ORAL FINDINGS OF TWO SIBLINGS WITH DYSKERATOSIS CONGENITA

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Abstract

Dyskeratosis Congenita (DC) is a rare inherited fatal disorder characterized by classic triad of oral leukoplakia, nail dystrophy and abnormal skin pigmentation. Variable somatic abnormalities may be present like pulmonary, neural, immune, oral complications. Bone marrow failure, pulmonary disease and malignancy are the main mortality causes of disorder. Oral and dental manifestations could be the first signs of DC, but there are a few reports on DC in the dental literature. This paper describes two siblings – 8 year old boy and 10 year old girl – with DC and their systemic, oral and dental conditions. Deep caries, gingival/periodontal problems, hypocalcified areas of teeth were noted. Congenital absence of 4 teeth of male sibling and 12 teeth of female sibling are important features of cases.

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Introduction

Dyskeratosis congenita (DC) is a rare inherited disorder first described in the early 1900s by Zinser.[1, 2] This disorder was detailed and recognized as a clinical entity several years later by Engman and subsequently by Cole et al.[1], and therefore, another popular name of the disorder emerged: Zinsser-Engman-Cole syndrome. The original mucocutaneous triad of the syndrome included oral leukoplakia, nail dystrophy, and abnormal skin pigmentation; this condition often develops in children, young adults or adolescents.[3, 4] Currently, progressive bone marrow (BM) failure with pancytopenia is an important well-known symptom of the disorder and the primary cause of mortality (in 60–70% cases); other common causes of mortality are pulmonary disease (10–15%) and malignancy (10%).[5] Further, DC includes a variety of somatic abnormalities, except for the "classic quartet" (abnormal skin pigmentation, nail dystrophy, oral leukoplakia, and BM failure), such as epiphora, mental retardation or developmental delay, pulmonary disease, short stature, premature hair loss, hyperhidrosis, malignancy, intrauterine growth retardation, liver disease, cerebellar hypoplasia, hypogonadism, microcephaly, and eye disorders. The incidence of the 4 classic symptoms is 80–90%, whereas that of other somatic abnormalities is approximately 5–30%.[5, 6] DC is associated with a male predominance, with a male-to-female ratio of 3:1 [7], and that 1 in 1 000 000 individuals are affected by DC worldwide.[8]

The genetic basis of DC has been understood in the last two decades. In the late 90s, the key role of the *DKC1* gene was identified, and three subtypes of DC were described: X-linked recessive (most common), autosomal dominant, and autosomal recessive.[9] Advanced studies on the genetics of DC revealed that mutations in one of eight genes, *DKC1* (most of the defined mutations), *CTC1, TERC, TERT, TINF2, NHP2, NOP10*, and *WRAP53*, causes this disease. Seven of these genes (except for *TINF2*) play roles in telomere maintenance because they encode components of the telomerase enzyme complex, whereas the *TINF2* gene encodes the shelterin complex. Despite

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substantial progress, about 40% of patients are presently not genetically characterized.[5, 10] Individuals with DC have very short germ-line telomeres for their age compared with those of normal individuals.[11]

The initial clinical findings involve dystrophic changes of the nails, abnormal skin pigmentation before 10 years of age, and BM failure that develops later, usually before 20 years of age.[12] Eighty percent of patients show signs of BM failure past 30 years of age.[5]

DC is a multisystem disorder that may affect oral tissues.[13] A series of reports have defined oral findings in DC. Oral leukoplakia is one of the basic characteristics of this syndrome [2, 6, 10] and is usually observed in the tongue and buccal mucosa.[14] In the literature, oral infectious findings include caries [15-17], periodontal disease [16, 17], tooth mobility [18], early exfoliation of the teeth [18], and ulcers.[19] Tooth-related conditions are spaces [17], hypocalcified enamel [15], hypodontia [16], delayed eruption [16], short roots [16], enamel defects [19], blunted apices [20], and taurodontism.[21] Other findings in DC include oral lichen planus [19], abnormal pigmentation [18], atrophic glossitis [15, 20], erythema [14], and bleeding.[16-18] Malignancy is a prominent cause of mortality in patients with DC, and squamous cell carcinoma is an important oral finding and a common malignancy type.[22]

This study describes oral, dental and medical findings of male and female siblings with DC.

