Case Report

Periodontitis Associated With Hajdu-Cheney Syndrome

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Background: Hajdu-Cheney syndrome (HCS) is an inheritable, rare disorder of bone metabolism, associated with acro-osteolysis of the distal phalanges, short stature, distinctive craniofacial and skull changes, premature tooth loss, and periodontitis. This report focuses on the periodontal manifestations of HCS.

Methods: A 22-year-old female presented with the characteristic clinical features of HCS, including short stature, small face, prominent epicanthal folds, thin lips, small mouth, and short hands. There were no abnormal biochemical, hematological, or hormonal data. Tests for bone mineral density were indicative of osteoporosis. Cephalometric analysis revealed hypoplasia of the midface and increased cranial base angle; the maxilla and the mandible were set posteriorly. The sella turcica was enlarged, elongated, and wide open with slender clinoids. Hair samples were examined by scanning electron microscopy, and tooth cementum and dentin were evaluated histologically.

Results: According to the periodontal evaluation, gingival inflammation was 12.5%, bleeding on probing score was 24%, probing depths averaged 4 to 6 mm, and clinical attachment loss averaged 3 to 6 mm. Class II furcations were found on three teeth. Almost all teeth exhibited pathological mobility of varying degrees. There was a generalized, horizontal bone loss of ~50%. Three teeth had to be extracted because of severe localized periodontal destruction. Histologic examination of the dentin and the cementum was normal.

Conclusions: HCS periodontitis is associated with an unpredictable and uneven, rapid rate of periodontal destruction of unknown etiology. Further research is required to identify the role of the possible pathogenic factors involved. J Periodontol 2007;78:1831-1838.

KEY WORDS
Diagnosis; disease progression; Hajdu-Cheney syndrome; pathogenesis; periodontitis.

Hajdu-Cheney syndrome (HCS), or acro-osteolysis, is an inheritable rare disorder of bone metabolism characterized by spinal, cranial, and facial bone abnormalities accompanied by progressive resorption of the distal phalangian bones.1,2 Synonyms of the syndrome include athro-dento-osteodysplasia,3 cranio-skeletal dysplasia with acro-osteolysis,4 hereditary osteodysplasia with acro-osteolysis,5 and acro-osteolysis with osteoporosis in skull and mandible.6 The most likely mode of transmission is autosomal dominant, although many cases are sporadic presentations.7,8

The main clinical features of HCS include short stature, scoliosis and kyphosis, elongation of the skull, small chin, clubbing of the fingers, coarse hair, and thick eyebrows.5,7 Radiographically, the most frequent findings are enlarged sella turcica, wormian bones, persistent wide cranial sutures, absence of the frontal and maxillary sinuses, and osteolysis of the distal phalanges.7 In some cases, progressive platybasia can occur and can lead to Chiari malformation with an obstruction of cerebrospinal fluid flow and cervicothoracic syringomyelia.9,10 Associated neurologic abnormalities, such as optic nerve head swelling and mild optic neuropathy, are often the result of progressive basilar invagination.11

Oral and dental manifestations of HCS include premature exfoliation of teeth,1,5 dental maleruption and malocclusion,7 increased tooth mobility,12,13 impaction of teeth,2,4 hypoplastic dental roots,3 atrophy of the alveolar processes,2,4 and structural changes in the dentin and cementum of teeth.14 Periodontal manifestations of HCS were documented first in the literature in 19847 and include rapidly progressive periodontitis, insufficient attached gingiva, and secondary occlusal trauma. With respect to bone morphology in HCS, studies showed a diminished bone density and bone formation, whereas the osteoblasts are characterized by widely dilated smooth endoplasmic reticulum.15 According to one theory, the disordered bone metabolism is attributed to an abnormality of a structural protein.16

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This report presents the clinical, radiographic, and laboratory findings and assesses the periodontal status of a young female patient with HCS. The possible pathogenic mechanisms involved in HCS periodontitis and its therapeutic approach are discussed.

