

Van Buchem disease

First case report in Taiwan

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Abstract

Rationale: Van Buchem disease (VBD) is a very rare autosomal recessive disease. According to our review of the relevant literature, this article is the first case report of VBD in Taiwan.

Patient concerns: A 54-year-old woman developed a protruding chin, frontal bossing, and macrocephaly at the age of 40 years. She noted the onset of progressive bilateral visual and hearing impairment at the age of 40 and 45 years, respectively. Intermittent headaches, peripheral facial palsy, recurrent bilateral trigeminal neuralgia, and back pain were also observed since age 40.

Diagnoses: She received a diagnosis of VBD based on the phenotypic abnormalities of the skull and mandible, facial nerve involvement, radiological images of the skeleton, and her family history.

Interventions: She received symptomatic treatment and surgical decompression for spinal stenosis.

Outcomes: Her clinical condition did not improve satisfactorily.

Lessons: We hope to promote clinician awareness of this very rare disease and its symptoms and signs. A comprehensive understanding of VBD might lead to the development of a curative therapy in the future.

Abbreviations: CT = computed tomography, ICP = intracranial pressure, MR = magnetic resonance, VBD = van Buchem disease.

Keywords: hyperostosis, van Buchem disease

1. Introduction

Van Buchem disease (VBD) is a rare autosomal recessive disease that was first described by van Buchem et al in 1955. The most characteristic feature is endosteal hyperostosis of the mandible, skull (both the calvaria and the cranial base), ribs, and clavicles as well as diaphysis of the long bones.^[1] Therefore, VBD has been classified as one of the craniotubular hyperostoses.^[2] Many subperiosteal osteophytes are formed on these bones, resulting in a rough bone surface. The principal exterior findings are macrocephaly and an enlarged mandible, which can be very broad. In most patients, the bone anomalies are symmetric and progressive, starting in the first decade of life.^[3] The clinical complications include cranial nerve paralysis, neuralgic pain,

sensorineural hearing loss, and visual problems.^[4] The prevalence of VBD is very low, with fewer than 35 cases reported so far.^[5] We present one such case and attempt to provide a detailed understanding of VBD to all physicians.

2. Case report

A 54-year-old Asian woman presented with dense ribs and clavicles on chest X-ray examination (Fig. 1), which were first observed at the age of 20 years. Subsequently, she developed a protruding chin, frontal bossing, and macrocephaly at the age of 40 years (Fig. 2). Mandible palpation revealed a bony enlargement over the anterior sides to angles without any symptoms of inflammation. She noted progressive bilateral visual and hearing impairments since the age of 40 and 45 years, respectively. Furthermore, intermittent headaches, peripheral facial palsy (House Brackman Scale grade III), recurrent bilateral trigeminal neuralgia, and back pain were observed since the age of 40 years. She was distressed by headaches, trigeminal neuralgia, and back pain, for which she had been treated with various painkillers including celecoxib (200 mg, twice daily), tramadol (100 mg every 6 hours), and pregabalin (75 mg, twice daily). However, her pain did not improve satisfactorily (visual analog scale score > 4). Therefore, she was later treated with oral morphine (15 mg every 4 hours) and duloxetine (60 mg daily) for severe pain and depression. Although her pain improved on the above, she frequently experienced drowsiness, dizziness, and nausea. In addition, she had frequent falls during this period. She also had a suicide attempt by overdose of sleeping pills in December 2016. She received surgical decompression for spinal stenosis in March 2017 for worsening back pain and progressive right arm clumsiness. After surgery, her back pain and right arm clumsiness improved considerably.

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Figure 1. Chest X-ray on May 26, 2005 revealed hyperostosis of the clavicles, particularly on the medial side. Hyperostosis of bilateral ribs was also observed.