Case Reports

An 8-year-old boy and a 10-year-old girl, who were siblings, were referred to the Department of Pediatric Dentistry at Süleyman Demirel University by the Dermatology Department where the siblings had been first diagnosed with DC 3 years earlier. Parents signed an informed consent form before examinations. The family history indicated that the parents had a cross-cousin marriage, and the father's sister in the family had psoriasis.

Case 1

The male patient was diagnosed with DC when he was 5 years old. On physical examination, fingernail dystrophy (Figure 1), skin hyperpigmentation on the face (Figure 2), short stature, premature hair loss, hyperhidrosis, strabismus, and amblyopia were noted.

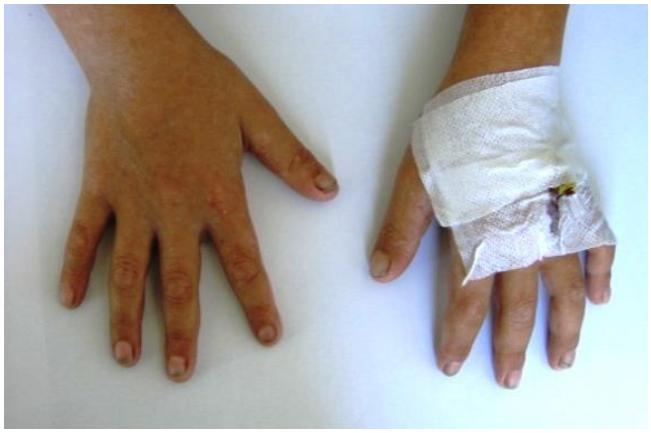

Figure 1. Fingernail dystrophy of male sibling

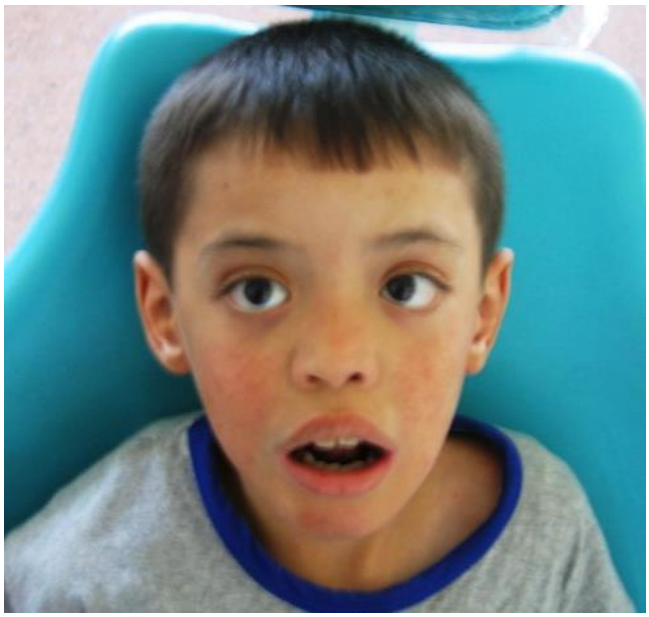

Figure 2. Skin hyperpigmentation of male sibling

He was using a moisturizing cream for dry skin. Further, he had mild learning difficulties and speech problems. Hematology tests revealed reduced white blood cell count (2700/mm^3), decreased percentages of neutrophils and eosinophils (22.9% and 0.1%, respectively), mean corpuscular volume (75.4 fL), mean corpuscular hemoglobin level (26.4 pg/cell), and uric acid and total bilirubin levels (2.37 and 0.27 mg/dL, respectively). Moreover, the patients' lymphocytes and monocytes (59.4% and 16.6%, respectively) as well as red cell distribution width (15.8%), and levels of alkaline phosphatase (263 U/L), aspartate transaminase (47 U/L), and lactate dehydrogenase (641 U/L) were elevated.

Intraoral examination revealed hypocalcified areas of the incisor teeth, gingivitis, atrophic glossitis, and dentin caries of most of the teeth (Figure 3).

