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HYPERBRACHYCEPHALY, SHORT FACE, MIDFACE HYPOPLASIA, FUSION OF CERVICAL VERTEBRAE, RADIOLUCENT BONE DEFECTS, AND SEVERE DESTRUCTION OF PERIODONTIUM – A NEW SYNDROME: CRANIOFACIOCERVICAL OSTEOGLYPHIC DYSPLASIA

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Summary: *Hyperbrachycephaly, short face, midface hypoplasia, fusion of cervical vertebrae, radiolucent bone defects, and severe destruction of periodontium – A new syndrome: Craniofaciocervical osteoglyphic dysplasia:* A patient with an unusual combination of findings, which do not fit in any of the known syndromes, is presented. The patient, a 24.5-year-old male of normal growth and intelligence, manifests craniofacial dysmorphism, radiolucencies in the skull and in the cervical vertebrae, progressive alveolar bone loss and fusion of cervical vertebrae. The young man does not exhibit any other systemic, hematological, biochemical, chromosomal or immunological abnormality, except for IgA deficiency.

Key-words: Craniofacial dysmorphism – skull and vertebral radiolucencies – fusion of cervical vertebrae – alveolar bone loss.

Résumé: *Hyperbrachycéphalie, hypoplasie midfaciale, fusion des vertèbres cervicaux, zones radiolucentes osseuses, et destruction périodontale sévère – Un nouveau syndrome: la dysplasie craniofaciocervicale ostéoglyphique:* Dans cet article, nous rapportons un malade avec un tableau clinique qui ne cadre guère dans un syndrome connu. Le patient, un homme âgé de 24.5 ans, avec un développement mental et corporel normal, présente une dysharmonie craniofaciale, des zones radiolucentes osseuses dans le crâne et les vertèbres cervicales, une perte progressive de l'os alvéolaire et une fusion des vertèbres cervicales. Le patient ne présente aucun autre signe systémique, hématologique, biochémique, chromosomique et immunologique sauf une déficience IgA.

Mots-clés: Déficience craniofaciale – Anomalies osseuses – Fusion cervicale – Destruction alvéolaire.

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INTRODUCTION

In every day practice, the clinical geneticist very often encounters with cases difficult to diagnose, a number of which may represent unknown entities. In such cases, a very careful, detailed and laborious investigation is needed, in order an entity to become delineated and characterized as a new one. A sporadic case with unusual combination of findings which does not fit to any of the known syndromes is presented in this paper. In addition to the phenotypic spectrum, data of the natural history of this unknown syn-

drome are provided, in order to become delineated.

CASE REPORT

A 24 5/12-year-old male was referred for genetic evaluation to the Department of Oral Pathology and Surgery because of severe periodontitis and unusual facies.

History

The patient was born to young (mother 22- and father 26-year-old), apparently normal, non-consanguineous parents after an uneventful, full-term pregnancy with no exposure to radiation or any unusual agent, and weighed 3.500 gr at birth. His growth and developmental milestones were reportedly normal. At 6 years of age the mobility of the neck started being restricted. The dysfunction was diagnosed as «torticolis», and an orthopedic cervical collar was used for treatment for a period of three months. When he was 8-year-old he fell off a balcony and sustained multiple injuries including fractures of the skull and lower limbs. A year later he started suffering recurrent episodes of meningitis and cerebrospinal fluid rhinorrhea, surgically treated at the age of 14 6/12 through frontal bone craniotomy with covering of the expected fracture of the anterior cranial fossa with muscle and fascia lata grafts and, finally, at the age of 16 1/12 with muscle graft in the ethmoid sinus, through an incision at the inner canthus of the right eye. During the first operation he was given a blood transfusion. At the age of 10 the mandibular incisors started presenting clinical mobility and were spontaneously exfoliated after five years. By the age of 23 he had generalized destruction of the periodontium, and lucent intrabone lesions in the cranium, face and cervical vertebrae, fusion of cervical vertebrae and restriction of neck mobility. Lateral and P.A. chest radiographs at the ages of 14 7/12, 15 7/12, 16, and 23 3/12 were normal. Brain tomography (22 11/12 y.o.) disclosed no pathologic findings of the brain, but multiple healed fractures of the frontal and parietal bones, a small defect of the squamous portion of the left temporal bone and of the left inner plate of the occipital bone, but no lysis of the cerebellar tissue.