Previously obtained radiographs revealed an increased thickness and hyperostosis of the calvaria and mandible (Fig. 3) and progressive hyperostosis at the diaphysis of the femur and tibia, which resulted in the narrowing of the medullary canal (Fig. 4). Her head computed tomography (CT) images in bone window in 2014 revealed a generalized thickening of the skull and mandible as well as a narrowing of the bilateral internal auditory canals (Fig. 5A). Furthermore, dense abnormal bone was encroaching on otherwise normal inner ear structures such as the vestibule; the cochlea facial canals were compressed and could not be clearly identified; and the optic canals were narrow (Fig. 5B). Magnetic resonance (MR) images of the C-spine in 2015 revealed diffuse

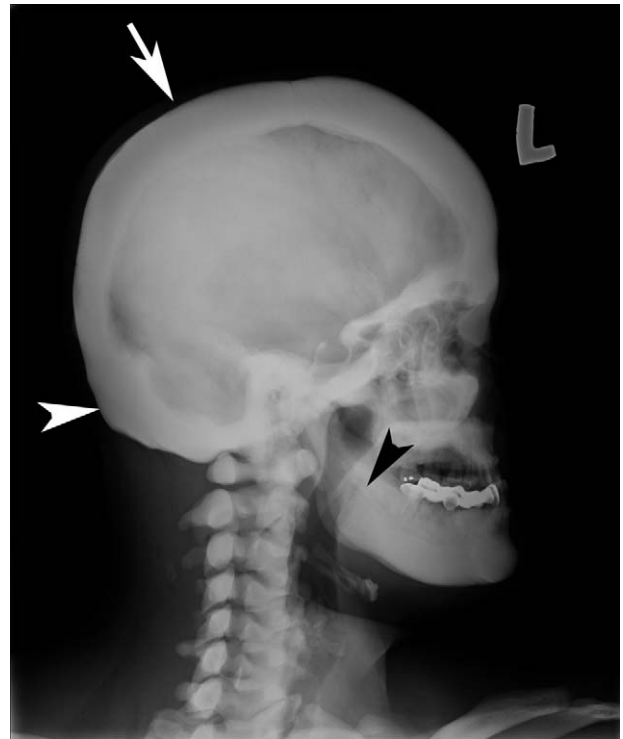


Figure 3. Skull X-ray on June 2, 2005 showed a generalized thickening and sclerosis of the calvaria (white arrow), skull base (white arrowhead), and mandible (black arrowhead).

sclerosis with blastic changes in the visible bones and canal stenosis with cord compression from the C3 to C6 levels (Fig. 6).

The results of laboratory investigations—including serum calcitonin and alkaline phosphatase levels—were within the normal range. She had 2 brothers, and her younger brother had similar symptoms (Fig. 7). A diagnosis of VBD was provided on the basis of the phenotypic abnormalities of the skull and



Figure 2. Our patient's images on March 30, 2017 showed (A) macrocephaly and (B) a protruding chin and frontal bossing.

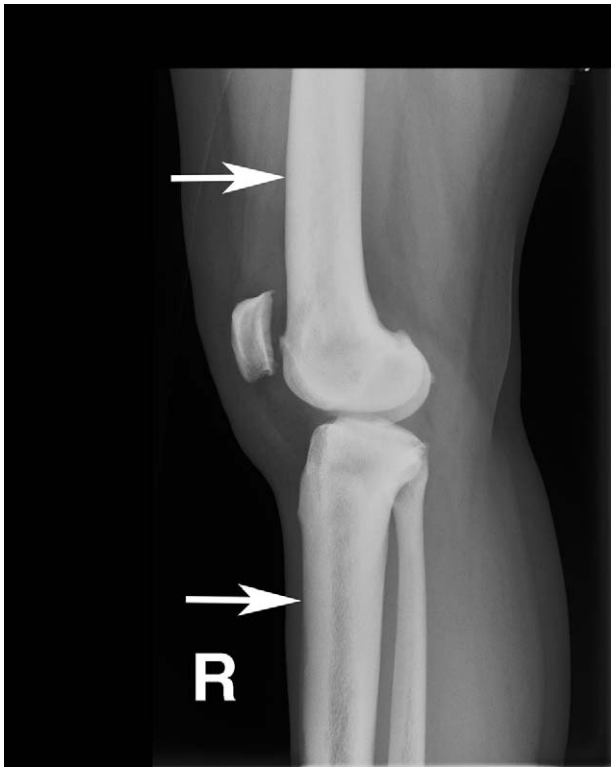


Figure 4. Lateral view of the right knee on June 25, 2005 showed hyperostosis at the diaphysis of the femur and tibia (white arrow), resulting in the narrowing of the medullary canal.

mandible, facial nerve involvement, radiological images of the skeleton, and her family history.