**CASE REPORT**

In 2003, a 22-year-old female was referred to the Department of Periodontology by the Department of Oral Pathology and Surgery at the School of Dentistry, University of Athens, with the diagnosis of HCS. According to the patient’s medical history, she was born to young, unrelated parents (mother 22 years of age; father 28 years of age) after uncomplicated 37 weeks of gestation. Birth weight was 3,400 kg (90th percentile), length was 50 cm (75th percentile), and occipitofrontal head circumference (OFC) was 33 cm (50th percentile). Growth curves for the first year of her life were available for length, weight, and head circumference and were found to be within normal limits. Concern about her short stature started at 8 years of age; however, all tests in an evaluation were normal, including an endocrine work-up. Her mother and her 18-year-old brother have normal dentitions and exhibit no signs of periodontal disease. The patient’s 50-year-old father has mobile teeth due to chronic advanced periodontitis. Her paternal grandfather and maternal grandfather and grandmother had lost all their natural teeth by the age of 40 years.

The patient’s medical history revealed emphysema and allergic rhinitis. Vitamin D and calcium were administered by mouth daily for the treatment of osteoporosis.

According to the patient’s dental history, she had undergone orthodontic treatment for a period of 9 years between the ages of 12 and 21 years. During the course of the treatment, at the age of 13 years, the patient had all of her four first premolars removed. At the age of 20 years, the patient received periodontal treatment, which included instruction in personal oral hygiene, scaling and non-surgical root surface debridement, and limited periodontal surgery of the lower anterior region. Unfortunately, detailed records of the nature and the extent of the applied surgical procedure were not available.

The patient was a non-smoker, visited her dentist every 6 months, brushed her teeth twice every day (Bass technique), and used dental floss and interdental cleaning devices (brushes).

**Physical Examination**

On physical examination, the patient’s height was 145 cm (7 cm <5th percentile), her weight was 45 kg (10th percentile), the upper/lower segment ratio was 0.95, OFC was 54 cm (50th percentile), and the cranial index score was 80.555 (mesocephaly). She had thick coarse hair, low-set ears with a prominent crease in both lower lobes, small face, prominent epicanthal fold on the right side, thin lips, small mouth (Fig. 1), and short hands with clubbing of the fingertips (Fig. 2).
Laboratory Investigation

All biochemical (sodium, potassium, calcium [Ca], magnesium, Ca/creatinine, and Ca urine), hematological, and hormonal (triiodothyronine, thyroxine, thyrotropin, parathyroid hormone, calcitonine, and osteocalcine) tests carried out upon presentation were within normal limits.

The results from the scan test for bone mineral density (BMD) showed that the femoral neck BMD measured 0.674 g/cm², the young adult femoral neck percentage was 69% (Z score = 2.55), and the age-matched neck percentage was 70% (Z score = 2.40). These were indicative of osteoporosis and established the diagnosis of the disorder for the patient.

Low-vacuum scanning electron microscopy (LV-SEM) images of the patient’s hair revealed random striations and a disorganized morphologic appearance compared to samples taken from a healthy individual of the same age (22 years) who was used as a control (Fig. 3). No marked differences were seen in hair thickness between the test and the control specimens (Fig. 3).

The lower left central incisor (tooth #24), which exhibited extensive periodontal destruction and had to be extracted, was processed for light microscopy. Immediately after extraction, it was fixed in a 10% buffered formaldehyde solution, followed by decalcification in EDTA for approximately 3 weeks; finally, it was embedded in paraffin. Hematoxylin and eosin–stained tissue sections of 5-μm thickness showed normal morphology of dental pulp, dentin, and cementum (Fig. 4). Because of the decalcification process, enamel was not available for observation.

Radiographs

The findings from radiographs included a number of significant findings. Hand–wrist radiographs demonstrated the typical picture observed in HCS, i.e., osteolysis of the distal phalanges (second and third right and first and second left) and clinodactyly of the fifth left finger (Fig. 5). Skeletal radiographs showed horizontal radiopaque lines beneath the epiphysis of the sacrum, exaggerated lordosis of the lumbar spine and

Figure 3. LV-SEM of control (A) and test (patient’s) (B) hair samples. The test sample shows random striations (arrows) and has a more disorganized morphologic appearance compared to control. No marked differences are evident in the hair samples thickness. (Original magnification x1,000.)

