Review Article

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Hajdu-Cheney syndrome: Report of a family and a short literature review

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SUMMARY

We report three members of an Armenian family with Hajdu-Cheney syndrome. The history suggested that five other members of the family were also probably affected. This disorder is important for the radiologist because distinctive radiographic findings make the diagnosis possible before clinical signs and symptoms are fully developed. Additionally, radiographic examination is essential in all patients suspected of Hajdu-Cheney syndrome for confirmation of the clinical diagnosis. Radiographic examination also detects complications of the syndrome not evident on clinical examination.

Key words: *acroosteolysis; cranial suture; Hajdu-Cheney syndrome; Wormian bone*.

INTRODUCTION

There are over 50 congenital and acquired disorders characterized by osteolysis. In half of these conditions, osteolysis is limited exclusively or predominantly to the hands and feet (acroosteolysis). Although there are several bone dysplasias with acroosteolysis, in none of them is this a sign of such diagnostic significance as in the Hajdu-Cheney syndrome (HCS).[1–23]

We present the study of three members of an Armenian family with HCS who were examined by us. History suggested that five other members of the family were also probably affected (Fig. 1). If the researcher is familiar with the disorder, radiographic diagnosis of HCS is possible even before clinical diagnosis is made.

CASE REPORT

Patient 1

A 12-year-old boy was referred for consultation because of dysmorphic features (Fig. 2a). His phenotype is similar to that of his father in whom acroosteolysis was diagnosed at the age of 12 years.

The boy was born to a 19-year-old G2P2AO mother after a normal pregnancy and delivery. His birthweight was 3500 g (50th centile) and his height was 50 cm (50th centile). No abnormal findings were noted at birth. From a preschool age, he was noted to share some facial similarities with his father. This became more evident with advancing age. His only complaint was transient back pain. His motor and mental developments were normal.

At clinical examination, dysmorphic facial features were noted, including frontal bossing, prominent supra-orbital ridges, widely set antimongoloid eyes, flared anteverted nostrils and micrognathia. The eyebrows were bushy and his hair was coarse. Dentinogenesis imperfecta was noted. The fingers were short and there was mild clubbing of the first three fingers. There was a mild thoracic kyphosis and hyperlordosis of the lumbo-sacral spine. The height was 149 cm (25–50 centile) and weight was 40.5 kg (normal).

Radiographic examination documented widened lambdoid suture with multiple Wormian bones, basilar invagination and spondylolisthesis L5/S1. In the hands, there was transverse osteolysis of the distal phalanges of the second and third fingers

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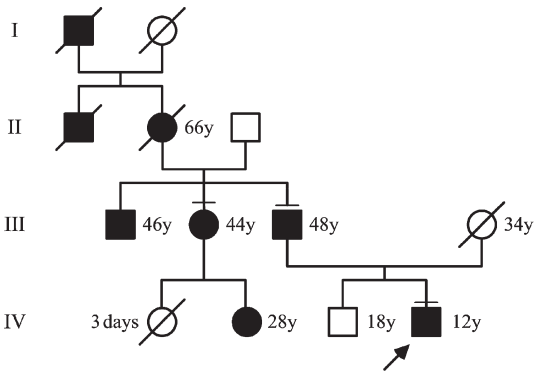

Fig. 1. Family pedigree of the patients with Hajdu-Cheney syndrome. Standard nomenclature used for the symbols. Roman numerals denote generation; y, years.

(Fig. 2b–d). Biochemical examination showed high markers of bone turnover.

Patient 2

The father of patient 1, aged 48 years, complained of feet and back pain. His height was 175 cm (50th centile) and his weight was 125 kg (>95th centile). His facial features were similar to that of his son. His hands were similarly, but more severely, affected than those of his son. He had lost almost all his teeth and had a dental prosthesis.

