CASE REPORT

Bilateral Compressive Optic Neuropathy from Renal Osteodystrophy Caused by Branchio-oto-renal Syndrome Stabilised After Parathyroidectomy

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ABSTRACT

Renal osteodystrophy can cause calvarial hypertrophy and narrowing of the neural canals and foramina. Compressive optic neuropathy is extremely rare in renal osteodystrophy and was reported once only. The authors report bilateral, simultaneous compressive optic neuropathy secondary to renal osteodystrophy with features of uremic leontiasis ossea in chronic renal failure caused by branchio-oto-renal syndrome. Because of the extensive calvarial hypertrophy and the surgical difficulties envisaged with optic canal decompression, conservative approach was pursued. The patient's visual acuity and fields improved after partial parathyroidectomy. Visual improvement may be explained by the arrest of renal osteodystrophy and reduced optic nerve compression after parathyroidectomy.

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Introduction

Chronic renal failure causes hypocalcaemia and hyperphosphataemia, which in turn results in increased release of parathormone. This secondary hyperparathyroidism leads to excessive bone resorption as well as new bone formation, called renal osteodystrophy (RO). Progressive thickening of the cranial bones in RO can result in massive calvarial hypertrophy and narrowing of the neural canals and foramina. Uremic leontiasis ossea (ULO) is a rare, severe form of RO with distinctive facial features. Parathyroidectomy stabilises ULO.¹ Compressive optic neuropathy secondary to narrowed optic canals in RO had been reported in only one patient.² It was felt that aggressive treatment with high-dose steroids and optic nerve decompression in early course can influence the visual outcome.² We report bilateral compressive optic neuropathy from RO in a patient who neither received high-dose steroids nor optic canal decompression surgery, but vision loss improved following parathyroidectomy.

Patient description

A 23-year-old woman was referred for progressive blurred vision in both the eyes for 2 months. She reported occasional dull generalised headaches once a month. She had end-stage renal disease secondary to branchio-oto-renal syndrome, a rare autosomal dominant condition characterised by branchial arch anomalies, pre-auricular pits, congenital sensory neural hearing impairment, and renal malformations. She was born with a solitary dysplastic left kidney. She had cadaveric renal transplant at age 6, which was unsuccessful. She had been on peritoneal dialysis since age 14. She suffered from hypertension and chronic anaemia. Her renal insufficiency was complicated by secondary hyperparathyroidism and at the time of our initial assessment, parathyroidectomy was already planned. Her medications included sevelamer hydrochloride, cinacalcet, darbepoietin alfa, calcium carbonate, and multivitamins. There was no family history of branchio-oto-renal syndrome or renal disease from any other cause.

On examination, the patient had a short stature and was thin. She had prominent cheek bones, widened nares, flattened nasal bridge, and widely

spaced teeth—facial features suggestive of ULO. Best-corrected visual acuity was finger counting at 6 feet distance in both eyes. Pupils measured 4 mm and both reacted sluggishly and equally to light. Colour vision was 2/17 Ishihara colour plates in either eye. Eye movements were normal. Funduscopy showed bilateral temporal pallor (Figure 1). Humphrey visual fields revealed bilateral central scotomas, worse superiorly in right eye (mean deviation: -7.59 dB) and inferiorly in left eye (mean deviation: -10.4 dB) (Figure 2A). She had diminished hearing bilaterally. The remainder of the neurological examination was normal. Lumbar puncture opening pressure was 24 cm H₂O. Cerebrospinal fluid (CSF) cell count, glucose, and protein were normal.

Magnetic resonance imaging (MRI) revealed massive calvarial hypertrophy, in keeping with bony sequelae of the secondary hyperparathyroidism. There was diffuse narrowing of the optic canals (Figures 3) as well as all the skull base neural foramina. Within the narrowed optic canals, the optic nerves appeared atrophic. MRI also revealed non-homogeneously enlarged diploic space as well as nodular areas of hypointensity consistent with brown tumours (Figure 4).

Computed tomography (CT) showed diffuse hypertrophy and hyperostosis of the calvarium and skull base. The optic canals were narrowed (Figure 5). The mandible was enlarged and expanded, with sclerosis and increased lucency. Dystrophic calcification was observed in several intracranial arteries, including the cavernous portion of the internal carotid arteries. The cochlea was hypoplastic, and there was a mild dilatation of the vestibule. The long process and the manubrium of the incus were shortened.

The malleolar heads were slightly enlarged and deformed bilaterally. The CT findings of the inner ear were typical of branchio-oto-renal syndrome. A sestamibi parathyroid gland scan and an ultrasound of the neck done prior to our evaluation showed bilateral parathyroid adenomas.

Conservative approach and observation was advised by the neurosurgeon because of the extensively thickened and deformed skull bones. Three months after the onset of the visual symptoms, she had a subtotal parathyroidectomy (three and three-quarters of the four parathyroid glands removed), which was proposed for the secondary hyperparathyroidism even before her visual loss. Five months after symptom onset (2 months after partial parathyroidectomy), she reported improvement of her vision. Visual acuity had improved to 20/70 OD and 20/200 OS, and Humphrey visual field showed improvement in the central scotomas (mean deviation: -4.32 dB and -4.24 dB in the right and left eyes, respectively) (Figure 2B). There was no improvement in the colour vision. Her pupillary light reflex transformed to a relative afferent pupillary defect in the left eye, compared with bilateral sluggish light reflex documented initially. The optic discs showed no changes. Her vision and funduscopy examination appeared stable during three follow-up visits at 5, 7, and 11 months after onset of visual symptoms. Patient compliance precluded visual evoked potentials testing, optical coherence tomography, and further neuroimaging. She was eventually lost for follow-up.

