Case Report

Hajdu–Cheney syndrome: A rare acro-osteolytic disorder

Mojisola Adejoke Olusola-Bello, Ayodeji A Olatunji, Oluyemisi O Toyobo

Department of Radiology, Olabisi Onabanjo University Teaching Hospital, Shagamu, Ogun State, Nigeria

Abstract We report a case of a 35-year-old woman with Hajdu–Cheney syndrome, a very rare connective tissue disorder with about 70 cases reported worldwide since 1948. No similar disease occurred in her family. She presented with clinical features of the syndrome and left seventh cranial nerve palsy after several dental procedures. The radiographs of the skull and the hands demonstrate the abnormalities clearly.

Keywords: Acro-osteolytic disorder, Hajdu–Cheney syndrome, Osteolytic disorder

Address for correspondence: Dr. Mojisola Adejoke Olusola-Bello, Department of Radiology, Olabisi Onabanjo University Teaching Hospital, Shagamu, Ogun State, Nigeria.
E-mail: mojisolabello@gmail.com

INTRODUCTION

There are over 50 congenital and acquired disorders characterized by osteolysis. In half of these conditions, osteolysis is limited exclusively to the hands and feet. Although there are several bone dysplasias, in none of them is acro-osteolysis a sign of such diagnostic significance as in Hajdu–Cheney syndrome (HCS).

HCS is a very rare connective tissue disorder. About 70 cases have been reported worldwide since its discovery in 1948. No case has been reported in Nigeria, to the best of the authors' knowledge. This disorder is important for the radiologist because of the distinctive radiographic findings that make the diagnosis possible.

CASE REPORT

A 35-year-old female patient presented to the rheumatology clinic with a history of pain and progressive shortening of fingers.

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She had been to the dental clinic on account of loose and premature loss of multiple teeth. She had multiple prosthetic teeth. After one of the procedures, she noticed that her face was pulled to the right and had difficulty in closing the left eye.

No other neurological deficit was noted.

On examination, the patient was short in stature and had a wide neck. The left corner of the mouth was drooping, and it was difficult for her to close her left eye. She had midfacial flattening and short stubby hands [Figure 1].

Radiographs of the skull and the hands were ordered and performed.

Lateral radiograph of the skull showed multiple Wormian bones in the lambdoid suture. There was delayed closure of the coronal and metopic sutures and prominence of the occipital bone. There was platybasia, but no basilar invagination seen.

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The frontal sinus was not pneumatized, and the maxillary sinuses were hypoplastic [Figures 2 and 3].

Multiple losses of the upper and lower teeth were noted, and two teeth were noted on the maxilla and the mandible.

Radiograph of the right hand showed a transverse band of osteolysis involving the distal phalanges of the thumb, second, third, and fifth fingers.

Radiograph of the left hand showed an osteolytic band involving the distal phalanx of the thumb and the distal phalanges of the second, third, and fifth fingers [Figure 4].

Based on clinical and radiological findings, the patient was diagnosed to have HCS with facial nerve palsy.

Genetic analysis for NOTCH2 mutation was not available.

DISCUSSION

HCS was first described by Hajdu and Kauntze in 1948 as a cranio-skeletal dysplasia.[1,2] Cheney brought in another case report in 1965 where he described additional radiological features of the disease including acro-osteolysis.[3]

HCS is a very rare, autosomal dominant disorder of connective tissue with <100 cases reported.[4]

It is known that restricted range of mutations in the terminal exon of neurogenic locus notch homolog protein 2, also known as NOTCH2, causes this syndrome. NOTCH is a regulator of the skeletal development and bone remodeling. Notch signaling is important in the early skeletal development as well as for the differentiation and function of osteoblasts and osteoclasts in postnatal life. However, the precise mechanism leading to osteoporosis and other manifestations in HCS is unclear.[5]

The severity of the disease and age at diagnosis varies, and the diagnosis may be made earlier in childhood in patients with family history. However, most often, it is diagnosed in adolescence or adulthood.

The main clinical features of HCS include short stature, scoliosis and kyphosis, elongation of the skull, small chin, clubbing of fingers, coarse hair, and thick eyebrows. They may also have micrognathia, premature loss of teeth, low set ears, and short web neck.[6]

Radiographically, the most frequent findings are seen in the skull, hands, and feet.

In the skull, there is delayed closure of sutures, persistent Wormian bones, especially in the lambdoid suture, bulging of squamous occipital bone, enlarged sella turcica, aplasia of the frontal sinus, platybasia with or without basilar invagination, and thickening of skull basal and mastoids.

There may be malalignment of teeth, premature loss of teeth due to periodontal disease, and hypoplastic maxilla and mandible. In the index patient, all the features were present, and only about four teeth were seen on the radiograph.

The spine may show features of osteoporosis, biconcave vertebrae, compression fractures, spondylolisthesis, and kyphoscoliosis; no evidence of spondylolisthesis and kyphoscoliosis was seen in the index patient.