Informed consent for the publication of this case report was provided by the patient. Review by Ethics Committee is not required for case reports beyond patient consent.

3. Discussion

VBD is a rare autosomal recessive disease. Most patients described by van Buchem resided in a small Dutch fishing



Figure 6. MR images of the C-spine on December 7, 2015 showed diffuse sclerosis with blastic changes in the visible bones and canal stenosis with cord compression from the C3 to C6 levels (white arrowhead).

village. Our patient is the first to receive a diagnosis of VBD in Taiwan. The bone tissue in VBD has a normal structure, with slight modeling defects. The pathogenesis of VBD has been suggested to involve increased osteoblast activity caused by deletion of the SOST gene on chromosome 17q, which is a characteristic molecular finding in patients with VBD.^[6]

The main features of VBD include hyperostosis of skull, mandible, clavicles, ribs, and diaphysis of the long bones.^[7] Skeletal dysplasia can result in severe neurological complications.^[8] In VBD, the clinical consequences of skull thickening are cranial neuropathies, which are caused by the narrowing of the neuroforamina in the skull base. The entrapment of the seventh and eighth cranial nerves is most common, causing facial nerve palsy and hearing loss in the second decade of life. The hearing loss can be conductive, sensorineural, or mixed.^[9] Furthermore,

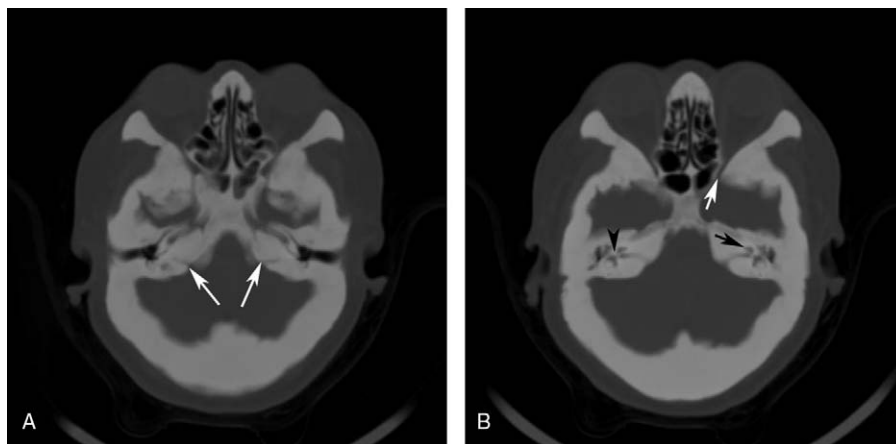


Figure 5. Head CT in bone window on March 27, 2014, showed (A) narrowing of the bilateral internal auditory canals (white arrow) and (B) encroachment of dense abnormal bone on the otherwise normal inner ear structures, such as the vestibule (black arrowhead). The cochlea facial canals were compressed (black arrow) and could not be clearly identified, and the optic canals were narrow (white arrow).



Figure 7. Right knee X-ray of our patient's brother (aged 28 years on September 21, 1994) showed hyperostosis at the diaphysis of the femur and tibia (black arrowhead), resulting in narrowing of the medullary canal.

the first, second, fifth, and twelfth cranial nerves are often involved.^[10] Late neurological complications, including spinal stenosis and increased intracranial pressure (ICP) caused by the hyperostosis of the calvaria with decreased intracranial space, have also been observed.^[9] Recurring headaches and dizziness can be caused by increased ICP. In the reported literature, there was very little information on spine complications in VBD. Spinal stenosis has been mentioned as a possible late complication, but without further detailed description. Patient age in most reports ranges from young to middle age adults. Spine complications usually occur in older adults. In addition, some reports observed a slowing of disease progression in older patients. Therefore, some patients may not experience spine complications at all. Our patient developed cranial neuropathies since the fifth decade of life. Her facial palsy, trigeminal neuralgia, and visual and hearing impairment were all bilateral. Notably, despite the diminished intracranial space for brain parenchyma, the intelligence of patients with VBD is not affected. The same applies to our patient. These individuals usually perform well in school and are often highly trained.^[11]