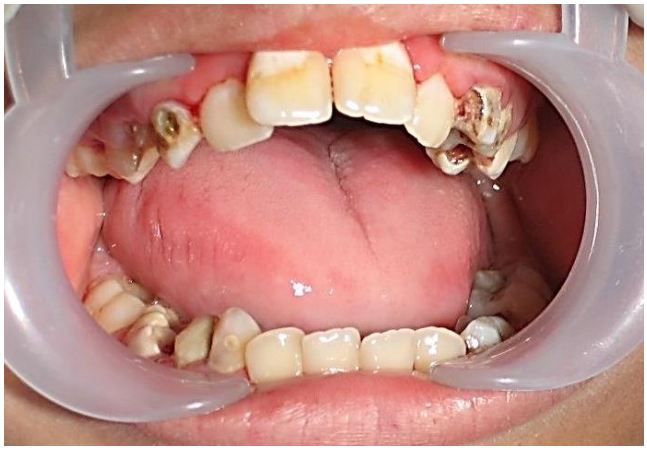

Figure 3. Oral cavity of male sibling

Poor oral hygiene and plaque retention were noted. Oral leukoplakia was not seen. Radiographic examination demonstrated congenital absence of maxillary right and left premolars as well as extensive caries of 16, 53, 26, 63, 64, 65, 36, 73, 74, 75, 46, 83, 84, and 85 (Figure 4).

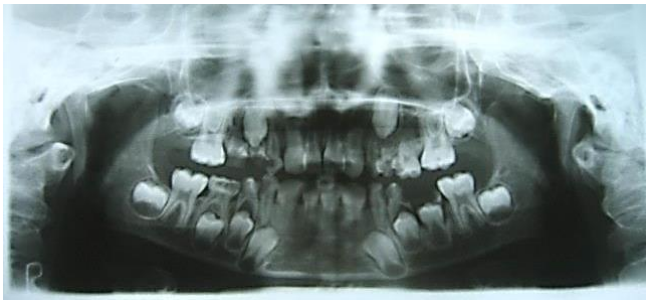

Figure 4. Panoromic radiograph of male sibling

Furthermore, an ectopic eruption of the right upper canine was noted, and the eruption path had changed distally to the first primary molar because of the congenital absence of the first premolar.

Case 2

The female sibling was diagnosed with DC when she was 7 years old. She was applying the same moisturizing cream that her brother had used and had been taking levothyroxine sodium for hypothyroidism for two years. Dystrophy of the fingernails (Figure 5), skin hyperpigmentation on the face (figure 6), short stature, premature hair loss, hyperhidrosis, learning difficulties, and speech problems were observed similar to her brother's results on physical examination.

