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Dyskeratosis congenita associated with leukoplakia of the tongue

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Abstract. Dyskeratosis congenita (DC) is an inherited disease characterized by the triad of skin pigmentation, nail dystrophy, and oral leukoplakia. Among other abnormalities, bone marrow failure and a predisposition to cancer are recognized as the major causes of premature mortality in patients with DC. This disease is associated with short telomeres and mutations in 10 genes associated with telomerase and telomere components. The case of a 35-year-old male patient diagnosed with DC, who presented with leukoplakia of the tongue and had a high degree of hypoplastic marrow, but no haematological abnormalities, is reported here. The diagnosis of DC was confirmed by detection of short telomeres in the blood cells and mutations in the *DKC1* gene. This encounter with the case presented suggests that an awareness of the classical forms of DC is important for oral clinicians so that an early diagnosis can be made and the patient can be managed appropriately. Furthermore, genetic analysis is necessary to establish the diagnosis of DC.

Key words: dyskeratosis congenita (DC); *DKC1*; leukoplakia.

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Dyskeratosis congenita (DC), also known as Zinsser–Cole–Engman syndrome, is characterized by skin pigmentation, nail dystrophy, and oral leukoplakia.[1] It is an inherited disease associated with bone marrow failure and a predisposition to cancer.[1] A variety of other abnormalities of the bones, teeth, eyes, gastrointestinal system, and lungs in DC patients have also been reported.[2] DC is a rare disease of defective telomere maintenance and its incidence rate is one in a million.[1] Patients with DC have very short telomeres and mutations in 10 genes associated with telomerase and telomere components.[1] It has become clear that bone marrow failure is a frequent complication in DC, and the main cause of mortality in DC patients is bone marrow failure (60–70%).[2] Therefore, it would be more appropriate to consider DC as a bone marrow disorder with multiple mucocutaneous manifestations.

This disease is often encountered in the paediatric and dermatology fields due to the abnormalities in blood profiles and skin pigmentations, but it is rarely seen in the field of oral surgery.[1] Therefore, it is necessary for oral surgeons to be aware of this inherited disease. The case of a 35-year-old male patient who presented with a white lesion on the tongue and who was diagnosed with DC is reported herein. This case presented an interesting phenomenon, in that the patient exhibited hypocellular marrow but no abnormalities in blood profile, making it difficult to classify this case as an inherited aplastic anaemia.

