

# Unilateral compressive optic neuropathy due to skull hyperostosis secondary to nutritional vitamin A deficiency

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## Summary

**We report a 17-year-old boy who presented with a chronic left unilateral optic neuropathy. Computerized tomography and magnetic resonance imaging demonstrated compression of the left optic nerve due to skull hyperostosis. He was found to be profoundly vitamin A deficient secondary to an unusual diet consisting predominantly of potato chips and crisps. Skull hyperostosis with cranial neuropathies and other neurological abnormalities has been described in growing animals fed vitamin A deficient diets but has not been previously reported in humans.**

*KEY WORDS: optic neuropathy; skull hyperostosis; vitamin A deficiency.*

## Introduction

Vitamin A is a structural component of the vision pigment rhodopsin, but it is also important in stem cell differentiation, embryo growth and epithelial function. The most common problems caused by vitamin A deficiency are night blindness and xerophthalmia (1). In addition, vitamin A is needed for normal bone growth and tooth development (2). It has been shown to both inhibit osteoblast proliferation and activity and stimulate osteoclast formation and bone resorption. In adults there is an inverse U-shaped curve of vitamin A intake and

bone mineral density (BMD), suggesting that both vitamin A deficiency and excess can lead to osteopenia (3). Since the early part of the last century it has been recognized that vitamin A deficiency can affect bone growth and structure in immature mammals, causing skull hyperostosis, leading to neurological deficits such as blindness due to compression of the optic nerves in the optic canal (4). This effect has never previously been reported in humans.

## Case report

A 17-year-old boy was referred to the Ophthalmology clinic by his optometrist due to decreased vision in his left eye. He had always felt his left eye was weaker than his right but had not noticed any recent deterioration. He was otherwise well, was on no medication, did not drink alcohol and did not smoke tobacco. There was no family history of vision problems.

He could only perceive hand movements with his left eye and had a left centro-caecal scotoma on Goldman perimetry. The visual acuity in his right eye was 6/6 with normal colour vision and a normal visual field. He had a left relative afferent pupillary defect and a pale left optic disc.

A computerized tomography (CT) scan showed generalized increase in the thickness of the bones of the orbit and sphenoid with an increased thickness of diploic spaces and cortices but no signs of bone destruction (Figure 1). Subsequent magnetic resonance imaging (MRI) confirmed that the increased bony thickness involved the whole calvarium and the skull base and the body of sphenoid was not aerated. There was atrophy of the intra-canalicular portion of the left optic nerve (Figure 2). Due to the longstanding nature of the optic nerve atrophy, it was felt that decompression of the optic canal was not indicated.

The bone mineral density in his lumbar spine and hip was very low; four standard deviations below the average for his age. A dietary review revealed that he had had a severely restricted diet since the age of 3, consisting predominantly of potato chips and crisps. Despite this, he was of normal height at 1.79m, although his body mass index was reduced at 18.9kg/m<sup>2</sup>.

His hemoglobin level was at the lower end of normal at 133g/l with a mildly elevated mean cell volume of 97.8fl (normal range [NR] 81.8-96.3fl). His serum vitamin B<sub>12</sub> and folate levels were within the NR. His serum albumin (33mmol/l, NR 35-48), total protein (60g/l, NR 63-79) and creatinine (61µmol/l, NR 83-124) were all low, consistent with his poor muscle bulk. His thyroid function, liver function and alkaline phosphatase were all normal.

A serum vitamin assay found severe vitamin A deficiency at 0.2µmol/l (NR 0.84-3.6µmol/l), mild vitamin D deficiency at 13µmol/l (NR 15.8-100µmol/l) and mild vitamin E deficiency at 9.0µmol/l (NR 11.6-35.5µmol/l).

