

An Incidental Diagnosis of a Rare Bone Disease in a Young Man-Van Buchem Disease.

Author's Details:

Dushantha Madegedara¹, S A Luckmy², B M L S Basnayake³, Prasanna Wijerathna⁵, I M Nawarathne⁴, Dharmadasa Sajani⁶

¹Senior Consultant Respiratory Physician, ^{2,3,4,6}Senior Registrars in Respiratory Medicine, ⁵Resident Respiratory Physician, National Hospital - Kandy, Sri Lanka. Corresponding author- Dushantha Madegedara (dmadegedara@yahoo.com)

Abstract

Van Buchem disease (VBD) is a rare autosomal recessive sclerosing skeletal dysplasia. The most characteristic feature is endosteal hyperostosis of bones, predominantly the skull, mandible, clavicle, ribs and long bones. Consequently, patients may present with various neurological complications such as cranial neuropathies, entrapment neuropathies and raised intracranial pressure. Here we report a 23-year-old male with bronchial asthma, who presented to the out-patient respiratory clinic with symptoms of allergic rhinitis, insidious onset frontal headache and neck pain. Later, the patient developed dizziness, blurred vision, hoarseness of voice and hearing impairment. The most striking features in examination were macrocephaly, frontal bossing, protruding chin and early optic disc edema with multiple cranial nerve palsies. Magnetic Resonance Imaging (MRI) of brain revealed diffuse calvarial thickening with bilateral optic canal stenosis and optic nerve atrophy along with features of increased intracranial pressure (ICP) and evidence of early tonsillar herniation. Results of biochemical analysis including serum calcium and phosphate, parathyroid hormone, calcitonin, and alkaline phosphatase levels were within normal range. Van Buchem disease was diagnosed based on the phenotypic and radiological features. The patient underwent urgent bilateral sub temporal craniotomy for decompression and subsequently showed marked symptomatic improvement.

Key words: Van Buchem disease, hyperostosis

Introduction

Van Buchem disease (VBD), also known as Hyperostosis Corticalis Generalisata is an extremely rare bone disease with autosomal recessive inheritance (1). It was first described in 1955 by Van Buchem. (2) The disease is characterized by endosteal hyperostosis of the skull, mandible, clavicle, ribs and the diaphysis of the long bones (3). The abnormal growth of bones may cause phenotypic abnormalities such as macrocephaly, frontal bossing, enlargement of the jaw and severe neurological complications such as cranial neuropathies, entrapment neuropathies, neuralgic pain, and visual problems. (4) The skull thickening and resultant narrowing of neuroforamina in the skull base can cause entrapment neuropathies of cranial nerve. The seventh and eighth nerve entrapment causing facial nerve palsy and hearing impairment are the most common cranial neuropathies encountered in these patients. Apart from these several of other cranial nerves such as first, second, fifth, tenth and twelfth nerves can get affected due to nerve entrapment. (1,5) Increased intracranial pressure due to hyperostosis of the calvarium can be life threatening and may require surgery for cranial decompression. Radiologically there are features of massive hyperostosis of the calvarium and mandible, resulting in increased weight of skull (6).

VBD is an extremely rare disease and according to the literature, fewer than 35 cases (7) have been reported worldwide, but none from Sri Lanka. Therefore, by reporting this case we attempt to improve the awareness regarding this rare disease among clinicians.

Case report

A 23-year-old gentleman presented to the outpatient respiratory clinic complaining of frontal headache, recurrent nasal block, runny nose and sneezing triggered by dust and cold weather for 2 years duration, with recent worsening of symptoms. He had a history of intermittent bronchial asthma since childhood, but had defaulted treatment in the last 10 years. The patient was commenced on inhalers, antihistamines and steroid

nasal drops for allergic rhinitis and follow up was arranged at clinic level. However, as there was only partial response to treatment, further investigations were arranged including chest radiography (Figure 1) and X ray of sinus view, which revealed generalized sclerosis of bones of the skull, clavicle and ribs.



Figure 1 – Chest radiography showing symmetrical thickening of ribs and the clavicles.

