Dyskeratosis Congenita: Dental Management of a Medically Complex Child

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Abstract

Dyskeratosis congenita (DKC) is a rare syndrome characterized by cutaneous hyperpigmentation, nail dystrophy, leukoplakia, and pancytopenia. The purpose of this case study was to describe the management of a 7-year-old girl diagnosed with DKC who urgently needed dental treatment under general anesthesia before bone marrow transplantation (BMT). The patient presented normal skin, nails, and hair, but oral examination revealed a number of ulcers, leukoplakia, gingival recessions, alveolar bone loss, and dental caries. Hematologic preparation included raising blood parameters, and the anesthesiologist to had consider pulmonary infection. The alveolar bone loss and the gingival recessions required the consultation of a periodontist. Avoiding stainless steel crowns was necessary due to potential plaque accumulation in the crown margins. The goal of this dental treatment was eliminating potential sources of infection before transplantation was conducted. It is important for the pediatric dentist to recognize the medical aspects associated with dental management prior to BMT, and to incorporate them into the treatment plan. (Pediatr Dent 2005;27;244-248)

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clinical section

Dyskeratosis congenita (DKC, or Zinsser-Engman-Cole syndrome) is a rare genodermatosis involving multiple organs.[1-5] The mucocutaneous features of DKC typically develop between 5 and 15 years of age. The median age of onset of the peripheral cytopenia is 10 years.[1-5] The common features of DKC are atrophy of the skin, reticulated hyperpigmentation, dystrophic nails, and oral leukoplakia. Other skin abnormalities include atrophic, wrinkled skin over the dorsum of the hands and feet and hyperhidrosis and hyperkeratosis of the palms and soles with the disappearance of dermal ridges (absence of fingerprints).[4-6] Leukoplakia may be present in any mucosal site, often involving the oral mucosa.

Mucosal surfaces such as the esophagus, urethra, and lacrimal duct may become constricted and stenotic—resulting in dysphagia in 59% of patients, dysuria, and epiphora.[4-6] Liver and/or spleen enlargement, portal hypertension, diverticula or strictures of the esophagus, gastroduodenitis, duodenal ulcers, anal stricture, and chronic diarrhea have been described.[6-8] Among DKC patients who suffer from dysphagia, most have esophageal webbing. Other findings are increased incidence of malignant neoplasms, particularly squamous cell carcinoma of the skin, mouth, nasopharynx, esophagus, rectum, vagina, and cervix. These often occur within sites of leukoplakia. An association with immunodeficiency has also been documented.[6-8]

Genetics

DKC is genetically heterogeneous, with autosomal dominant, autosomal recessive, and X-linked forms.[9] The genes for the X-linked and the autosomal dominant forms of DKC have been identified as *DKC1* and *hTERC*, respectively.[9-11] *DKC1* encodes dyskerin, a nucleolar protein associated with a class of small nucleolar RNA molecules. Dyskerin interacts with the RNA component of telomerase, an enzyme involved in the maintenance of telomere length. Therefore, dyskerin is involved in the regulation of the proliferation capacity of the cell.[9-12]

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The recent elucidation of the genetic basis of DKC enables prenatal testing and carrier detection.[4,5] Early diagnosis of DKC through genetic analysis will allow identifying patients for early harvest and storage of their bone marrow for use after anticipated marrow failure.

Treatment and prognosis

Short-term treatment options for bone marrow failure in DKC patients include erythropoietin and granulocyte colony stimulating factor. The long-term, curative option is allogenic bone marrow transplantation (BMT). Success of BMT is low, due to a high incidence of fatal pulmonary complications. It has been suggested that nonmyeloablative hematopoietic stem cell transplantation conditioning regimens utilizing fludarabine could afford better outcomes in these patients, emphasizing the potential importance of detecting *hTERC* mutations in transplantation candidates.[9]

A recent report showed that approximately 70% of patients with DKC died either directly from BMT failure or its complications at a median age of 16 years. Eleven percent died from sudden pulmonary complications, and another 11% succumbed to pulmonary disease in the BMT setting. Seven percent died from malignancies (eg, Hodgkin's lymphoma and pancreatic carcinoma).[1-3]

Oral and dental manifestations

Oral findings may include gingival inflammation, bleeding or recession, leukoplakia, and a smooth atrophic tongue.[13,14] Dental abnormalities in DKC include hypodontia, diminutive maxillary lateral incisors, and short-blunted roots. Delayed eruption, tooth mobility, severe alveolar bone loss resembling aggressive periodontitis, and crowding have also been reported.[15] Extensive dental caries and early tooth loss are also common.[6]

The purpose of this case study was to describe the general and dental phenomena in a patient with DKC and elaborate on the medical considerations associated with dental treatment.