Histologic reports on biopsy specimens taken from the body and the ramus of the mandible at age 23 3/12 concluded that there were lesions of a non-specific chronic active inflammation. Histiocytosis X, myeloma and giant cell lesion were ruled out.

Repeated laboratory testing of the patient about the age of 23 showed normal values and morphology for red and white blood cells, calcium, phosphorus and alkaline phosphatase. Test for Bence-Jones protein in the urine was negative. Tests for bone metabolism and parathyroid hormone disclosed no pathologic findings.

Since the age of 22 he has had repeated infections (3-4 times per year) of the frontal sinuses.

At age 25 4/12 he manifested symptoms of intracranial pressure due to brain abscess of the right frontal lobe. He was subjected to an operation of stereotaxic suction of the abscess with good postoperative course. Since then he takes phenytoin 200 mg per day.

Physical examination

On physical examination on first admission, his height was 170 cm (U/L segment: 1.07) and weight 77 kg. He had (Fig. 1 and 2) eurycephaly (H.C. 53 cm, 10th P., H.W. 15.9 cm, >2 SD, H.L. 17.1 cm < 2 SD), hyperbrachycephaly (C.I.: 93.52), low anterior and posterior hairline, protruded supraorbital ridge, deeply set eyes, normotelorism (I.P. distance 63 mm 90th P.), short, slightly asymmetric, face with hypoplastic maxilla and malar bones (narrow upper face), short filtrum, protruded nose, microstomia with narrow upper lip,

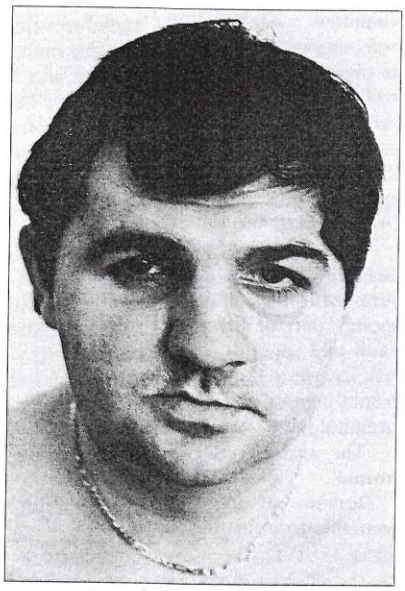

Figure 1: Face of patient with eurycephaly, slight facial asymmetry, short philtrum, microstomia, thin upper lip.

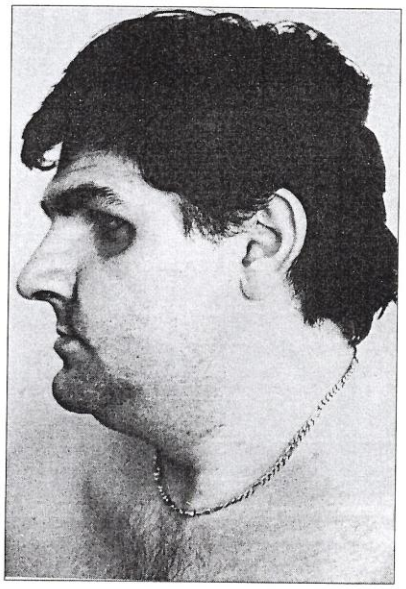

Figure 2: Lateral view of head and neck. Protruding supraorbital ridge, prominent nose, deeply set eyes, hypoplastic maxilla and malar bone, prognathic mandible, brachycephaly, low anterior and posterior hairline, short and thick neck.

a short, thick, with severely restricted (flexion, extension, lateral, circular) mobility neck, limitation of head movement, frontal and lateral cross-bite, flat palate, wide tongue, malaligned left upper second premolar, and advanced tooth mobility with non-significant plaque accumulation, minimum bleeding on probing and non-contributory calculus formation. Sense of touch of the lower lip was normal.