Figure 4. Histologic section of extracted tooth #24 showing normal morphology of radicular dentin and cementum. (Hematoxylin and eosin; original magnification x400.)
slight right scoliosis of the lower part of the lumbar spine, sacralization of L5, and markedly reduced bone density (Fig. 6).

The lateral view of the skull demonstrated brachycephaly, wormian bones in lambdoid suture, failure of ossification of the coronal suture, and basilar invagination. Cephalometric analysis revealed hypoplasia of the midface anteroposteriorly and vertically (Fig. 7). The maxilla and the mandible were set posteriorly, although their relation was within normal limits. The cranial base was increased (measurement of two SDs). The sella turcica was enlarged, elongated, and wide open with slender clinoids (Fig. 7).

**Oral Examination**

The patient’s dentition consisted of 24 erupted teeth. Five teeth (#5, #12, #16, #21, and #28) were missing, and three wisdom teeth (#1, #17, and #32) were impacted as shown radiographically (Fig. 8).

In the upper arch, most teeth exhibited pathological mobility. Biting stress mobility (fremitus) was present in teeth #7, #8, #9, and #10. Tooth #4 had a mobility degree of 3, with depressibility; teeth #6 and #14 had a mobility degree of 2; and teeth #2, #3, and #11 had a mobility degree of 1. Tooth #7 also exhibited external cervical resorption. Carious lesions were detected on tooth #2.

In the lower arch, both canines and bilateral incisors were splinted through a temporary construction of composite resin, which had been placed by her dentist 2 years ago, to stabilize them. The lower teeth also exhibited pathological mobility, ranging from degree 1 (#22, #23, #24, #25, #26, #27, and #29), to degree 2 (#20 and #30). Tooth #26 exhibited external cervical resorption and had been detached from the splinting. Carious lesions were detected on teeth #19 and #30, with the latter exhibiting supereruption.

**Periodontal Evaluation**

According to the periodontal evaluation, the patient exhibited good oral hygiene, with a plaque index\(^\text{17}\) of 25% (Table 1). Her ability to clean her teeth was compromised by the presence of the temporary splinting because of its excessive thickness and almost complete closure of the interdental spaces, thereby limiting the efficient use of the interdental cleaning devices. In general, the gingiva was mildly inflamed, with a gingival index\(^\text{18}\) of 12.5%. It also exhibited a smooth texture and soft consistency (Fig. 9). Bleeding in response to probing to the bottom of the pocket was scored at 24% (Table 1).

Probing depths averaged 4 to 6 mm, with extremes of 7 to 10 mm at teeth #2, #4, and #14 (Fig. 10). Clinical attachment level (CAL) measurements averaged 3 to 6 mm, with extremes of 7 mm (#14, #24, and #30) to 10 mm (#4) (Fig. 10). A Class I furcation was noted.
on tooth #3. Class II furcations were noted on teeth #13, #19, and #30. Probing measurements were performed by a single calibrated examiner at six aspects of each tooth (mesio-buccal, mid-buccal, disto-buccal, mesio-lingual, mid-lingual, and disto-lingual) using a straight graded periodontal probe and rounded off to the nearest millimeter. The cemento-enamel junction was used as a reference for the CAL measurements. Assessment of the horizontal attachment levels at each furcation was made with a color-coded, calibrated Nabers probe, marked at 3-mm intervals.

Evaluation of the panoramic and periapical radiographs revealed a number of significant findings (Figs. 8 and 11). There was a generalized horizontal bone loss of ~50%. However, alveolar bone loss around teeth #4 and #14 was extensive, reaching almost 100%. The crown/root ratio of most teeth averaged 1:1, although it was unfavorable in some teeth (teeth #4, #6, #7, #8, #14, #19, #24, and #30). In general, tooth roots appeared short and conical in shape; these features were more pronounced in all four first molars (Fig. 11). Cervical resorption lesions also were evident (teeth #3, #7, and #26). The periodontal ligament space generally was widened, especially at teeth #6 and #20, whereas the radicular lamina dura generally was absent.

