Van Buchem Disease: First Case Report from the Indian Subcontinent with an Early Presentation

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Abstract

Van Buchem disease is a rare autosomal recessive genetic disorder that causes a compromised inhibitory feedback mechanism resulting in increased bone formation and overgrowth of the skeleton leading to a variety of neurological symptoms. It has been reported in less than 50 patients most of which were in western Europe. We report the first case of this condition from the Indian subcontinent with an early presentation. This patient presented with a global delay in attaining the developmental milestones and progressive reduction in visual acuity and loss of hearing. He had dysmorphic facies, multiple cranial nerve palsies, and severe visual and auditory deficits. Imaging revealed sclerosing bone dysplasia. This case illustrates the clinical and imaging findings of this rare condition.

Keywords

- Van Buchem disease
- cranial nerve
- hyperostosis
corticalis generalisata

Introduction

Van Buchem disease (VBD) is characterized by the increased bone formation and overgrowth of the skeleton. It is listed as entry # 239100 in Online Mendelian Inheritance in Man (OMIM) database. It derives its name from its first documentation by Van Buchem in 1955.1 Clinically facial dysmorphism, progressive cranial nerve involvement, and increased intracranial pressure are noted. It most commonly involves the skull and skull base, the mandible, the clavicles, the ribs, and the diaphysis of the tubular bones. We report the case of a 5-year-old boy with classical imaging features of VBD. It is the first case of this condition from the Indian subcontinent. This case is also unique in its early presentation.

Case Report

A 5-year-old boy was brought to the hospital by caregivers with a global delay in attaining the developmental milestones and progressive reduction in visual acuity and loss of hearing. The symptoms started at the age of 3 years. The child was the product of a nonconsanguineous marriage. There was no family history of similar symptoms.

Clinical examination revealed facial dysmorphism with macrocephaly, flat prominent nasal bridge, hypertelorism, prognathic mandible, and protruding tongue (Fig. 1). The patient had short stature with a global developmental delay. The child had bilateral seventh cranial nerve palsy (House–Brackmann grade III on the right side and grade IV on the left side) on examination.

The ophthalmologic examination found reduced visual acuity having only light perception bilaterally. The child also had horizontal nystagmus at extremes of gazes with temporal pallor and altered pigmentation at the macula. Visual evoked potential study showed no recordable potentials. Otological examination showed intact tympanic membranes on both sides. Pure tone audiometry revealed severe bilateral mixed conductive and sensorineural hearing loss. The dental examination showed malocclusion, mild decay, and diastema between lower central incisors. The rest of the clinical examination was unremarkable.

Given the suspicion of a syndromic disorder, the patient had a skeletal survey. Posteroanterior and lateral view radiographs...
of the skull (► Fig. 2) showed generalized thickening of the skull vault, maxilla, and mandible involving both inner and outer tables with partial obliteration of diploic spaces. The skull had a patchy copper-beaten appearance. The maxillary sinus was not visualized. The rest of the skeletal survey was normal.

A corroborative noncontrast computed tomography scan of head was performed which confirmed the findings seen on skull radiograph (► Fig. 3). Characteristic bony excrescences were seen along the inner table of the skull. Also, there was a narrowing of the bilateral optic canals, internal auditory meatuses, and facial nerve canals. Diffuse hyperostosis of the temporal bone was seen to cause severe narrowing of the middle ear cleft. The scan had a Computed Tomography Dose Index of 32.3mGy.

The child had reduced vitamin D3 levels at 9.3 ng/mL (reference values: 12–20 ng/mL) with mildly raised alkaline phosphatase levels at 382 units/liter (reference values for age: 92–309 U/L). The rest of the hematological and biochemical investigations was normal including serum calcium, serum phosphorus, serum parathyroid hormone levels, and urine calcium/creatinine ratio was within the normal range. We could not perform serum osteocalcin level analysis. Genetic analysis could not be done as caregivers did not provide the consent for the same.

The patient is being managed by nonsurgical measures. He has been prescribed hearing aids with mild improvement in the hearing and has been started on glucocorticoids to suppress further bone formation. His parents have undergone genetic counselling. The child is on regular follow-up.

Discussion

VBD is an uncommon autosomal recessive hereditary condition with bone dysplasia.\(^2\) Recessive type of VBD (OMIM 239100) segregates with 17q21.31 locus harboring SOST. There is a homozygous 52-kb deletion downstream of the SOST gene that is thought to decrease gene expression of sclerostin. Sclerostin is an inhibitor of bone formation. The reduction in its expression leads to unrestricted bone
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The treatment of VBD is symptomatic as no cure is available. Various treatment modalities range from medical therapy in the form of glucocorticoids to surgical interventions in the form of bone-anchored hearing aids, surgical nerve decompression, and decompressive craniectomy. A detailed discussion of these is beyond the present submission.

Ethics Approval and Consent to Participate
Ethical approval was waived by the local Ethics Committee of Armed Forces Medical College given the retrospective nature of the study and all the procedures being performed were part of the routine care. The patient reported in this article had signed a written informed consent form to participate in the study and have their data published in a journal article under anonymity. This case report was a reporting of a case in a medical educational center, in which all patients are informed that they may be subjects of scientific experiments and are informed of the ethical codes of conduct. This study was in compliance with the latest version of the Helsinki Declaration.

Consent for Publication
The patient had written and signed an informed consent note that the findings may be published without any personal detail.

Availability of Data and Material
All data are available based on a reasonable request.

Authors’ Contributions
All authors contributed to the study conception and design. Material preparation, data collection, and analysis were performed by S.M., A.N. SH, and U.R. The first draft of the manuscript was written by S.Y. and K.U.B. All authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.
All authors have agreed to both to be personally accountable for their contributions and they have ensured that questions related to the accuracy or integrity of any part of this work, even ones in which they were not personally involved, were appropriately investigated, resolved, and the resolution was documented in the literature.

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Conflict of Interest
None declared.

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References