Radiographs documented acroosteolysis of the distal phalanges of fingers 1–3 with subluxation of the metacarpophalangeal joints of the first and second fingers. There were acroosteolysis of minor degree at the distal phalanges of the

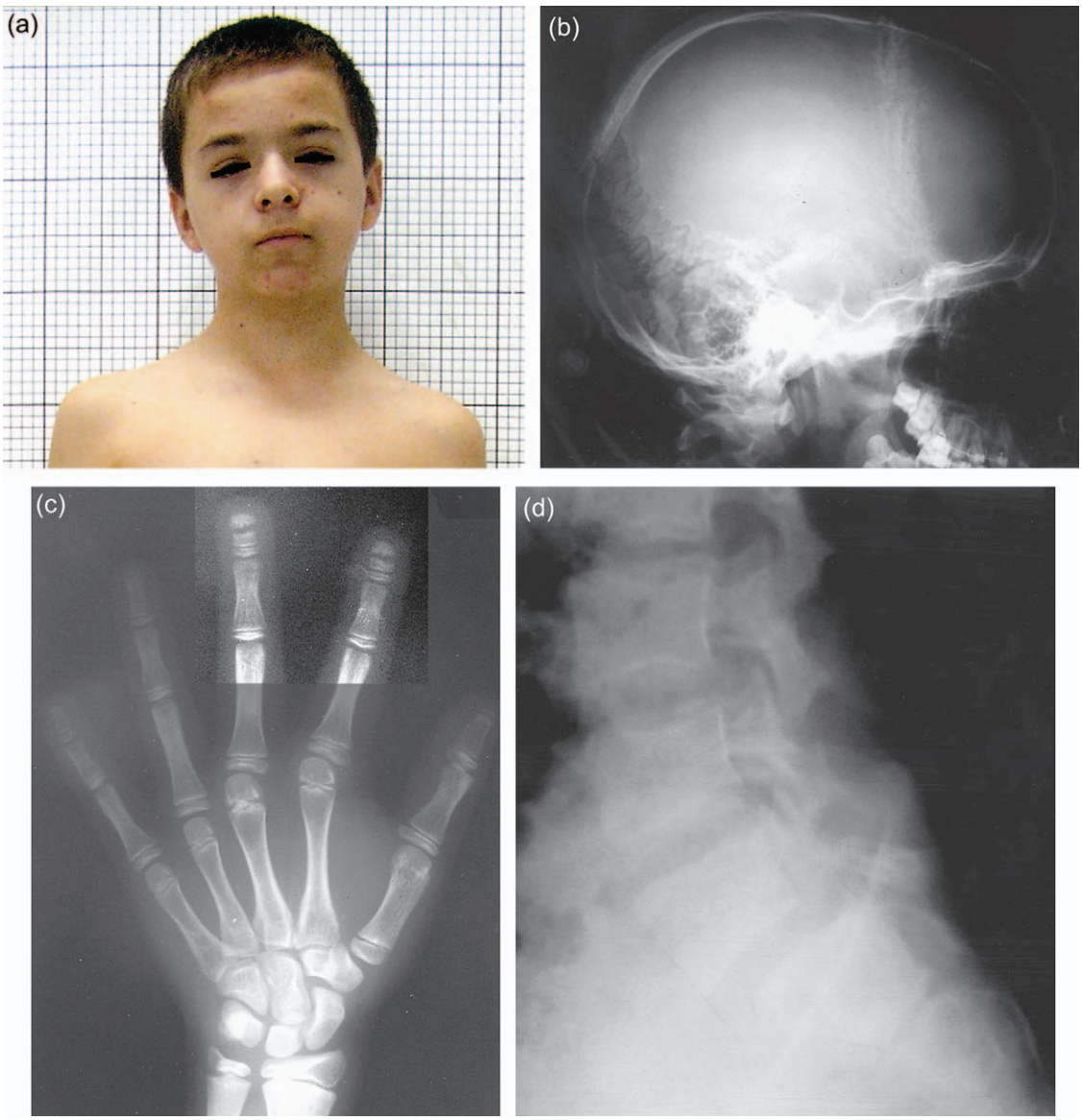

Fig. 2. Patient 1, 12-year-old proband. (a) Prominent forehead, coarse hair, bushy eyebrows, antimongoloid slant, flared anteverted nostrils, small mandible, (b) wide lambdoid suture with multiple Wormian bones, dentinogenesis imperfecta, (c) transverse osteolysis in the distal phalanges of the second and third fingers, and (d) spondylolisthesis L5/S1.

feet and at the fifth metacarpo-phalangeal joint. There was osteoporosis of the spine with compression fracture of the L2 vertebral body (Fig. 3).

