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CASE REPORT

Seckel syndrome associated with oligodontia, microdontia, enamel hypoplasia, delayed eruption, and dentin dysmineralization: a new variant?

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Seckel syndrome (SCKL) [OMIM Entry 210600] is a rare, autosomal recessive syndrome, characterized by severe intrauterine and postnatal growth retardation, microcephaly, mental retardation, and typical facial appearance with beaklike protrusion of the midface (bird-headed). Associated findings may include limb anomalies, dislocation of femoral heads, scoliosis, and gastrointestinal malformation. A 14-year-old boy is presented with brain hypoplasia, pachygyria, hydrocephaly, enamel hypoplasia and root dysplasia in the temporary dentition, and oligodontia, severe microdontia, and delayed eruption of the permanent dentition. The association of SCKL with the above unusual dental findings may represent a new phenotype.
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Case report

The proband, a Caucasian 14-year-old boy, had been followed and treated at a private practice at Bad-Segeberg (Germany) since the age of 6 years. He was born after 36 gestational weeks, and had low birth weight (lower than the 5th percentile). Body height and head circumference were indicative of severe prenatal growth retardation (< P5). At the age of 3 years, the patient was diagnosed with Seckel syndrome (SCKL) on the basis of primordial dwarfism with severe pre- and post-natal dystrophy, microcephaly, and typical craniofacial features with protrusion of the midface (bird-headed; Fig. 1). Additional findings were hypoplasia of the corpus callosum and the frontal brain horn, and pachygyria with internal and external hydrocephaly. During infancy, the proband started to develop severe autoaggressive behavior accompanied by mental retardation, muscle spasticity, contractures of the major peripheral joints, grand mal epilepsy, alalia, anemia, progressive degeneration of the optic nerve, and a progeroid habitus with an unusually thickened and dry skin. The patient did not walk until the age of 7 years, which was characterized by an uncoordinated and tip-toe fashion of movement. At the age of 6 years, he presented a full deciduous dentition with generalized enamel hypoplasia (rough surface type), irregular and small crown shape, severe root dysplasia and progressive loosening of all teeth. With the exception of the first molars, no permanent teeth had erupted at the age of 14 years. On oral tomography, a number of extremely small tooth structures (microteeth) were seen in both the jaws, which were fully encapsuled by the mucosal/periodontal tissues without any connection to the alveolar bone (Fig. 2). No signs of osteolysis or follicular cysts were found in association with these structures. The temporomandibular joints appeared hypoplastic without a clear delineation of the condyles and the synovial cavities.

Nine microteeth (five from the frontal maxilla and four from the mandible) were removed surgically. Tooth height ranged from 1.7 to 2.9 mm and tooth width from 1.3 to 2.2 mm. Part of the teeth were demineralized with EDTA 0.33 mol/l and prepared using standard histological techniques (paraffin sections). With light microscopy, the roots appeared short and distorted, and in most cases the pulp chambers were completely obliterated by tertiary dentin (hematoxyline and eosin stain; Fig. 3). Root cementum was consistently hypoplastic and, in the absence of a clearly delineated periodontal ligament at the apical third, the root dentin was continuous with the surrounding periodontal tissues. Immunostaining for type I collagen (polyclonal human antibody no. R1038, Acris

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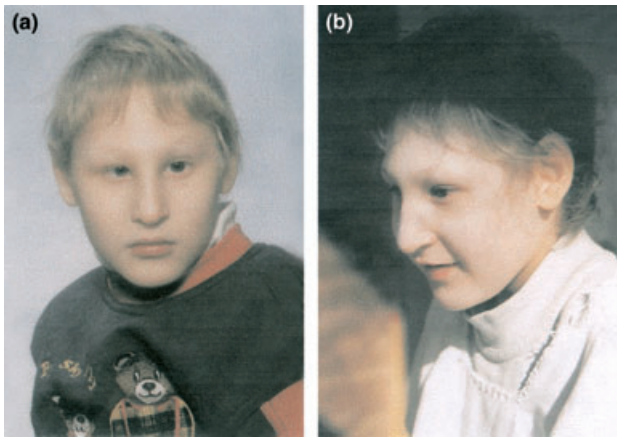

Figure 1 Proband at the age of 6 (a) and 13 years (b), presenting typical protrusion of the midface and the nose (bird-headed) as an intrinsic craniofacial feature of Seckel syndrome.