No abnormality was found in any of the rest anatomic regions and organ systems of his body. His intelligence was normal.

X-ray studies

Examination of a skull and cervical spine lateral radiograph, done at the age of 23 3/12 (Fig. 3), showed wide frontal sinus, deep sella turcica, multiple well-defined radiolucencies in the occipital bone, few in the parietal bone and quite a few along the craniotomy line of the frontal bone, a focal defect of the inner table of the occipital bone, concave profile with severely hypoplastic maxilla, fusion of the vertebra C1 to the occipital bone (atlanto-occipital joint), fusion of the bodies of vertebrae C1 to C4, radiolucencies in the spinous processes of the C1 to the C6 vertebrae, partial fusion of the spinous processes of the C2, C3, C4, fusion of those of the C5-C6 vertebrae, and fusion of the C1 to the C6 glinding joints. The bodies of the C5 and C6 were characteristically small, the lower of the C5 and upper back corner of the C6 were missing, and the intervertebral disk space was narrow. The mobility of the neck seemed feasible at the level of the C6-C7 vertebrae. Skull and cervical spine lateral radiograph, done

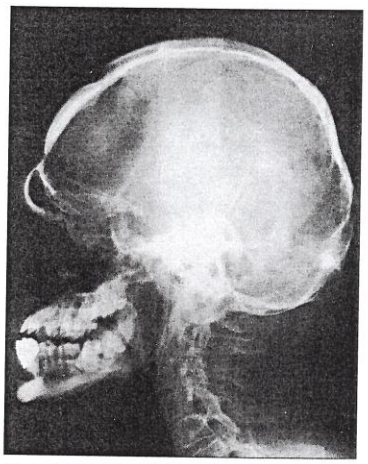

Figure 3: Lateral cephalometric radiograph of the patient. Brachycephaly, short anterior and posterior cranial base, concave profile, short facial height, multiple radiolucencies in occiput, along the frontal craniotomy line and spinous vertebral processes, fusion of superior vertebrae.

at the age of 25 9/12 showed no noticeable changes from that of age 23 3/12.

Panoramic radiograph at age 23 3/12 (Fig. 4) showed destruction of the periodontium, characterized by generalized, horizontal, advanced (more than 75 per cent), alveolar bone loss with floating mandibular right molars and root proximity in the upper dental arch, small condyle, absence of coronoid process, antegonial notching, rounded mandibular angle, impacted third molars, and flattened dental radicular apexes; extended radiolucencies with well-defined borders in both right and left mandibular ramus and maxillary tubercles.

Panoramic radiograph at age 25 9/12 (Fig. 5) showed that during the 2.5 year meantime the maxillary incisors and mandibular right molars were lost (spontaneously exfoliated), while the remaining alveolar bone seemed to be stabilized somehow. Multilocular radiolucencies were shown in the right mandibular ramus in the same region, where there was a well-defined unilocular radiolucency before (Fig. 4). Shortly after the previous panoramic radiograph was done, the patient had his third right mandibular molar extracted and a biopsy specimen taken from the close intrabone lucent lesion.

CT-scanning (25 10/12 y.o.) of the head revealed extended lesions with severe disturbance of the architecture of the spongy part of the bones of the cranial vault and superior vertebrae, also osteolytic lesions in the cranial base and the left frontal region, and fusion of the antlanto-occipital joint.

The rest skeletal X-ray survey was normal.

Review of informative radiographs available from his file showed that at the age of 13 10/12 (Fig. 6 and Fig. 7) extended radiolucencies in both mandibular ramis were already present and alveolar bone loss was evident in the mandibular incisor and molar area (Fig. 6), as well as multiple well-defined radiolucencies in the occiput, few scattered in the rest cranial vault and in the spinous processes of the first two cervical vertebrae (Fig. 7). Part of the coronal suture was illustrated, and the rest was completely fused.