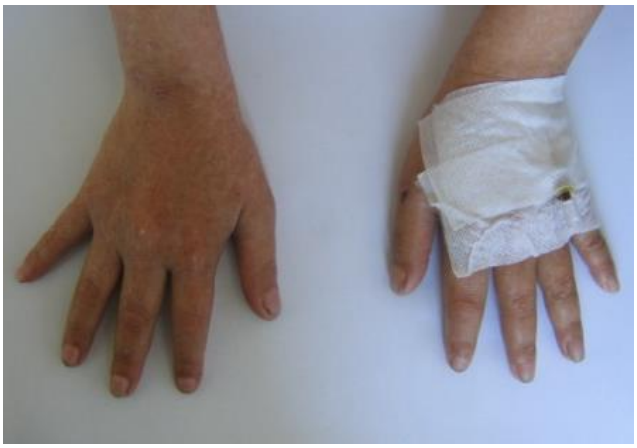

Figure 5. Fingernail dystrophy of female sibling

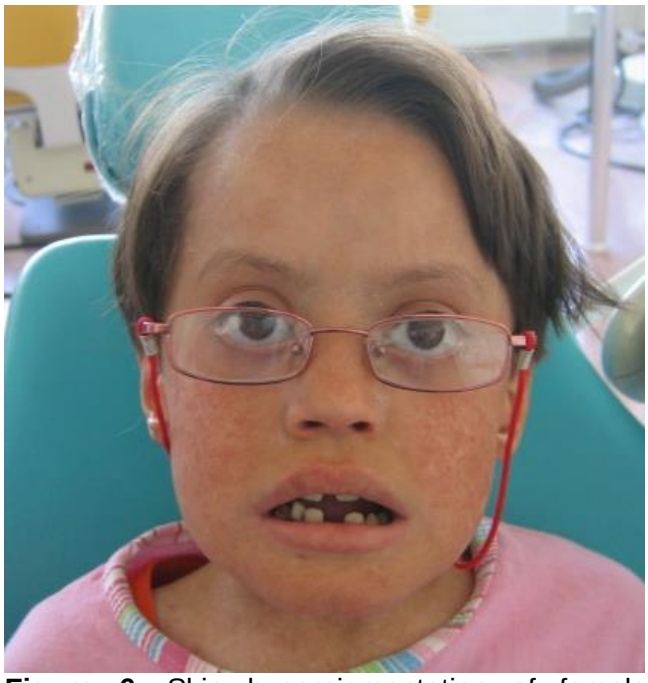

Figure 6. Skin hyperpigmentation of female sibling

Amblyopia and myopia were also noted. Hematology tests were similar to those of her brother: low white blood cell count (2900/mm^3), decreased percentage of neutrophils (19.9%), and decreased uric acid and total bilirubin levels (2.06 and 0.29 mg/dL, respectively), increased percentages of lymphocytes and monocytes (63.5% and 13.1%, respectively), red cell distribution width (16.8%), as well as increased levels of alkaline phosphatase (164 U/L),

aspartate transaminase (48 U/L), and lactate dehydrogenase (904 U/L). Intraoral findings included hypocalcified sites on the incisor teeth, aggressive periodontitis, including wide hyperemic bands in the gingiva, gingival bleeding, and poor oral hygiene with bacterial plaque accumulation (Figure 7).

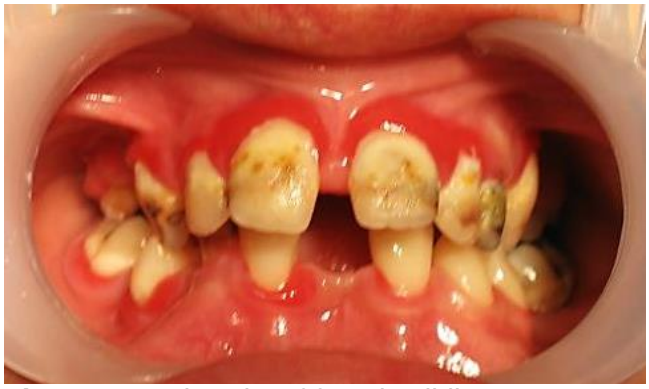

Figure 7. Oral cavity of female sibling

Similar to her sibling, there was no oral leukoplakia. Radiographic examination showed the congenital absence of 12 permanent teeth (14, 15, 18, 24, 25, 28, 31, 35, 38, 41, 45, and 48); ectopic erupted left upper canine; dentin caries in 11, 12, 13, 21, 22, 63, 23, 36, and 46; excessive crown damage of 16 and 26 with periapical lesions; and periodontal bone loss mostly around the first permanent molars (Figure 8).

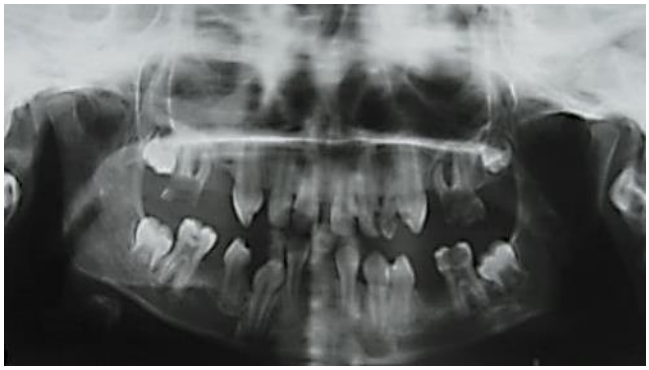

Figure 8. Panoromic radiograph of female sibling

Periodontal treatments performed for both patients consisted of scaling the whole dentition and gingivoplasty for maxillary anterior teeth. Detailed oral hygiene technique recommendations were provided to both the patients and their parents. Decayed teeth were restored, and hopeless teeth were extracted.