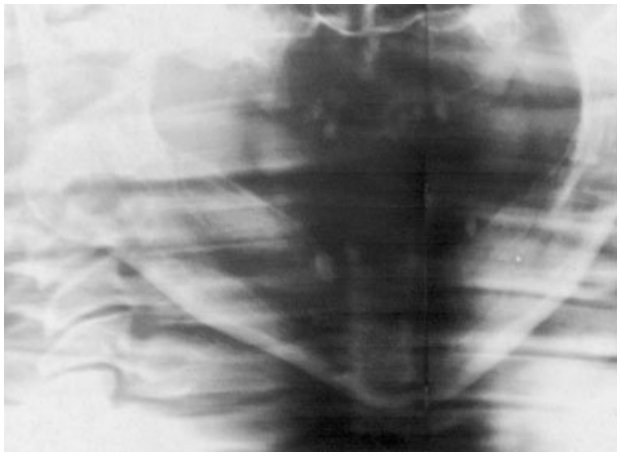

Figure 2 Oral tomography at the age of 13 years, showing only a few permanent microteeth without connection to the alveolar bone.

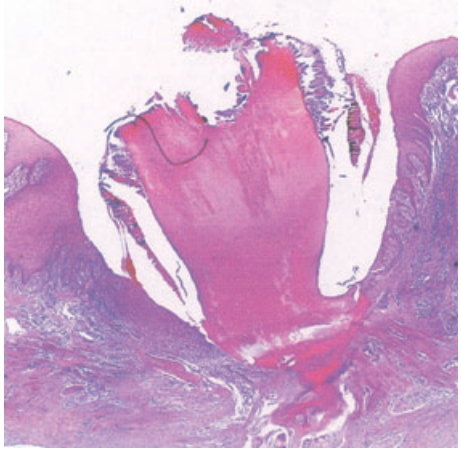

Figure 3 Histological appearances of a permanent mandibular microtooth with short and distorted root, complete pulp obliteration, and cementum hypoplasia. Hematoxyline and eosin stain on paraffin section, 100×.

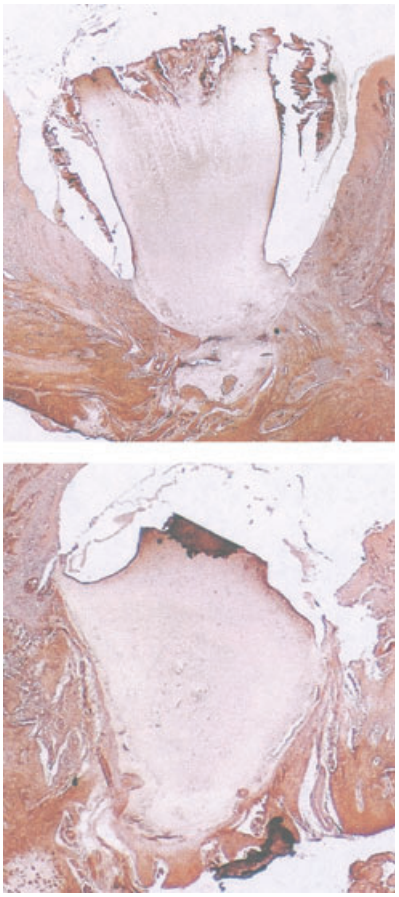

Figure 4 Immunostaining of two permanent mandibular microteeth for type I collagen, showing an abnormal distribution of collagen fibers in dentin, and an ill-defined, atrophic periodontal ligament. Paraffin section, 100×.

Antibodies GmbH, D-32120 Hiddenhausen, Germany; dilution 1:75–1:125) showed an abnormal distribution of collagen fibers in dentin, and confirmed the previous finding of an atrophic and ill-defined periodontal ligament (Fig. 4). A broad, laminated zone (over 100 μm wide) with scarse and abnormally enlarged dentinal tubules was present beneath the mantle dentin and running parallel to the dentin-enamel junction. Planoparallel sections of 120 μm thickness were cut from the other teeth using a water-cooled diamond saw (Microslice2, Ultra Tec, Santa Ana, CA, USA). Each section was mounted on a microradiographic plate-holder bearing an aluminum stepwedge (seven 25-μm steps). Microradiographs (MRG) were taken at 3 min exposure on high resolution glass film plates (Millimask HD, Agfa, Mortsel, Belgium) using a Cu(Kα) X-ray source (PW1830, Philips, Almelo, The Netherlands) operating at 25 kV and 15 mA at a focus-specimen distance of 30 cm. The plates were developed using standard techniques. The MRGs were evaluated using a light microscope (Axioplan MPS20, Carl Zeiss, Oberkochen, Germany). The laminated submantle dentin zone was characterized by globular zones of dysmineralization (interglobular dentin) extending from the crown to the apical third of the roots (Fig. 5).