Patient 3

The sister of patient 2, aged 44 years, complained of feet pain. Her height was 158 cm and her weight was 64 kg. Her phenotype was similar to that of patients 1 and 2. In the hands, only the second fingers were short with clubbing of the distal phalanx. She had lost all her teeth and had a dental prosthesis. Radiographs documented acroosteolysis of the distal phalanx of the second fingers. In the feet, there was osteolysis with subluxation at the first metatarso-phalangeal joints (Fig. 4).

Patients 4–8

We did not examine these individuals, but were told that all of them were short and had similar facial features to the members of the family we examined. We also saw the photographs of the hands of patient III/1 and patient IV/2 that showed distal shortening of the fingers, particularly at the second digit.

DISCUSSION

Hajdu-Cheney syndrome presents at birth with a dysmorphic, but not distinctive, diagnostic face. With advancing age, the characteristics of HCS became more evident. The diagnosis of HCS is usually made in teenagers[3,6,10,15,17–19] or adults.[5,9,11,14,16,21] Presence of affected relatives makes earlier diagnosis in the first decade of life possible.[2,8,12,22]

The distinctive clinical features of HCS consist of general features and facial dysmorphism. These features are suggestive or characteristic but not diagnostic of HCS. The former include short stature, short fingers with pseudoclubbing, hyperextensible joints, kyphosis, conductive hearing loss and speech impairment. The latter is characterized by frontal bossing, broad nose with flared nostrils, receding chin, bushy eyebrows, coarse thick hair and low-set ears with large ear lobules. Dentinogenesis imperfecta consists of premature loss of deciduous teeth with permanent absorption of alveolar processes, delayed eruption and premature loss of permanent teeth.[2,5,9]

Decisive for the diagnosis are two radiographic signs – acroosteolysis of variable degree of the distal phalanges of the hands and feet and wide cranial sutures, particularly the lambdoid suture with multiple Wormian bones. Acroosteolysis usually develops after the first few years of life and progresses through adulthood. Hypoplastic mandible and maxilla, dentinogenesis imperfecta, osteoporosis, basilar impression with ensuing complications, spondylolisthesis and fractures are less distinctive, supportive diagnostic features of the disorder.[1,13] Wide lambdoid suture with multiple Wormian bones is present at birth and persists after the first few years of life.

The radiographic differential diagnoses of HCS are the acroosteolytic syndromes and disorders with multiple Wormian bones. The mandibuloacral syndrome share similar skull and hand changes, but osteolytic changes in the former are more severe and include some other bones, particularly the clavicles.[2,3] Giaccai syndrome (a neurological condition with