Following parathyroidectomy, her parathormone level reduced to 67.9 (range: 1.3–7.6) mmol/L compared with 177 mmol/L at the time of visual symptoms.

Figure 1. Fundus photographs obtained during the initial assessment showing bilateral temporal pallor.

Figure 2. (A) Humphrey visual field: Central 24-2 threshold test. Visual fields done 2 months after the onset of blurred vision, during the first neuro-ophthalmological evaluation show dense central scotomas, worse superiorly OD (MD: -7.59 dB) and inferiorly OS (MD: -10.47 dB). (B) Repeat visual fields 2 months after partial parathyroidectomy (5 months after the onset of visual symptom) show improvement in the bilateral central scotomas (MD: -4.32 dB OD and -4.24 dB OS).

Figure 3. MRI of the brain: coronal T1 image shows narrowing of both optic canals (arrows). Optic nerves are atrophic.

Figure 4. MRI of the brain: sagittal T1 image showing significantly enlarged diploic space, with arrows pointing to nodular areas of hypointensity caused by brown tumour.

Figure 5. Coronal CT scan shows massive calvarial hypertrophy and narrowed optic canals bilaterally (arrows).

Discussion

This patient with branchio-oto-renal syndrome and chronic renal failure developed bilateral compressive optic neuropathy due to RO. She had spontaneous visual improvement following parathyroidectomy, which remained stable during follow-up.

Involvement of the cranial bones in RO causes massive calvarial hypertrophy and narrowing of the neural canals and foramina. Widening of the diploic space secondary to expanded marrow is a common radiological finding in RO, as in our patient. Parathormone stimulates osteoclasts, which results in localised replacement of bone by vascularised fibrous tissue, called osteoclastomas or brown tumours. Brown tumours are a much less common finding in RO.³

An extreme form of facial bone involvement in RO is called ULO or “bighead” disease, which is characterised by prominence of the maxillary bone, thickening of the mandible, flattened nasal bridge, and widely spaced teeth,^{1,4,5} as evident in our patient. ULO secondary to hyperparathyroidism has been known to affect animals that are fed with diet rich in phosphate and deficient in calcium.⁶ Lee et al. reported five patients with radiological features of ULO associated with RO, treated with parathyroidectomy.¹ They concluded that facial changes in patients with ULO stabilised or even mildly improved following parathyroidectomy. Our patient had clinical as well as radiological evidence of RO, and some facial features of ULO.

The cause of renal failure in our patient was the rare autosomal dominant disorder, branchio-oto-

renal syndrome. Melnick et al.⁷ described this syndrome in a family with branchial fistulae, small cup-shaped ears, prehelical pits, mixed hearing loss, and renal anomalies. Mutations are found in the *EYA1* gene on chromosome 8q13.3.⁸ The *EYA1* gene is thought to be expressed during the development of the otic placode and renal anlage, between the 4th and 10th weeks of embryonic life. CT scan of the temporal bones can identify the abnormalities in the middle and inner ear structures and facilitate the diagnosis, without costly genetic testing that is not widely available.⁹ Our patient did not have a family history of branchio-oto-renal syndrome and probably had the disease because of a sporadic mutation, although genetic testing was not available for confirmation. To our knowledge, ULO has not been reported in branchio-oto-renal syndrome.

Due to narrowing of the neural canals, RO can cause bilateral facial palsies and bilateral hearing loss. RO is in the differential diagnosis of multiple cranial nerve palsies.¹⁰ However, compression of optic nerves secondary to narrowing of optic canals is extremely rare in RO. There is only one prior report of optic nerve compression as a result of RO² in a patient who was treated with high-dose corticosteroids followed by optic canal decompression surgery for one eye, which resulted in significant visual field restoration.² When the opposite eye was affected 16 months later, that patient was treated with high-dose corticosteroids alone because of the surgical difficulties encountered previously due to the thickened calvarium.² There was visual improvement initially with high-dose corticosteroids, but eventually visual field deteriorated in that medically treated eye. Hence, it is felt that visual loss could be progressive without optic nerve decompression in this rare condition.² Our patient was not treated with steroids.

Optic nerve compression initially causes axonal conduction block, which is reversible.¹¹ Prolonged compression eventually leads to retrograde and orthograde (Wallerian) axonal degeneration, and the visual loss can be irreversible.^{12,13} Sometimes, visual loss can be precipitous, in which case a superimposed ischaemic mechanism may be responsible.

The role of decompression surgery in optic neuropathies caused by intra-canalicular compression is not clear. Although decompression is reported to be successful in some cases,^{14,15} acute visual

deterioration and failure to arrest progressive visual loss is also reported to occur with optic canal decompression.¹⁶ Generally, surgical interventions are reserved for acute visual loss,¹⁷ or for continuous visual deterioration¹⁸ despite other treatment.

Although decompression surgery was deferred, our patient had partial parathyroidectomy for multiple parathyroid adenomas. Following this, her vision and visual fields improved. The recovery may be explained by reduction of parathormone levels and arrest of the RO as reported earlier in uraemia.¹ Arrest or relief of the compression on the optic nerves appears to have preserved our patient's vision, although the exact mechanism remains elusive.

The ultimate goal in compressive optic neuropathy should be aimed toward stopping damage to the optic nerves within the optic canals. Decompression surgery is more difficult when the craniofacial bones are abnormally thick in RO,² and parathyroidectomy may be an alternate management if the parathormone level is elevated. Parathyroidectomy may also be beneficial for patients with renal hyperparathyroidism who have unilateral optic nerve compression, as involvement of the other side may ensue if RO is not arrested.

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Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the article.

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