At age 14 5/12 the bodies of the C1 and C2 were already fused, the upper articular surface of the C3 was irregular, and

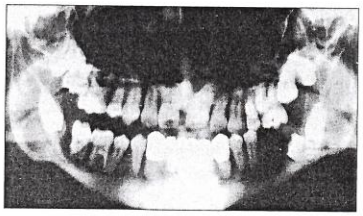

Figure 4: Panoramic radiography of the patient at age 23 3/12. Extended well-defined radiolucencies in mandibular rami and maxillary tubercles, severe, generalized, horizontal alveolar bone loss.

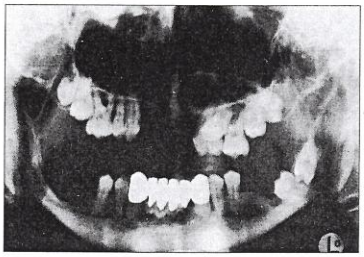

Figure 5: Panoramic radiography of the patient at age 25 9/12. Multilocular radiolucencies in the right ramus after extraction of impacted third molar and biopsy. Stabilization of alveolar bone destruction after exfoliation of mandibular right molars.

the mandibular incisors were still in place. At age 15 2/12 the mandibular incisors were already lost and he weared a bridge; the destruction of the alveolar bone had progressed; the spinous processes of the C3 and C4 were almost fused; there was olisthesis to the front of C4 vertebra.

At age 15 6/12 extended radiolucencies in both mandibular rami were well-defined and horizontal destruction in the molar area of the alveolar bone was clearly shown; the radiolucencies in the spinous processes of the C1 to the C5 vertebrae were clearly shown; there was fusion of the bodies of C1-C2 and C3-C4; the articular space of the gliding joints of the C1 to the C4 had disappeared, but it was illustrated in those of the C4 to the C7. At age 15 7/12 the C1 to C4 vertebrae

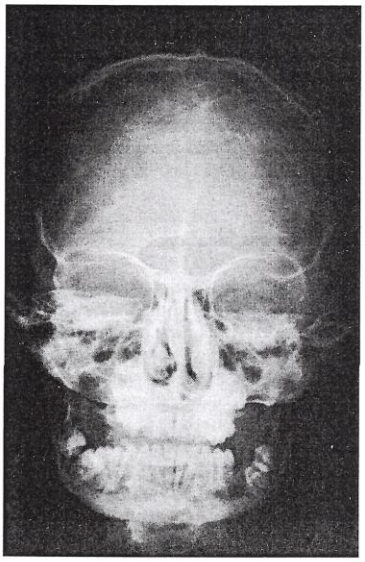

Figure 6: P.A radiography of patient's skull at age 13 10/12. Extended radiolucencies in both mandibular rami and alveolar bone loss evident in the mandibular incisor and molar area.

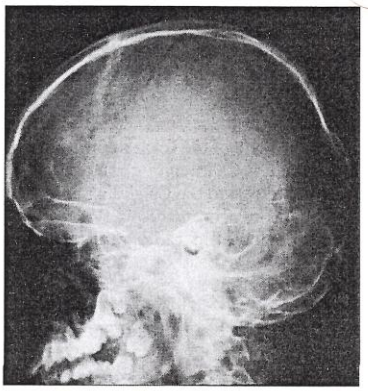

Figure 7: Lateral radiography of patient's skull at age 13 10/12. Multiple well-defined radiolucencies in occiput, few scattered in rest cranial vault and in spinous processes of first two cervical vertebrae. Part of the coronal suture is illustrated, and the rest is completely fused.

were fused; there were radiolucencies in the lower of the C5 and in the upper back corner of the C6 vertebral bodies. A consecutive radiograph (exact age unknown) showed destruction of the lower back cor-