Discussion

DC is a fatal multisystem genetic disorder that mainly affects ectodermal tissues.[16] This disease is classically characterized by three mucocutaneous defects (oral leukoplakia, nail dystrophy, and abnormal skin pigmentation) as well as BM failure.[5] All DC patients may not exhibit all of these classic features, and clinically, it has been accepted that at least two features of the classic quartet and two of the somatic features are sufficient for the diagnosis of DC.[23] Both our patients had two of the four main characteristics of disorder; dystrophy of fingernails and skin hyperpigmentation, but neither exhibited BM failure or oral leukoplakia. Further, these patients had many somatic manifestations such as short stature, premature hair loss, hyperhidrosis, learning difficulties, speech problems, and eye disorders. Mucocutaneous features of this disorder usually occur between the ages of 5 to 10 years. The siblings were 8 and 10 years old, and therefore, oral leukoplakia may occur in the near future because of the progressive nature of this disorder.

Patients with BM failure and many somatic abnormalities younger than 10 years old are considered to have a severe phenotype.[9] The siblings' complete blood counts revealed decreased numbers of white blood cells (leukopenia), reduced percentages of neutrophils (neutropenia), and elevated levels of hepatic enzymes. One of the important causes of leukopenia and neutropenia is BM abnormality because of a congenital disorder such as DC. BM failure includes anemia, leukopenia, and thrombocytopenia. Half of the patients developing pancytopenia before 10 years of age.[2]

Female patients with DC are few and have milder phenotypical features than male patients.[9, 16] In the present cases, the general phenotypes of the siblings were similar, but the female sibling had more complex oral features such as the absence of 8 permanent teeth and severe problems, including intensive gingival and periodontal damages, as well as periapical lesions in several permanent teeth. The reason for observing more severe dental-periodontal problems in the female sibling could be due to her being older. There is an approximately two and a half years age gap between the siblings.

DC is a progressive disorder, and oral tissues could become affected with age; poor oral hygiene over time contributes to intraoral problems.

Congenital absence of teeth has been reported in a few studies on DC.[2,16,17]

Yavuzyılmaz et al.[17] reported a 13-year-old girl with oral leukoplakia, nail dystrophy, and pancytopenia. Oral findings included caries, short-blunted roots, alveolar bone loss, especially in the mandibular incisor and first molar areas, and congenital absence of all second molars. Another report described a 14-year-old girl with the classical triad.[16] Dental abnormalities in this case included caries; alveolar bone loss; short roots; delayed eruption; small-sized laterals; and hypodontia of 18, 35, 38 and 48. Baran et al.[2] reported a 25-year-old oligodontia patient with the classical triad of DC. He had 20 missing permanent teeth including all maxillary teeth, except for the first and second molars; left mandibular central, lateral, canine, second premolar, and third molar teeth; and right mandibular lateral, canine, and third molar teeth. In our cases, the male sibling lacked 4 teeth (14, 15, 24, and 25), and the female sibling lacked 12 teeth (14, 15, 18, 24, 25, 28, 31, 35, 38, 41, 45, and 48) due to congenital absence. The lack of teeth is due to defects in the ectodermal and ectomesenchymal derivatives in DC cases. Agenesis of numerous teeth is often associated with congenital ectodermal problems.

Oral and dental findings in DC are variable. Ectodermal problems such as thin enamel and epithelial defects are important features of disorder. Defects in ectoderm-based tissues, including enamel and epithelium, could predispose a patient to caries and periodontal disease. Poor immune function resulting from neutropenia could also be the main cause of periodontal disease. Moreover, these siblings have very poor oral hygiene habits, and apparently, this factor can aggravate the oral situation.

The treatment plan was based on improving oral hygiene, extracting of severely damaged teeth, eliminating periodontal problems mechanically and pharmacologically, restoring dental caries, and supplementing the edentulous areas with removable prostheses to improve function, speech, esthetics, and psychosocial condition.

In regular intraoral controls, a baseline evaluation of oral hygiene and an assessment for leukoplakia and squamous cell cancer are suggested in DC cases. Dentists should be aware of the increased cancer risk and perform a thorough examination at each visit. Suspicious oral leukoplakia lesions should be biopsied because squamous cell carcinoma is usually found in areas of leukoplakia.[10] Preventive measures should be taken at an early stage to effectively avoid rapid destruction of dental and periodontal tissues.

Conclusions

Oral symptoms may be the earliest signs of DC. The main purpose of treatments in these cases should be to increase life expectancy and quality of life of patients with DC.

Declaration of Interest

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