledema resolved on treatment with vitamin D and calcium supplements even though lumbar punctures were not done. A single lumbar puncture may lower CSF pressure in some patients with pseudotumor cerebri.³ As lumbar punctures were not done in the four patients noted above, the papilledema

may have responded to vitamin D and calcium supplementation alone, suggesting that hypoparathyroidism (or hypocalcemia) may cause an elevation in CSF pressure.

There is some indirect evidence that mechanisms exist which might explain this relationship between hypoparathyroidism and pseudotumor cerebri. Choroid plexus adenylate cyclase may have an important role in CSF physiology.¹⁴ A specific beta-adrenergic adenylate cyclase which is activated by isoproterenol and other beta agonists is present in mammalian choroid plexus epithelium.¹⁵ Although a role for parathyroid hormone in the regulation of CSF production has not been demonstrated, recent work has shown that parathyroid hormone stimulates adenylate cyclase in cerebral microvessels.¹⁶

Stimulation of the known adenylate cyclase system in the choroid plexus might result in CSF hypersecretion, as cholera toxin, a potent activator of adenylate cyclase, results in a markedly increased rate of CSF production when given intraventricularly.¹⁷ Based on this evidence, however, the reduced parathyroid hormone levels seen in our patient would be expected to result in CSF hyposecretion rather than hypersecretion. Other evidence suggests that the profound hypocalcemia could possibly result in an increased rate of CSF production. Nathanson¹⁵ has shown that when divalent cations (including Ca^{++}) are removed from choroid plexus tissue homogenates by chelating agents (EGTA), basal and isoproterenol stimulated adenylate cyclase activity is increased. This could possibly result in CSF hypersecretion. Although pseudotumor cerebri occurs in only a small proportion of patients with hypoparathyroidism, this does not rule out the possibility that the parathyroid hormone abnormality or the resultant hypocalcemia is the cause of the increased intracranial pressure in these patients. If for example hypoparathyroidism increased the rate of CSF formation, only those patients with the fewest low resistance absorptive channels would be prone to develop pseudotumor cerebri. Such a mechanism has been proposed to explain the occasional occurrence of pseudotumor cerebri in obese women, in whom increased estrone levels may lead to an increased rate of CSF formation.¹⁸

The mechanisms responsible for the increased CSF pressure in pseudotumor cerebri remain controversial. The frequently low CSF protein level in pseudotumor has often been cited as evidence for CSF hypersecretion, and obese young women with pseudotumor have shown net rates of CSF production several times greater than normal.¹⁸ Others have found CSF outflow to be reduced in pseudotumor.¹⁹ It may be that both mechanisms alone or in combination may result in pseudotumor cerebri. Although our patient's CSF protein was quite normal (0.40 g/L) on his first lumbar puncture, it was relatively low (0.25 g/L) on his second lumbar puncture, perhaps in keeping with some degree of CSF hypersecretion.

Hypoparathyroidism is only rarely associated with pseudotumor cerebri, but should be looked for in all patients presenting with intracranial hypertension of unknown etiology. Lumbar puncture is indicated in patients with pseudotumor cerebri and hypoparathyroidism, to document CSF pressures. The potentially therapeutic effects of lumbar puncture on the elevated CSF pressure may also be important, particularly in patients with visual symptoms. Treatment of the hypoparathyroidism with a rapid acting vitamin D metabolite (such as calcitriol) and calcium supplements may also contribute to reduction of CSF pressure in these patients.

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