He had no signs of xerophthalmia and denied night blind-

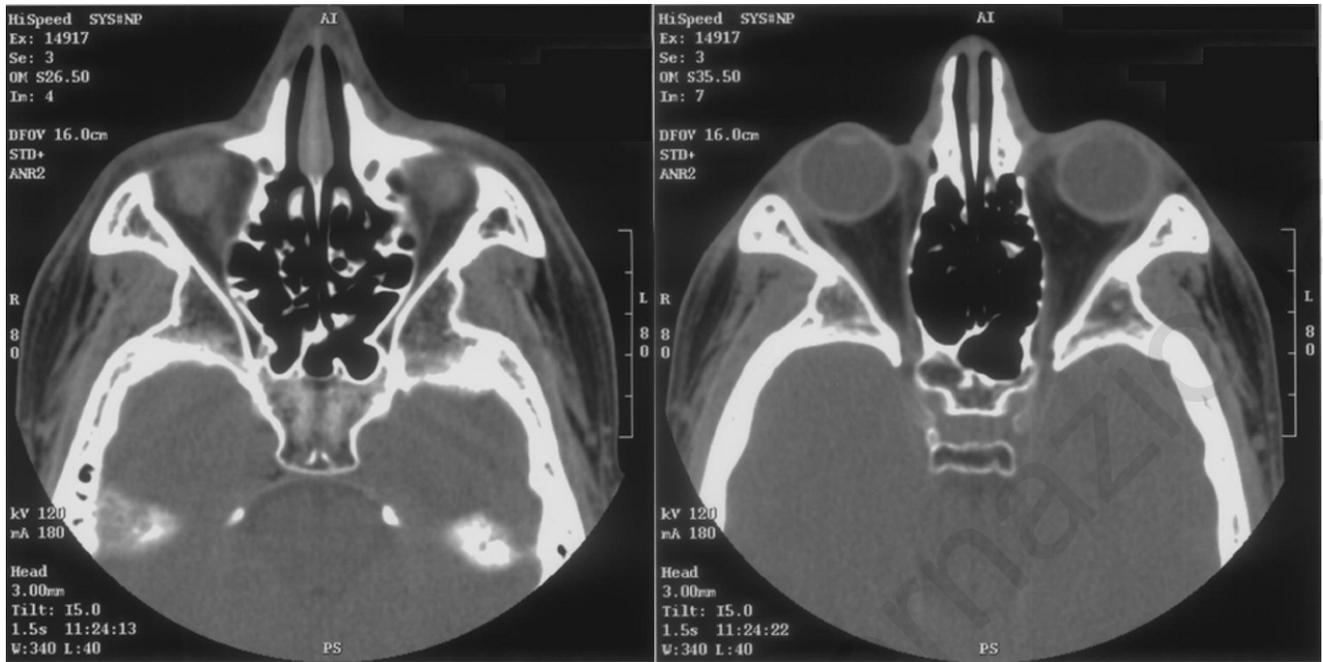


Figure 1 - Axial computerized tomography scans demonstrating generalized thickening of bones with increased thickness of both diploic spaces and cortices and narrowing of both optic canals.



Figure 2 - Coronal T2-weighted magnetic resonance imaging demonstrating atrophy of the intra-canalicular part of the left optic nerve (arrowed).

ness. An electroretinogram (ERG) found normal cone and rod responses but the left eye pattern ERG was attenuated with an absent cortical pattern visual evoked response, consistent with a left optic neuropathy.

He was given dietary advice and was prescribed vitamin supplements. Over 10 years of review his vision remained stable. His diet had diversified to a degree and his bone density had shown some improvement, although it remained re-

duced for his age. A spectralis optical coherence tomography examination found severe thinning of the retinal nerve fibre layer on the left at 49 $\mu$ m, with normal overall thickness on the right at 84 $\mu$ m, although the temporal segment on the right was slightly thinned at 46 $\mu$ m.

## Discussion

Optic canal stenosis causing vision loss has been previously reported due to skull abnormalities in fibrous dysplasia, renal osteodystrophy, osteopetrosis and extramedullary haemopoiesis (5). We speculate that severe, prolonged vitamin A deficiency during growth caused the optic canal stenosis in our patient, since no other cause was found on investigation and the imaging features were not suggestive of any of the above disorders. We do not feel that he had a nutritional optic neuropathy, due to the normal vision in the right eye.

Mellanby, who reared puppies on a vitamin A deficient diet, found increases in both osteoblastic and osteoclastic activity, resulting in the proliferation of cancellous bone at the expense of compact bone, with the bone becoming thickened and enlarged. The particular bones affected were the basi-occipital bone and the spine (6). Gallina et al. and Harris et al. found only increases in osteoblastic activity and no change in osteoclastic activity in vitamin A deficient calves and guinea pig respectively (7, 8). Similarly though to Mellanby, Gallina et al. found that the vertebrae and optic canals of these calves tended to have less compact bone than control calves.

The asynchrony of brain and bone growth in animals has been observed to cause foramen magnum compression, raised intracranial pressure and multiple cranial nerve compression in the skull foramina, not just optic nerve compression (4, 6, 7, 9). Signs reported in lion cubs fed a vitamin A

deficient diet, principally consisting of lean meat, included ataxia, apathy, apparent blindness, "star gazing", convulsions and death (9). Skull abnormalities in vitamin A deficient lions have now been reported from *in vivo* studies using both CT (10) and MRI (11), with changes similar to those seen in our patient.

There have been no previous reports of bone abnormalities in humans secondary to hypovitaminosis A. This may be because vitamin A deficiency usually occurs in the presence of generalized poor nutrition and stunted growth (12), which may prevent the development of skull hyperostosis, unlike in our case and in reported cases in animals where the predominant dietary deficiency was just vitamin A. Also, vitamin A deficiency tends to occur in regions of the world with poor access to health care, so there may be under-reporting of the problem. We are not aware of any systematic surveys of bone abnormalities in human populations with vitamin A deficiency.

It is interesting that our patient did not have xerophthalmia or night blindness. In a study of pre-school children in Indonesia 8 out of 169 (4.7%) children who had severe vitamin A deficiency did not have either xerophthalmia or night blindness (1), suggesting innate resistance to low vitamin A levels in the eyes of some individuals.

This is the first report in humans of neurological abnormality secondary to skull hyperostosis due to nutritional vitamin A deficiency. The likely mechanism, from previous animal studies outlined above, is an increase in osteoblastic activity causing a shift from compact to cancellous bone.

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