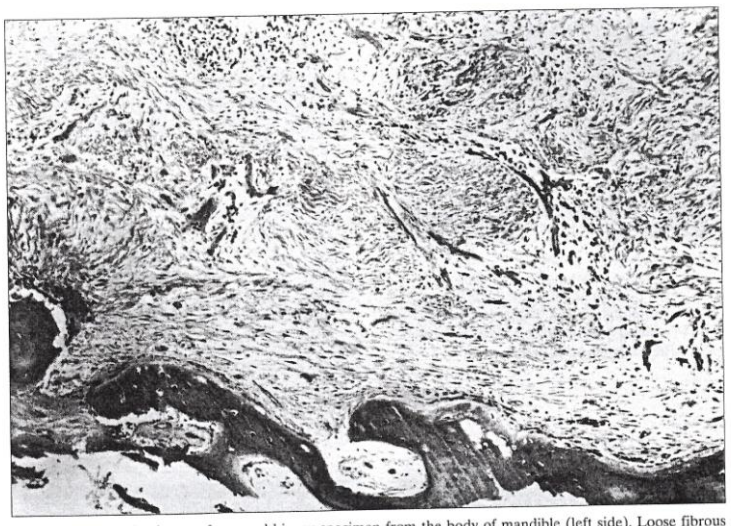

Figure 8: Histologic picture of mucosal biopsy specimen from the body of mandible (left side). Loose fibrous connective tissue with focal, perivascular inflammatory infiltration. Notice immature bone trabeculae with osteoid and osteoblastic rimming (hematoxylin and eosin, x25).

ner of the body of the C5 vertebra, narrowing of the C4- C5 intervertebral disc space, fusion of the C4 to the C6 gliding points.

Cranial measurements on P.A. and lateral cephalometric radiographs (fig. 3) were as follows: head breadth (14 y.o.) 17 cm (4.89 SD), head length (23 y.o.) 16.4 cm (-4.36 SD), head height (23 y.o.) 14 cm (2.72 SD), forehead height (23 y.o.) 9.5 cm (-3 SD).

Cephalometrics (Fig. 3) revealed: severely short anterior (72.6 mm, -2.8 SD) and posterior (38 mm, -3.0 SD) cranial base; moderately short saddle angle (116 dg, -2.0 SD); extremely short maxilla (maxillary length 44.2 mm, -4.7 SD); mandible mild prognathic to the forehead (facial angle [PN-FH]: 97.6 dg, 1.4SD); severely concave skeletal profile (convexity 180-[NAP]: -28.5 dg, -5.7 SD); severely short upper facial height (47.7 mm, -3.1 SD); overclosure pattern (mandible Y-axis: 46.7 dg, -2.1 SD, mandibular plane: 11.4 dg, -1.8 SD); short lower facial height (upper FH/lower FH: 45.5%).

Histologic examination

The histologic sections of biopsy specimens taken at the age of 23 3/12 from the body of the left mandible (Fig. 8), superficial cortical bone of anterior edge of the right ramus, and deeply situated cortical bone and osteolytic lesion of the right mandible from the vicinity of an impacted third molar, presented similar microscopic findings. They consisted of mostly hypocellular fibrous connective tissue with limited cellular areas presenting prominent fibroblasts, that were diffusely infiltrated by chronic inflammatory cells. A few immature and hypocalcified bone trabeculae were also identified. They presented osteocytes in well-defined lacunae, focal rimming by flattened osteoblasts, as well as a

few osteolytic lacunae. No osteoclast, however, was identified. Specimens from the osteolytic lesion of the right mandible showed, in addition, bundles of striated muscle fibers.

Laboratory investigation

Hematological testing of the patient showed normal values and morphology for red and white blood cells, calcium, phosphorus and alkaline phosphatase. Test for Bence-Jones protein in the urine was negative. Tests for bone metabolism and parathyroid hormone disclosed no pathologic findings. Urinary mucopolysaccharide excretion and excretion pattern on one dimensional electrophoresis were normal. Serum lysosomal hydrolases, a-manosidase and b-manosidase were within usual limits.

Tests for both cellular and humoral immunity gave normal values except for **very low IgA** (<5 mg/dl, n.v. 70-230), slightly **elevated IgG** (2.650 mg/dl, n.v. 900-1900) due to **increased IgG1** (1.860 mg/dl, n.v. for adults: 422-1292 mg/dl), and **slightly increased IgE** (258 Ku/l, n.v.: 2-195 Ku/l).

Intradermal test for aspergillosis was negative.

Cytogenetic studies

G-banded chromosome analysis revealed a normal male karyotype (46,XY).