Case report

A 35-year-old male presented with the complaint of a white lesion on the tongue

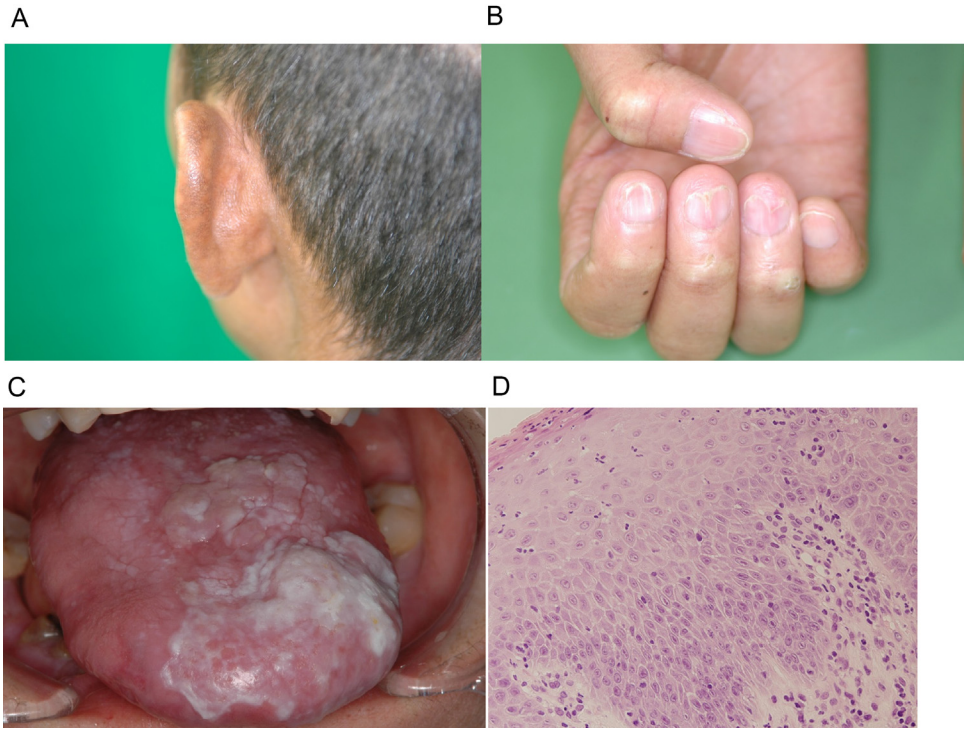

Fig. 1. (A) Reticulated pigmentation of the skin of bilateral ears and neck. (B) The nails appeared atrophic and dystrophic, with longitudinal ridging. (C) An extensive white lesion of varying thickness on the dorsal and ventral tongue surfaces. (D) Histopathology of the biopsied mucosal lesion: thickening of the entire stratified squamous epithelium and dyskeratosis in the prickle cell layer, indicating moderate dysplasia (haematoxylin–eosin stain, original magnification 200×).

and was referred to our department from the department of otorhinolaryngology of another hospital. The patient had noticed a white lesion on the tongue surface 1–2 years ago, which had gradually increased in size. Furthermore, his parents had noted the pigmentation of the skin of the bilateral ears since childhood. This cutaneous abnormality led to a consultation with the department of dermatology, where the disease of DC was suspected and a further genetic analysis for DC-related genes was suggested. The diagnosis of DC was confirmed by the detection of the mutations in the *DKC1* gene.

The patient had a smoking history of 20 years, but no other significant medical history. Further, there was no family history relevant to the disease.

An external examination showed reticulated pigmentation of the skin of the bilateral ears, neck, and other areas such as the limbs, precordium, and back (Fig. 1A). The nails appeared atrophic and dystrophic, with longitudinal ridging (Fig. 1B). The patient presented no other obvious abnormalities such as fatigue, a pale colour, bruises, bleeding, or infection. Intraoral examination showed an extensive white lesion of varying thickness on the dorsal tongue surface (Fig. 1C). Biopsy of a specimen taken from the white lesion revealed thickening of the entire stratified squamous epithelium and dyskeratosis in the prickle cell layer, indicating a change of moderate dysplasia (Fig. 1D). In addition, multiple caries, missing teeth, and periodontitis involving numerous teeth were observed. Laboratory findings were as follows: white blood cell count 3.44×10^9/l with 51.1% neutrophils, red blood cell count 4.73×10^{12}/l, platelets 124×10^9/l, and haemoglobin 15.4 g/dl.

Bone marrow aspiration showed a hypoplastic marrow containing prominent fat tissue and few nucleated cells and megakaryocytes (Fig. 2). A bone marrow biopsy also showed a high degree of hypoplastic marrow characterized by prominent occupation of a large amount of fat tissue and the presence of few haematopoietic cells (a hypocellular marrow). Examination by magnetic resonance imaging (MRI) and short-tau inversion-recovery (STIR) method showed that the chest lumbar vertebrae presented low signals, and T1 emphasis indicated a high signal. These findings led to further examination of the telomere length and genetic analysis

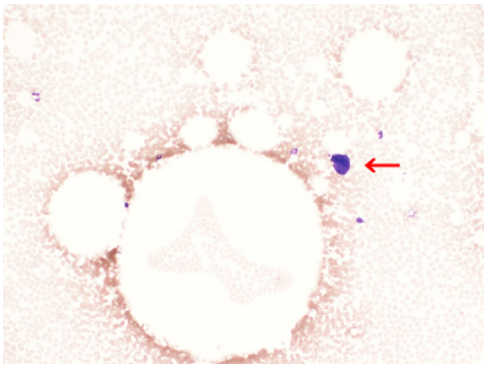

Fig. 2. Bone marrow aspiration showed hypoplastic marrow containing prominent fat tissue and few nucleated cells. Megakaryocytes were stained with May–Giemsa, as indicated with the arrow (May–Giemsa stain, original magnification 100×).