He was a product of a consanguineous marriage. Apart from mild intermittent asthma and allergic rhinitis, he had been apparently well until a year ago, when he developed insidious onset neck pain with radiation to both upper arms causing mild functional impairment. There was no history of fractures, back pain or bone pain. He also complained of intermittent frontal headache for the same duration for which he had been treated with multiple analgesics. Further questioning also revealed a hearing impairment in the preceding six months, without any associated vertigo or unsteadiness. There were no other neurological symptoms. His parents and two siblings were healthy and revealed no family history of bone diseases.

On examination he was a well-built young man with a height of 160cm and BMI of 23.5kg/m². His macroscopic appearance was significant with protruding chin, frontal bossing and macrocephaly. (Figure 2) There were no dysmorphic features, or other features to suggest acromegaly. He had clinical evidence of severe cervical-radiculopathy with wasting of both upper limb muscles with marked wasting of small muscles of the hands. Rest of the neurological examination as well as other systems examination were unremarkable. Plain radiography of skull revealed diffusely increased bone density with calvarial thickening, prominent frontal sinuses and mild prognathism. (Figure 3A) X ray assessment of the humerus (Figure 3B) and femur also showed diffuse hyperostosis of the diaphysis.



Figure 2 - Patients images showing frontal bossing and prognathism.

He was referred for specialized neurological management with regard to his neurological symptoms. But unfortunately, due to circumstances relating to Covid 19 pandemic, the patient defaulted follow up for nearly 5 months. When the patient presented later, he was found to have new onset blurred vision, hoarseness of voice and dizziness. Neurological examination revealed multiple cranial nerve palsies involving bilateral VIIth, VIIIth, IXth, Xth and XIth nerves with early optic disc oedema.

Urgent Computed tomography of the brain revealed diffuse bone thickening and increased density in skull, facial and upper cervical bones without evidence of bone lesions or fracture. Furthermore, there was narrowing of internal acoustic canals (Figure 4A) with compact middle ear cavities and poorly formed mastoid air cells. MRI brain revealed diffuse calvarial thickening (3cm) and sclerosis along with bilateral optic canal stenosis and optic nerve atrophy (Figure 4B). There were features of increased intracranial pressure (ICP) and evidence of early tonsillar herniation.



Figure 3 (A) X ray of skull showing diffuse thickening and sclerosis of calvaria (thick arrow), skull base (thin arrow) and mandible. (black arrow) (B) X ray of the humerus showing hyperostosis of the diaphysis (arrow)

The patient was immediately referred for neurosurgical interventions and underwent urgent decompression surgery with bilateral sub temporal craniotomy. (Figure 5) He showed marked symptomatic improvement following surgery with total resolution of headache and dizziness. Radiological screening of his asymptomatic siblings revealed negative findings.