The diagnosis of VBD is based mainly on the phenotypic abnormalities of the skull and mandible, facial nerve involvement, and radiological images of the skeleton. Facial nerve grading (House Brackman Scale) is an effective diagnostic criterion because severe dysfunction (grade V) on at least one side was observed in all 11 patients who were examined in a previous study, with the exception of one patient, who demonstrated a moderately severe dysfunction (grade IV) on both sides.^[3] The diagnosis can be supported by establishing the deletion of the SOST gene on chromosome 17q. Genetic testing is useful for the diagnosis of VBD. Before 1998, the diagnosis of VBD can only be made by the phenotypic abnormalities and radiological pictures of the skeleton. Since 1998, some researchers believed

that VBD is caused by deletion of the SOST gene on chromosome 17q. Therefore, lots of the cases reported after 2000 were also proven to have the chromosome 17q deletion. Whether deletion of the SOST gene on chromosome 17q is necessary for the diagnosis of VBD, however, is not conclusive. Clearly, more studies are needed to clarify this issue. Biologic markers are not used to try to diagnosis of VBD. Serum calcium and phosphate levels are within the normal range.^[12] In addition, histological examination reveals that the increased quantity of bone was essentially normal in appearance and mineralization.^[13]

The key differential diagnosis of VBD is sclerosteosis, which has a high phenotypic resemblance to VBD. The main difference between the 2 disorders is that sclerosteosis patients show excessive height and hand abnormalities (radial deviation, syndactyly, or both).^[14] In addition, premature death has been reported in several cases of sclerosteosis. Increased ICP is the main cause of death in patients with sclerosteosis.^[15,16] However, increased ICP is less frequently observed in patients with VBD (20%). In contrast to patients with sclerosteosis, none of the 3 patients with VBD who had increased ICP in one series required craniotomy.^[17] Our patient has normal height and normal hands. With regards to genetics, both disorders have an autosomal recessive mode of inheritance. Van Buchem disease is believed to be caused by deletion of the SOST gene on chromosome 17q. However, sclerosteosis is caused by homozygous mutations in the SOST gene. The major limitation of our case report is the lack of genetic testing, which was unfortunately not available at the time the patient presented.

To date, curative treatment for VBD is unavailable. Current treatments are strictly symptomatic. Partial craniectomy has been used for increased ICP.^[18] In addition, a ventriculoperitoneal drain can be implanted to control increased ICP.^[19] In the Netherlands, 6 adult patients with VBD have undergone decompressive facial nerve surgery. However, facial nerve palsy recurred in all of these patients after the surgery.^[5] Symptomatic spinal stenosis is an indication for surgical decompression. Our patient had symptomatic spinal stenosis; and she therefore received surgical decompression. After the surgery, her symptoms improved considerably. Moreover, the placement of a bone-anchored hearing aid can be useful to treat extensive narrowing of the external meatus.^[9]

Glucocorticoids (prednisone for 2 years with a mean dose of 10mg per day) may represent a new treatment modality, resulting in biochemical and histologic suppression of bone formation.^[19] However, prolonged administration of glucocorticoids will negatively affect the growth of children. Two patients were reported to receive prednisone treatment during exacerbation of facial nerve palsy. Although a decrease in the abnormally high levels of biochemical bone parameters was observed, no clinical improvement was achieved.^[5] Additional research is warranted to evaluate the possible beneficial effects of glucocorticoids in both adults and children with VBD. We hope that clinicians can become more aware of this very rare disease when they encounter patients with similar symptoms and signs. A comprehensive understanding and identification of VBD might lead to the development of a curative therapy in the future.

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