Case report

A 7-year-old girl was urgently referred to the Department of Pediatric Dentistry at the Hebrew University–Hadassah School of Dental Medicine, Jerusalem, Israel, by her hematologist for dental treatment before BMT. The patient was diagnosed as suffering from DKC. Her general condition had deteriorated due to progressive immunodeficiency in the last year that mandated urgent BMT. Family history revealed that the patient had 4 siblings: 2 boys (who died from DKC at the ages of 5 and 12), a 17-year-old sister with DKC, and a healthy 21-year-old sister. At the time of the dental visit, the patient had pulmonary cytomegalovirus (CMV) infection, and bronchitis. She was treated with gancyclovir (5 mg/kg BID), trimethoprim, and sulphamethoxazole (resprim, 10 mg/kg twice a week), and immunoglobulins transfusion (0.5 g/kg) was administered for the agammaglobulinemia.

At the time of the dental examination, blood parameters were as follows: (1) white blood cells (WBC)=$2.4x10^4$; (2) red blood cells (RBC)=3.07×10^6; and (3) platelets=73,000. Body examination revealed normal skin, nails, and hair. Clinical examination of the oral cavity revealed a number of ulcers on the hard palate. One ulcer was elliptical, sized 10×5 mm (Figure 1). No definite diagnosis of the ulcer was made, although it was suspected to be a neutropenic ulcer. The ulcer did not resolve, despite the administration of gancyclovir. Leukoplakia was noted on the mucosal lining of the left and right cheeks. The oral mucosa appeared red, and bleeding upon probing around all teeth was noted. Gingival recessions around all primary canines and molars were observed (Figure 2), and dental caries was evident in the cervical areas of these teeth.

Radiographs revealed extensive alveolar bone loss in all quadrants extending from the primary canines to the second primary molars (Figure 3). The alveolar bone loss and the gingival recessions required the consultation of a periodontist. Both the hematologist and periodontist recommended avoiding stainless steel crowns because of the concern that the crown margins might be sources of plaque accumulation, and thus an origin of infection, which could worsen graft vs host disease (GVHD) after BMT. In addition, these foci of plaque

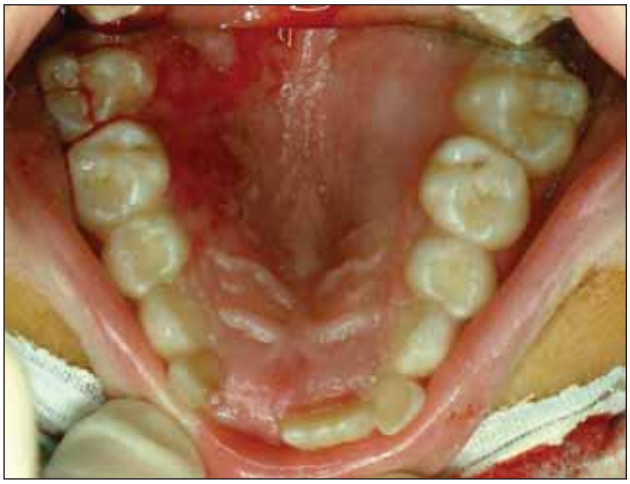

Figure 1. An elliptical ulcer on the patient's hard palate, sized 10×5 mm.

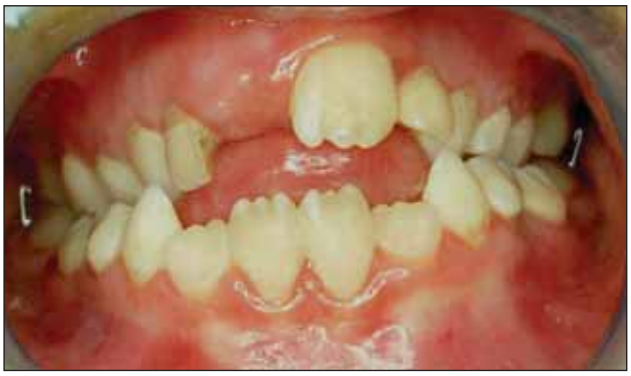

Figure 2. Gingival recessions around all primary canines and molars.