DISCUSSION
Approximately 58 cases of HCS have been published. Our patient manifests most of the characteristic features of HCS.

Table 1.
Clinical Parameters at Initial Examination

<table>
<thead>
<tr>
<th>Sites (N)</th>
<th>Plaque Index (%)</th>
<th>Gingival Index (%)</th>
<th>Bleeding on Probing (%)</th>
<th>Probing Depth (mm)</th>
<th>Clinical Attachment (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>144</td>
<td>25</td>
<td>12.5</td>
<td>24</td>
<td>4-6</td>
<td>3-6</td>
</tr>
</tbody>
</table>

1 PCP-15, Hu-Friedy, Chicago, IL.
# PQ2N, Hu-Friedy.
hematological, or hormonal tests probably indicates that the osteoporosis was idiopathic.

Of special interest are the results of the microscopic (LV-SEM) examination of the patient’s hair samples. There were no marked differences in thickness between the patient’s (test) and healthy (control) hair specimens. However, the test samples had a more disorganized morphologic appearance, with random striations, compared to the control samples. To our knowledge, this test has not been done before.

Histologic evaluation of the dental tissues of the extracted mandibular incisor showed normal morphology of the dental pulp, the dentin, and the cementum. Our findings contradicted those of Grant et al., who described dentin with a globular arrangement and a scalloped and undulating border forming on the walls of the pulp cavity and the absence of normal secondary cementum from the root surface.

The etiology of HCS is genetic. Our case is sporadic, probably indicating that it represents a new mutation.

The periodontal and general dental management of patients with HCS poses a difficult task for the clinician because of the pathology of the disease itself and the compromised ability of the host for regeneration. Information regarding the treatment of HCS periodontitis has been scarce in the dental literature, mainly because of the rarity of the syndrome.

It is known that periodontal treatment applied at early stages of adult life can be effective in halting disease progression in rapidly progressing types of periodontitis, thus minimizing the chances of premature tooth loss. This was confirmed in the present case, with the periodontal treatment put into effect at the age of 20 years. Although the average clinical measurements and radiographic evaluation were indicative of a periodontitis of moderate severity, certain sites exhibited extensive loss of periodontal support, leading to the subsequent loss of the respective teeth. This pattern of localized destruction is associated commonly with rapidly progressing periodontitis (especially the early-onset types) and may be attributed to a variety of factors.
of etiological and/or contributing factors, including dental abnormalities.

Site-specific factors, such as orthodontic forces and hypoplastic tooth roots, may be the major determinant of the initial outcomes of treatment in severe periodontitis.27 Orthodontic therapy in patients with HCS may be contraindicated by the severe mobility and the short roots of the teeth, as well as the unpredictable bone response to orthodontic forces.7 However, in the present case, the application of mild orthodontic forces for a long period of time was tolerated well by the dentition. This favorable response may be attributed to the ability of the periodontal tissues to adapt to the structural and functional demands, providing that inflammation is well controlled. Furthermore, successful orthodontic movements of periodontally affected teeth in children28,29 and, more recently, in a case of Papillon-Lefèvre syndrome30 have been documented in the literature.

Our patient was placed on a strict maintenance protocol, with recall visits every 3 months, to maintain periodontal health on a long-term basis. Furthermore, the introduction of such a scheme is a prerequisite for the successful prosthetic rehabilitation (conventional or implant-based) of the patient in the future.

CONCLUSIONS

The present case represents a typical case of HCS: osteoporosis, acro-osteolysis of the distal phalanges, distinctive craniofacial and skull changes, proportionate short stature, periodontitis with a rapid rate of progression, tooth mobility, and hypoplasia of the roots.

Although the etiology of the syndrome remains obscure, it becomes evident that diagnosis of the disorder in the early stages of life may contribute significantly toward the management of osteoporosis and periodontal disease. Efficacious control of inflammation of the periodontium, combined with mild orthodontic and/or occlusal adjustment interventions and a strict long-term maintenance program, may be the keys to preventing further periodontal and tooth loss.

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