The mean number of sister chromatid exchanges (SCE) in cultured peripheral lymphocytes of the patient was 5.63 per cell (normal values: 5.0 to 11.6 SCE per cell). The proliferation rate index (PRI) of cultured peripheral lymphocytes of the patient was 2.0 (186 cells studied), while it was 1.3 of the control (259 cells studied). Normal values of the laboratory range between 1.2-2.5.

The percentage of lymphocytes in three consecutive divisions in the patient were: 1st 42.5, 2nd 16.1, 3rd 41.4. In the control it was: 1st 77.2, 2nd 12.0, 3rd 10.8.

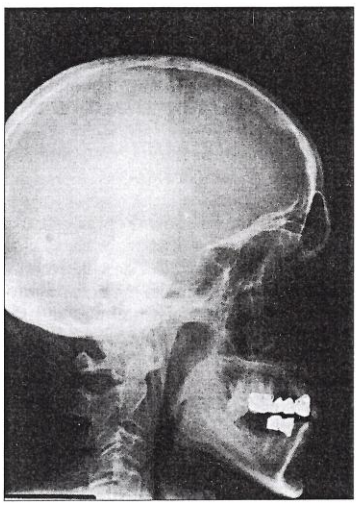

Figure 9: Lateral cephalometric radiograph of the father. Short anterior cranial base, short maxilla, normal facial height.

Family investigation

His 52-year-old father, 48-year-old mother, and 23-year-old brother were apparently normal. On physical examination the father, to whom the patient looks like, was 167 cm tall (U/L segment: 1.01) and weighed 77 kg. He had slight eurycephaly and brachycephaly (C.I.: 81.5, H.C.: 56.3, 80P., H.W.: 15.5 <2 SD, H.L.: 19 cm, mean), normotelorism, narrow upper face, normal in length face, small mouth with normal filtrum, and narrow upper and lower lip.

Cranial measurements of the father (Fig. 9) were as follows: head length 19 cm (-0.70 SD), head height 14.5 cm (3.86 SD), and forehead height 10.5 cm (-1.3 SD).

Cephalometrics of the father (Fig. 9) were normal except for severely short an-

terior cranial base (71.1 mm, -3.2 SD) and maxillary length (48.2 mm, -3.6 SD).

Immunoglobulin A in the family members was for father 270 mg/dl, mother 313 mg/dl, brother 207 mg/dl (n.v. 70-230).

DISCUSSION

Four main components of the patient's phenotype merit a discussion: the craniofacial dysmorphism, the destructive (radiolucent-«osteoglyphic») bone lesions, the fusion of cervical vertebrae, and the IgA deficiency.

The patient has a hyperbrachycephalic (breadth +4.89 SD, length -4.36), and height (+2.72 SD) head, severely short both anterior (-2.8 SD) and posterior (-3.0 SD) cranial base, moderately short cranial base saddle angle (-2 SD) severely concave (-5.7 SD) profile, extremely short maxilla (-4.7 SD) and upper facial height (-3.1 SD), and short lower facial height (-1.8 SD). His father has severely short anterior (-3.2 SD) cranial base and maxilla (-3.6 SD), mildly concave profile (-1.0 SD), but normal posterior cranial base, saddle angle and upper and lower facial height.

The hyperbrachycephaly and the severe shortness of anterior cranial base (and therefore the maxilla) could be considered as primary change attributed to synostosis of the coronal ring e.i. the coronal sutured, the frontosphenoidal sutures and the sphenoethmoidal synchodrosis. The severe shortness and the concavity of the midface could be considered as secondary growth effects following the sutural growth restriction, although this model of craniofacial change is considered only applicable to simple craniosynostosis, not to cases with complete coronal ring involvement or to syndromic cases [3]. However, although his father's anterior cranial base is even shorter, his midface is mildly affected (it is noted that 8% of patients with coronal synostosis represent familial examples [3]). In addition, the patient manifests a severe shortness of the posterior cranial base which could be attributed to synostosis of the sphenoccipital synchodrosis, while in his father this area is normal.

The fact that the patient manifests additional abnormal features, although he shares some basic features with his father, which do not seem to have secondary effects in the father, suggests that in the syndromic patient there probably is a pathogenetic mechanism different from that in the normal father.