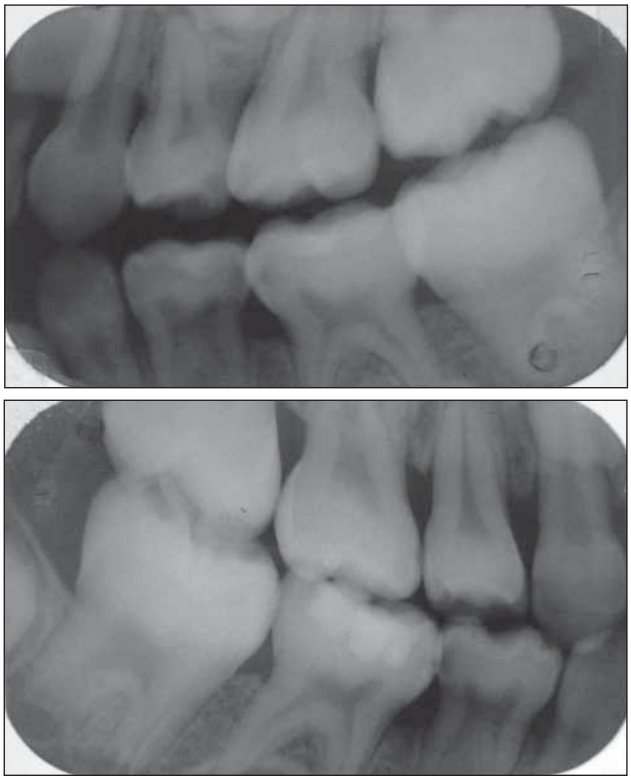

Figure 3. Extensive alveolar bone loss in all quadrants, extending from the primary canines to the second primary molars; interproximal caries is noted on the left side (top) and the right side (bottom).

accumulation could further exacerbate the already severe alveolar bone loss.

Scaling and curettage were not recommended due to lack of calculus and the laboratory findings. Chlorhexidine oral rinse was prescribed, but the patient could not bear its burning sensation, and did not comply. The treatment plan included a strict prevention protocol:

1. cleaning;
2. fluoride application (Duraphat 2.26% F, A. Nattermann & Cie GmbH, Colonge, Germany);
3. meticulous oral hygiene instructions;
4. restorations of the canines and the molars in the upper right, upper left, and lower left quadrants;
5. sealing the occlusal surfaces of the permanent molars;
6. extraction of the upper right and left lateral incisors.

Due to the immunodeficiency, the large extent of dental treatment which required several visits, and lack of cooperation, the patient was scheduled for dental treatment under general anesthesia. Because blood counts were still very low 4 days before the treatment (RBC=3.09×10^6, WBC=1.8×10^4, platelets=16,000), gancyclovir was substituted with foscarnet, and granulocyte colony stimulating factor (GCSF, 5 mg/kg/day) was administered.

On the morning of the treatment day, RBC and WBC counts were low (2.87×10^6, 4.7×10^4, respectively), and the platelet count was 31,000. The patient received platelets from a single platelet donor (SPD) as well as 500 mg tranexamic acid (Hexakapron) and 500 mg amoxicillin IV as prophylaxis for infection during the dental treatment.

The dental treatment was performed according to plan, with the decayed teeth restored with amalgam. Bleeding stopped 10 minutes after the extraction of the upper primary lateral incisors, despite the low platelet count. Fluoride varnish was applied after the restorative treatment. In the postanesthesia care unit (PACU), the patient received an additional dosage of 500 mg tranexamic acid (hexakapron) and 500 mg amoxicillin PO. The parents were instructed to continue the administration of the antibiotics and tranexamic acid for the next 48 hours (500 mg TID).

Due to elevated body temperature a few hours after treatment (39°C), the patient remained hospitalized. No pulmonary infection could be disclosed via the chest x-ray, and the elevated body temperature was suspected to be a postgeneral anesthesia phenomenon. Two days later, the oral mucosa appeared intact and neither pain nor sensitivity was reported. Bone marrow transplantation took place 3 weeks later. The patient died 6 months later as a result of pulmonary complications.

Discussion

The present case demonstrated the dental management of a 7-year-old patient with DKC who urgently needed dental treatment before BMT. The complexity of the patient's disease and its clinical manifestations required a multidisciplinary approach before dental treatment could be performed. Prior to the BMT, it was important to eliminate potential sources of infection, which may endanger the transplantation.[16,17]

Table 1 summarizes the preoperative, operative, and postoperative considerations that are important in such cases. Preoperatively, the medical condition must be ascertained. Of particular importance is the consultation with the hematologist, anesthesiologist, and periodontist. The goals of the dental treatment must be clear and are mainly dictated by the general medical condition. Above all, active infection or potential infection due to caries or of periodontal origin must be treated or eliminated. Attention should be paid to the blood parameters that allow the dental treatment.