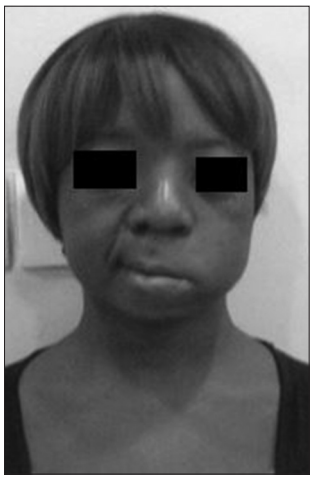

Figure 1: Photograph of the face of the patient showing wide neck and midfacial flattening. The mouth was deviated to the right and the left corner of the mouth is noted to droop

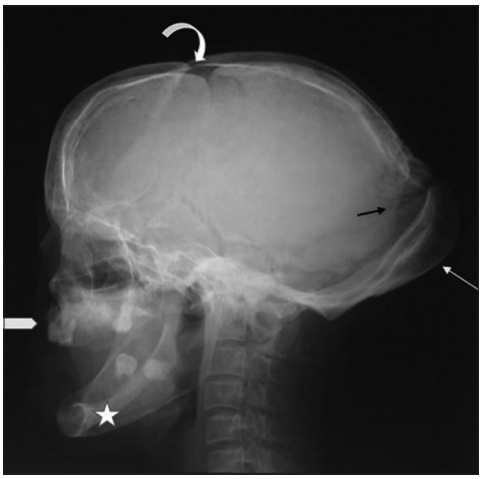

Figure 2: Lateral view of the skull. Multiple Wormian bones are noted in the lambdoid suture (black arrow). The prominence of the occipital bone also seen (white arrow). Delayed closure of the coronal suture seen (white curved arrow). Micrognathia (thick white arrow) and edentulous mandible (white star) also highlighted. The frontal sinuses are absent, and there is platybasia; however, there is no basilar invagination

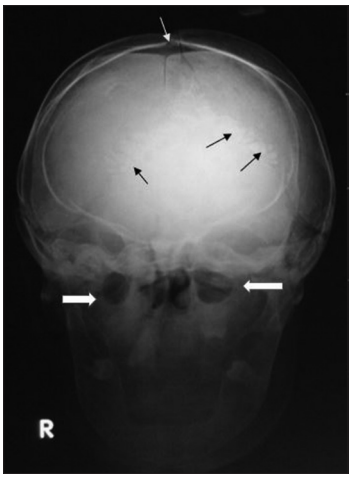

Figure 3: Posteroanterior view of the skull. Anterior fontanelle is seen (white arrow) with persistent metopic suture. The maxillary sinuses are hypoplastic (thick white arrows). Multiple Wormian bones are noted in the lambdoid suture (black arrows). Premature loss of teeth noted with four teeth noted in the alveolar portion of the mandible and maxilla seen

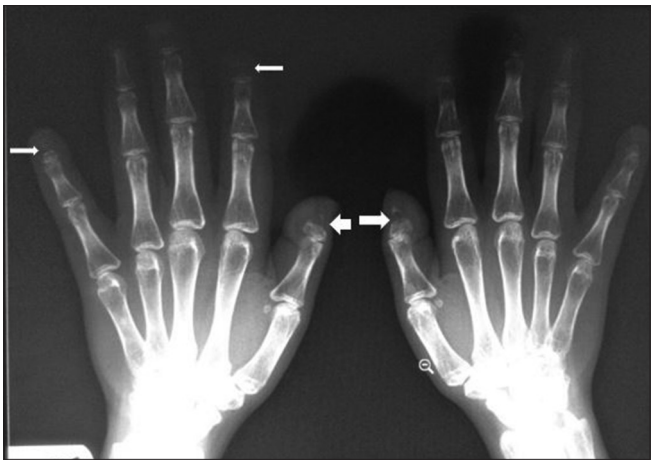

Figure 4: Radiograph of the right and left hands, Anterior–posterior view. Showing transverse band of osteolysis involving the distal phalanges of the thumb, second, third, and fifth fingers bilaterally (arrows). Osteoporosis of the distal phalanges when compared to the carpal bones also noted

Acro-osteolysis is considered to be the hallmark of the syndrome, and this is usually caused by increase in mast cells and by elaboration of osteolytic cytokines.

The hands and feet usually show a characteristic transverse band of osteolysis involving the distal phalanges and distal to proximal type of osteolysis.[7] The patient discussed in this article has a characteristic band of osteolysis in both hands, sparing the distal phalanges of both index fingers.

There is no known association between HCS and facial nerve palsy. However, the patient may have developed this palsy as a result of multiple dental procedures or dental anesthesia; Inferior alveolar nerve block or posterior superior nerve block.[8,9]

Other abnormalities that may be seen in HCS include recurrent respiratory tract infection, congenital heart diseases such as atrial septal defect, patent ductus arteriosus, mitral regurgitation, and polycystic kidney disease.[6]

The diagnosis in this syndrome is based on the characteristic clinical features and imaging findings in hands, feet, and skull. The presence of positive family history makes the diagnosis easier. The gold standard of diagnosis is demonstration of truncating mutation in terminal exon of NOTCH2.

No specific treatment is known for HCS. Management is symptomatic and is aimed at preventing osteoporosis. The index patient is presently on bisphosphonate and Vitamin D therapy by the rheumatologist.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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