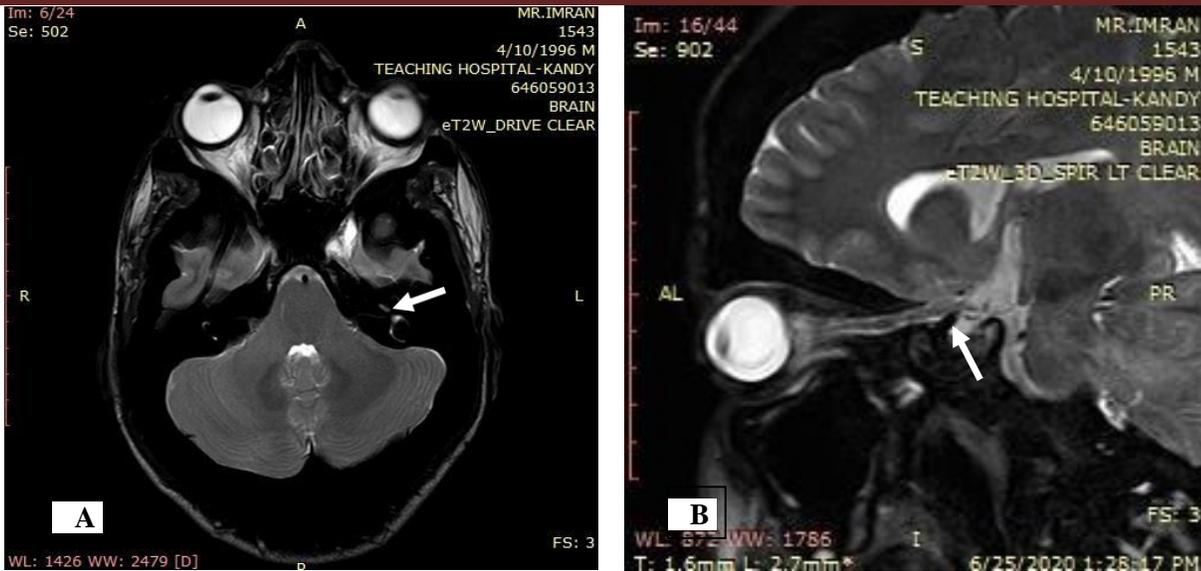


Figure 4 – (A) MRI brain showing narrowing of the internal acoustic canals (arrow) (B) MRI brain showing narrowing of optic canals causing optic nerve compression.



Figure 5 – Computed tomography of brain taken after bilateral sub temporal craniotomy.

Discussion

This patient was incidentally found to have a sclerosing bones in the skull which pointed towards further investigations. With the given history and investigations several differential diagnoses were made including adult onset osteopetrosis, Paget disease of bones, primary hyper parathyroidism, osteofluerosis, sclerosteosis

and VBD.

According to the clinical findings and investigations Paget disease of bone, primary hyper parathyroidism and osteofluerosis were excluded. Since the patient had minimal symptoms at initial presentation with radiological findings of bone sclerosis, our most probable diagnosis was adult onset autosomal dominant osteopetrosis. But the rapid deterioration of patient with multiple compressive cranial neuropathies and increased intracranial pressure together with absent fractures were against the diagnosis of adult onset osteopetrosis but more suggestive of sclerosteosis and VBD.

Slerosteosis and VBD are two forms of SOST-related sclerosing bone dysplasia, and share many phenotypic abnormalities (6,8). Of the two conditions, sclerosteosis causes a more severe form of bone disease with most of the affected people developing symptoms in early childhood or adolescence. Also, patients with sclerosteosis often show excessive height and hand abnormalities such as radial deviation, syndactyly or nail abnormalities (8).

Since our patient had normal height and absent hand abnormalities, a diagnosis of VBD was made. Both of these disorders have autosomal recessive inheritance. In VBD there is a 52-kb noncoding deletion of the SOST gene on chromosome 17q and sclerosteosis is caused by a homozygous mutation in the SOST gene (9). Therefore, genetic testing provides useful information to support diagnosis of VBD. In our case this was a major limitation as gene analysis could not be performed due to unavailability.

In VBD the genetic defect causes uninhibited activity of osteoblasts leading to excessive bone formation causing hyperostosis mainly involving the skull and the tubular bones (10). This may manifest as multiple cranial nerve palsies and entrapment neuropathy. The seventh and eighth cranial nerve palsies are the most common cranial neuropathies. Patients may present with several episodes of acute facial palsy during the course of the disease. The hearing loss can be conductive, sensorineural, or a mixed, due to eighth nerve entrapment as well as narrowing and elongation of the external auditory meatus and reduced middle ear space (11). Thickening of the nasal septum and turbinates causes obstruction of the nasal passage. Excessive bone formation in the skull causes reduced intracranial space giving rise to increased intracranial pressure and reduced space for brain parenchyma. Despite this, patients with VBD display normal intelligence and academic performance. (12,13)

Up to date, curative treatment is not available for VBD and the mainstay of management aims at symptomatic relief. According to literature, decompressive craniectomy has been successfully carried out in several patients with increased ICP to prevent subsequent brain herniation. (13,14) In addition ventriculoperitoneal shunts can be placed to reduce the intracranial pressure. (15) Hearing loss due to extensive narrowing of the external meatus can be improved with the placement of a bone anchored hearing aid(16). Some reports have suggested long term glucocorticoids as a new treatment modality, but considering the adverse effects profile, needs more research for further evaluation (15).

This case report highlights some important features of an extremely rare bone disease. Early recognition of features of increased ICP is crucial to prevent sudden death from brain herniation. Moreover, the awareness of the disease would help in early diagnosis, minimizing its life-threatening complications as well as genetic counseling.

Contribution:

DM, SAL, IMN and BMLSB, DS contributed to the manuscript preparation. DM supervised the all the aspects and was the supervising care physician. PW was involved in management.

Ethical statement:

Informed written consent was obtained from the patient for the publication of the case report and all the accompanying images.

Conflicts of interest:

All the authors have declared that they have no conflicts of interest.

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