In the operative stage, hematologic preparation is required. Attention must be given to bleeding problems,[18] and antibiotic prophylaxis must be considered.[18] Balanced anesthesia is recommended: fentanil and isoflurane through a nasotracheal tube with a moistened pack, positioned to block the entrance of the esophagus and around the endotracheal tube, just above arytenoids, so that blood and dental debris are kept above the esophagus.

The dental treatment must follow the treatment goals. Restorative materials may include amalgam or glass ionomer when a dry field cannot be achieved. It is important to apply preventive means such as fluoride varnishes.

In the postoperative stage, the patient must be carefully monitored, adequate hemostasis must be assured, and antibiotic prophylaxis must be continued. After the initial

Table 1. Dental Management of a Child With DKC Undergoing BMT

Preoperative
Consult
Confirm diagnosis and status of medical condition.
Consult hematologist for blood parameters and pulmonary infections as well as medications.
Consult anesthesiologist for possible risk of respiratory complications under general anesthesia (esophageal webbing or stenosis, bronchitis).
Consult a periodontist for periodontal status (gingival inflammation, recessions, alveolar bone loss).
Goals of dental treatment
Free from acute infection.
Free from potential dental infections: eliminate decay and restore.
Free from potential gingival infection: eliminate inflammation.
Observe the oral mucosa for ulcers and leukoplakia.
Meticulous oral hygiene and prevention protocol (chlorhexidine, fluoride, cleaning).
Operative
Meticuluos hematologic preparation before and during the treatment under general anesthesia.
Confirm status of RBC, WBC, and platelets.
Administer platelets from single platelets donor (SPD) if necessary.
Administer tranexamic acid (hexakapron).
Administer amoxicillin IV as prophylaxis for infection during the dental treatment.
Control bleeding by local means.
Administer balanced anesthesia.
Meticulously eliminate plaque and apply fluoride (gel or varnish).
Radical dental treatment approach is recommended.
Restorations: use amalgam or glass ionomer when potential wet area is suspected.
Avoid stainless steel crowns.[17]
Extract mobile teeth and teeth with questionable prognosis.
Postoperative
Monitor the patient in PACU for a longer period of time than is required for a regular dental care.
Administer tranexamic acid for the next 48 hours after dental treatment to ensure adequate hemostasis.
Administer antibiotics for 48 hours after dental treatment to ensure infection control due to anesthesia and dental treatment.

dental treatment, the pediatric dentist must follow the children thoroughly to supervise the maintenance of oral hygiene and detect any possible focus of infection and eliminate it.

Conclusions

The present case demonstrated the multidisciplinary approach in the dental treatment of a child suffering from dyskeratosis congenita. The roles of the hematologist, anesthesiologist, periodontist, and pediatric dentist were crucial in the planning and performing of the dental treatment.

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clinical section

Abstract of the Scientific Literature

State Tobacco Control Spending and Youth Smoking

Significant resources are currently being devoted to programs aimed at reducing tobacco use and the damage it causes to the public. Comprehensive programs have been developed to: (1) prevent the initiation of tobacco use among young people; (2) promote cessation of tobacco use; (3) eliminate exposure to environmental tobacco smoke; and (4) identify and eliminate disparities among population groups. The purpose of this study was to examine the relationship between state-level tobacco control expenditures and youth smoking prevalence and cigarette consumption. The authors estimated a 2-part model of cigarette demand using data from the 1991 through 2000 nationally representative surveys of eighth-, 10th-, and 12th-grade students participating in the Monitoring the Future project. The authors found that real per capita expenditures on tobacco control had a negative and significant impact on youth smoking prevalence and on the average number of cigarettes smoked by smokers. It was concluded that the prevalence of smoking among youths would have been between 3% and 14%—lower than the rate observed over this period—if states represented by the Monitoring the Future sample and the District of Columbia had spent the minimum amount of money recommended by the Centers for Disease Control and Prevention.

Comments: Although much is known about the impact of some individual state programs on cigarette smoking within the state, very few studies have examined the impact of state programs on cigarette smoking at the national level. This study adds to the growing body of evidence on the impact of state tobacco control programs on smoking. Using data taken from the nationally representative surveys, this study examined the relationship between state-level per capita tobacco control expenditures and youth smoking prevalence and consumption. Policies found to decrease youth smoking included: (1) higher cigarette prices; (2) stronger restrictions on youth access to tobacco; (3) smoke-free air laws; and (4) purchase, use, and possession laws. FSS

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