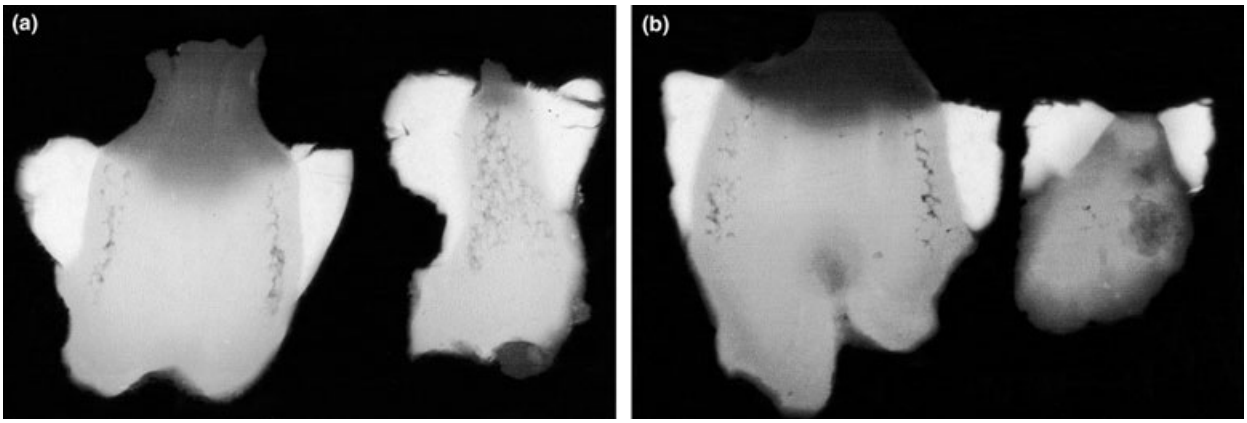

Figure 5 Interglobular dentin (dysmineralization defects) of two microteeth (a, b) presenting on microradiographs either as ribbon-like (left) or isolated radiolucencies (right) depending on the position of the section (transversal or near the surface, respectively).

Comments

The craniofacial features of SCKL allow for differentiation from other syndromes of growth deficiency such as Dubowitz syndrome, fetal alcohol syndrome, trisomy 18 syndrome, de Lange syndrome, Bloom syndrome and Fanconi syndrome. In contrast with these syndromes, SCKL has a great phenotypical and genotypical heterogeneity (1), and a number of unsorted variants have been reported. Three types have been proposed on the basis of variable clinical manifestations, and, in a small number of instances, their loci have been assigned respectively to chromosome 3q22.1-q24 (encoding ataxia-telangiectasia and RAD3-related protein) [Online Mendelian Inheritance in Man gene database, http://www3.ncbi.nlm.nih.gov/Omim (OMIM) Entry 210600], 18p11.31-q11.2 (unspecified gene) [OMIM Entry 606744], and 14q21-q22 (region comprising the MNAT1 gene which has a role in DNA repair) [OMIM Entry 608664]. Majoor-Krakauer et al. (2) reported a SCKL-like variant with additional hydrocephaly, abnormal gyral pattern, and delayed cortical neuronal migration. The dentition has been described sporadically in SCKL, focusing on enamel hypoplasia (3), malocclusion, microdontia, dentin dysplasia (4), and taurodontism (4, 5). The pattern of tooth agenesis observed in the dentition of SCKL patients appears to be similar to the pattern in normally developed persons (5). It is postulated that the present association of classical SCKL features with hydrocephaly, pachygyria, enamel hypoplasia and root dysplasia of the deciduous dentition, and oligodontia, microdontia, delayed eruption and dentin dysmineralization of the permanent dentition may represent a new SCKL phenotype. Genetic analysis of the patient presented is still ongoing, and the identification of the locus involved could probably lead to a new genotype-phenotype correlation.

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