Most of the destructive (osteoglyphic) bone lesions, restricted in the craniofaciocervical region and shown as intrabone well-defined radiolucencies in the mandible, maxilla, cranium and cervical vertebrae, were already present in the earliest available radiographs from the age of 13 10/12, but it is not easy to see and compare details because of the different standards of the radiographs. The latest 2.5 year follow-up, based on lateral cephalometrics and panoramic radiographs of same standards, failed to show any noticeable changes in the radiolucencies except for those located in the right mandibular ramus. The destruction of alveolar bone and the fusion of the bodies of cervical vertebrae can be also traced back at that early age and it is easier to see their progress.

Fusion of the C1-C2 vertebrae was traced in radiographs of the neck taken at the age of 14 5/12; the fusion of the C3-C4 was completed by the age of 15 6/12. According to the patient's history, the restriction of neck mobility started at the age of 6. This is an indication that the fusion of the C1 and C2 vertebrae started at that age, but there are no radiographs available from that age. The radiologic follow-up since the age of 14 5/12 shows that the fusion of vertebrae is progressive.

As it is shown from the radiologic follow-up, this disorder destroys the cranial, facial and cervical bones. It seems that the intrabone lesions are rather very slowly progressive, if not being stable, but the lesions of bone surfaces, in the alveolar

bone and the surfaces of the vertebrae as well, are evidently progressive and lead to exfoliation of the teeth and fusion of the vertebral bodies and processes respectively. It is striking that all the rest bones of the skeleton are absolutely normal. It is worth noting that the unilocular radiolucency of the right mandibular ramus became multilocular, indicating that it developed bone septa after the biopsy and the simultaneous extraction of the impacted third molar.

The histologic picture of specimen from «deeply situated cortical bone and osteolytic lesion of the mandible» was not purely representative of an absolutely intrabone lesion, since there were bundles of striated muscles next to the fibrous connective tissue of the lesion, and the gross specimen included the extracted tooth. Nevertheless, there is enough histologic evidence that the lesion consisted of fibrous connective tissue exhibiting cellular, as well as acellular areas. The inflammatory infiltration is well understood in the mucosal (periodontal) specimens, but not so in the intrabony lesion. The latter could be due to the vicinity of the impacted tooth. The intrabone lesions would be expected to be more progressively destructive than they are. Instead, bone septa were developed in the unilocular radiolucency, present in the right ramus before the extraction of the impacted 3rd molar and the biopsy, after two and a half years. The surgical intervention for treatment comes into question.

The IgA deficiency was revealed at the age of 24 6/12 and confirmed at the age 25 10/12. No immunity tests were performed before. The patient's IgA deficiency could be primary or acquired. It is certain that the patient takes phenytoin 100 mg x 2 per day, for preventing «headaches», after the suction of the abscess, i.e. since he was 25 4/12-year-old. Acquired IgA deficiency is reported to occur in patients taking phenytoin [1]. The patient had low levels of IgA (3 mg/dl) after he started taking phenytoin, as it was shown from the test performed at age 25 10/12, but these low levels also existed before, as it is shown by previous test (age 24 6/12, <5 mg/dl, n.v. 70-230). All the other members of his family have normal IgA values. As it is known, IgA is the predominant immunoglobulin class in body secretions, including saliva. It may serve both to defend against local infection and to prevent access of foreign antigens to the general immunity system. About 1 in 700 Caucasian persons have no demonstrable serum IgA, and no apparent disease [11], while others may have recurrent infections, gastrointestinal disorders, autoimmune diseases, allergies, malignancies and a variety of associated genetic disorders [13]. The alveolar bone destruction of our patient can not be explained on the basis of his IgA deficiency since periodontal involvement is not observed in IgA deficient individuals [9, 10]. Hence, the destruction of periodontium seems to be etiologically and pathogenetically connected with the intrabony lesions of the craniofaciocervical region and not with the IgA deficiency.