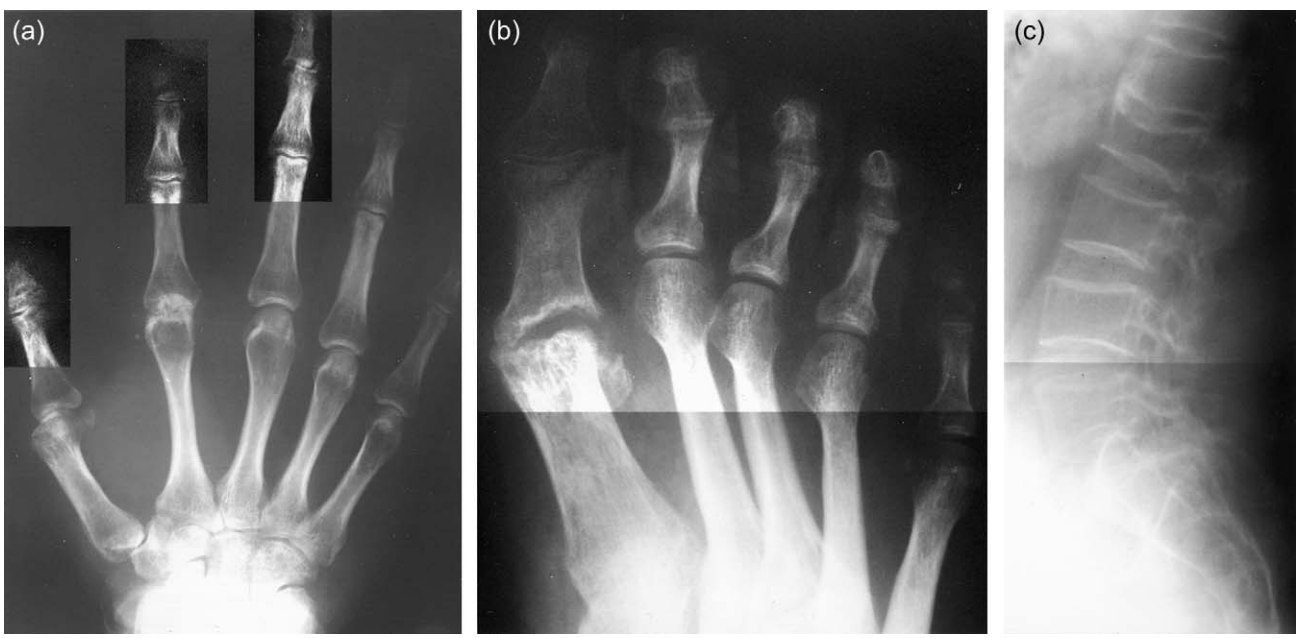

Fig. 3. Patient 2, father of patient 1. (a) Osteolysis at the proximal end of the distal phalanx of fingers 1–3. Subluxation at the proximal metacarpo-phalangeal joint of the first and second finger, (b) osteolysis at the first metatarso-phalangeal joint, (c) osteoporosis, post-traumatic flattening and deformity of L2 vertebral body.