The SCE (5.63/cell) frequency and the PRI (2.0) in the peripheral blood lymphocytes of the patient were normal according to our and international standard values. However, the PRI of the patient (2.0), although normal, was higher compared with that of the normal control (1.3). This finding may be a result of the differences in PRI values which characterize the human subpopulation subsets [8, 12]. The patient has normal values for T- and B-lymphocytes and normal CD_4, CD_8 subsets.

There are several syndromes which should be taken under consideration in the differential diagnosis of our case. Thus, our case should be differentiated from:

Osteoglophonic dysplasia characterized by gross dwarfism, craniofacial abnormalities, marked changes throughout the skeleton, and unerupted teeth [2]. Radiographically the bone lesions of our patient share similarities with those of the

osteoglophonic dysplasia, but are strictly limited to the craniofaciocervical bones. That is the reason that we called our patient's disorder craniofaciocervical osteoglyphic dysplasia. Osteoglyphic, not osteoglophonic, is the correct term for «hollowed bone». We have the same opinion on the term with Greenberg and Lewis [5]. Histologic picture of biopsy from metaphyseal lytic defects in a case with osteoglophonic dysplasia showed moderately cellular fibrous tissue having a slightly whorled pattern with no inflammatory infiltration [7].

In our case biopsy from both the periodontal and mandibular intrabony lesions showed hyperplastic fibrous connective tissue with non specific chronic inflammatory infiltrations. The chronic inflammatory infiltration of the connective tissue in our case could be due to the vicinity of the mandibular lesions to the periodontal tissues, which are seldom free of inflammation.

Job's syndrome consists of unusual facies, elevated IgE level, and leukocyte dysfunction [4]. There are three essential similarities between our case and Job's syndrome, that is coarse face, hypoplastic midface, and involvement of periodontium. However, there are much more dissimilarities: in our case there are no eczematous dermatitis, no recurrent pyogenic infections of the skin and lower respiratory tract, and different skeletal findings in comparison with Job's syndrome, in which there is craniosynostosis with fusion of the sagittal and lambdoid sutures and scaphocephaly [6]. In our case there is IgA deficiency, but no chemotactic defect, neither elevated serum IgE levels as it happens in Job's syndrome.

Hajdu-Cheney syndrome (acroosteolysis). This syndrome consists of dissolution of the terminal phalanges, bizarrely shaped skull, premature loss of teeth, and short stature [4]. The only similarity between our case and Hajdu-Cheney syndrome is the early loss of teeth due to destruction of the alveolar bone. All the other features are different. In Hajdu-Cheney there is dolichocephaly, bathrocephaly, widening of the cranial sutures, absence of the frontal sinuses, elongation of sella turcica (J-shaped), lysis of terminal phalanges in contrast to the hyperbrachycephaly, deep sella, wide frontal sinuses, fusion of cervical vertebrae and intact terminal phalanges of our case.

Frontometaphyseal dysplasia consists of pronounced bony supraorbital ridge, mixed hearing loss, and generalized skeletal dysplasia [4]. The facies of our case, at the first glance, reminds the facies of the frontometaphyseal dysplasia, mainly because of the pronounced supraorbital ridge, but this protuberance is due to the wide frontal sinuses in our case and not to bony torus as in the frontometaphyseal dysplasia. There is no generalized skeletal dysplasia in our case.

Klippel-Feil anomaly is characterized by fusion of two or more cervical vertebrae, short neck, limitation of head movement, and low posterior hairline [4]. Clinically and radiologically our case exhibits these characteristics, but our patient, in fact, does not have the Klippel-Feil anomaly. The mobility of his neck started being restricted at the age of 6 years. Therefore, the severe limitation of the neck and head mobility that he eventually developed is due to the fusion of the previously normally jointed cervical vertebrae as it is shown from the radiological follow-up. In the Klippel-Feil anomaly the condition is resulting from failure of normal segmentation to vertebrae, which can be traced back to the third embryonic week when segmentation of mesodermal somites takes place [14].

As it is shown from the differential diagnosis the combination of hyperbrachycephaly, short face, midface hypoplasia, fusion of cervical vertebrae, radiolucent bone defects of the skull and cervical vertebrae, and severe destruction of periodontium, most likely, represents a new unknown entity.

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