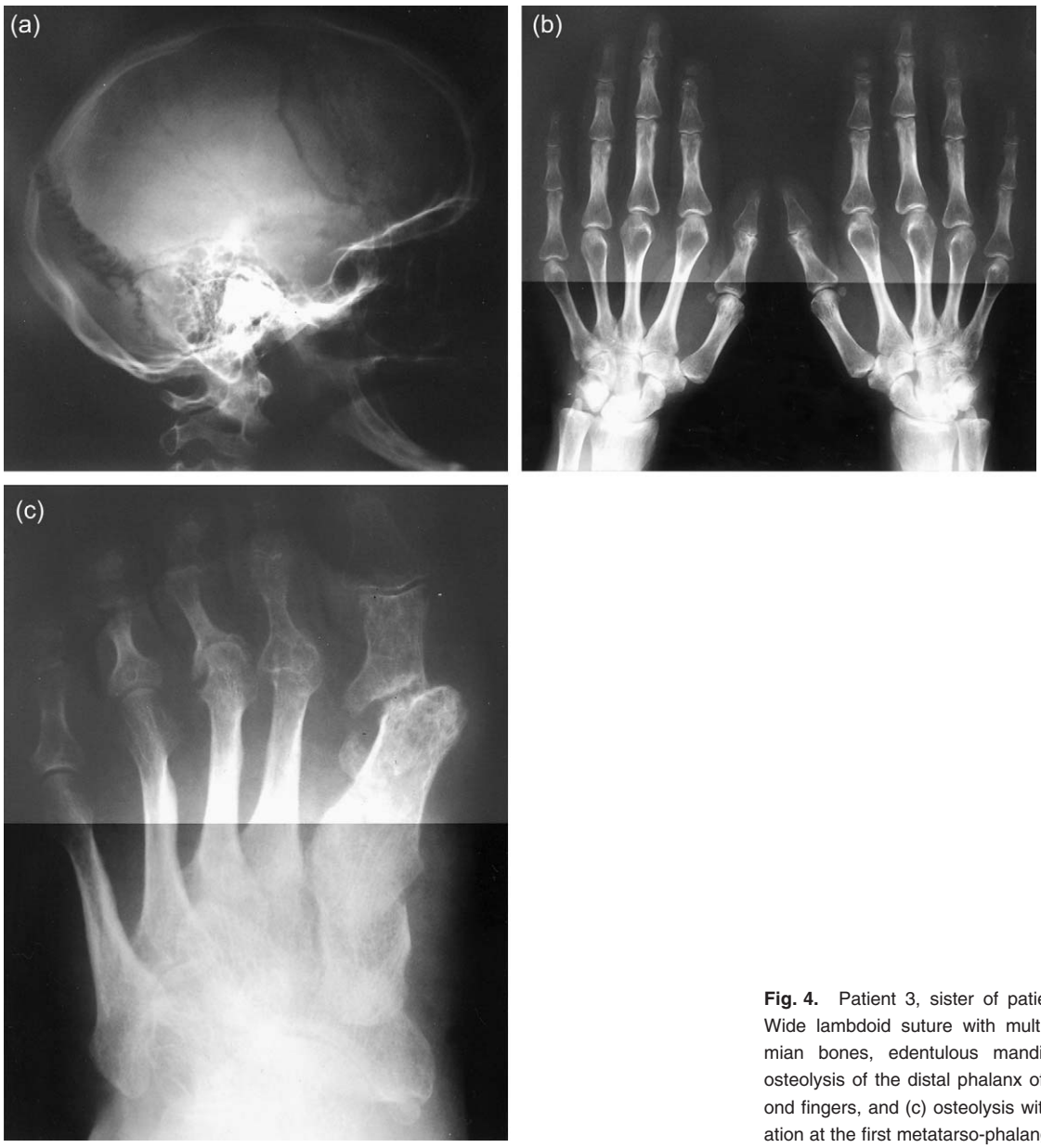

Fig. 4. Patient 3, sister of patient 2. (a) Wide lambdoid suture with multiple Wormian bones, edentulous mandibles, (b) osteolysis of the distal phalanx of the second fingers, and (c) osteolysis with subluxation at the first metatarso-phalangeal joint.

acroosteolysis) is associated with skin ulcerations. Some ill-defined acroosteolytic syndromes may show similar phalangeal changes, but usually without wide lambdoid suture and multiple Wormian bones. The pattern and severity of bone involvement varies from that of HCS. These ill-defined disorders may be the effect of partial penetration of the HCS gene or result of modifying genes. Until the molecular pathology of HCS is known, the correlation of these poorly differentiated acroosteolytic disorders to HCS is likely to remain unknown. Confusion with diseases with multiple Wormian bones, such as osteogenesis imperfecta, cleidocranial dysplasia, pycnodysostosis, hypothyroidism and rarer syndromes such as progeria or Rothmund–Thompson syndrome is highly unlikely in view of the other distinctive clinical (phenotype) and radiographic features characteristic of these conditions. The presence of thin bones, multiple fractures, 'German helmet' shape of the skull and blue sclerae in osteogenesis imperfecta; clavicular hypoplasia and large anterior fontanelle in cleidocranial dysplasia; osteosclerosis in pycnodysostosis; skin and eye changes in Rothmund–Thompson syndrome; and retarded bone age in hypothyroidism make confusion of these conditions with HCS unlikely.

Hajdu-Cheney syndrome is a rare autosomal dominant condition with approximately 50 cases published to date. The chromosomal location and molecular basis of HCS is unknown.

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