

Case report



ORAL FINDINGS AND CLINICAL BEHAVIOR IN PATIENT HAVING AUTOIMMUNE POLYENDOCRINOPATHY CANDIDIASIS ECTODERMAL DYSTROPHY (APECED)

Kremena Markova, Nikolay Simeonov.

Department of Operative Dentistry and Endodontics, Faculty of Dental Medicine, Medical University of Plovdiv, Bulgaria.

ABSTRACT

Introduction: APECED (Autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy) is a rare autosomal recessive disease with significant impacts on oral health, including oral candidiasis and varying degrees of enamel hypoplasia.

Objective: To present the oral findings of a girl with APECED and the minimally invasive approach taken in recovery and rehabilitation, taking into account the complexity of her medical condition.

Material and methods: A case of a 16-year-old girl with APECED, who visited the dental clinic due to defects of the hard dental tissues and severe dentinal hyperesthesia, is described. There was an underbite with a reduced lower facial floor and enamel hypoplasia in the coronal and middle third of the anterior teeth and first molars.

Results: Through direct composite restorations and a minimally invasive approach, a good healing, functional and aesthetic result was achieved.

Keywords: APECED, enamel hypoplasia, dentin hyperaesthesia,

BACKGROUND

Autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy (APECED), also known as autoimmune polyglandular syndrome type I (APS 1), is a rare inherited disease characterized by a broad clinical spectrum of signs that fall into three main categories: (1) multiple endocrine deficiencies (2) chronic mucocutaneous candidiasis (CMC), and (3) different forms of ectodermal dystrophy including hypoplasia of the dental enamel [1].

Autoimmune polyendocrinopathy candidiasis ectodermal dystrophy is an autosomal recessive disorder identified with mutations in the AIRE gene, in which there is a violation of tolerance to self-antigens, leading to a multiorgan autoimmune reaction [2, 3]. Chronic mucocutaneous candidiasis (CMC) is often the first manifestation of the disease, and all additional symptoms can appear at any

time at a later stage. It typically affects the mouth and, much less frequently the genitalia, conjunctivae, and other mucosae. Candidal infection of the nail bed gives rise to dystrophic nail changes and skin infection, which manifests as wartlike granulomas [4]. APECED usually has an early onset, between 3rd and 4th year, more commonly affecting girls, with an increased prevalence in populations with high rates of consanguineous marriage due to the autosomal recessive pattern of inheritance [5]. Hypoparathyroidism is the most common result of autoimmune destruction of the parathyroid glands, affecting 79 to 96% of individuals with APECED [6]. Symptoms of hypoparathyroidism include numbness around the mouth, hands or feet, seizures, low blood pressure, dental problems, and coarse/ brittle hair. Addison's disease is another common endocrine disorder in patients with APECED due to insufficient production of cortisol and aldosterone [7]. A common symptom is hyperpigmentation of the mucous membrane and skin, which usually precedes all other symptoms by months to a year [8]. This is important for dental professionals because hyperpigmentation of the oral mucosa can be the first observed manifestation of Addison's disease and can aid in rapid diagnosis.

The most characteristic ectodermal manifestations of APECED are enamel defects, nail dystrophy, and alopecia. The etiology of enamel defects remains unclear. Some authors [9] associate them with hypoparathyroidism, while others do not suggest such a dependence. The development of the aberrations appears to be time-dependent, following chronologically the enamel deposition.

CASE DESCRIPTION

A 16-year-old female attended the dental clinic for the management of tooth defects and hyperaesthesia. Patient informed consent was taken before the clinical examination. Medically, the patient was diagnosed with APECED when she was 6 years old. Since her initial diagnosis, the patient

was also diagnosed with hypoparathyroidism and Addison's disease. Steroid drug coverage was therefore required for invasive procedures or periods of illness. She had no known allergies, and a previous general anesthetic was uneventful.

Examination

Extraoral examination revealed sparse hair (Fig 1.) and persistent angular cheilitis.

Fig. 1. Extraoral photo of alopecia.



The oral mucosa was normal, with no evidence of candidiasis. Hypoplastic lesions are found on all anterior teeth and first molars. Only the enamel in the middle and incisal 1/3 of the tooth surface was affected, with a clearly defined horizontal band of macroscopically unaffected enamel, both vestibular and lingual (Fig. 2-3). Dental hyperaesthesia was present and no caries lesions, despite the moderate oral hygiene. On the x-ray, denticles were observed in the pulp chamber of the upper molars (Fig. 4). Based on the clinical and paraclinical studies, we diagnosed the patient with enamel hypoplasia.

Fig. 2. Intraoral view of the hypoplastic lesions of the anterior teeth.



Fig. 3. Intraoral view of the hypoplastic lesions of the anterior teeth.



Fig. 4. X-ray OPG



Treatment

On the first visit, oral hygiene motivation was done, and intraoral and facial scans were obtained using Trios and Bellus3D face scanners and superimposed in Dental Designer Studio (DSD) to create a virtual patient. Dental Designer Studio and virtual wax-up were performed using the patient's facial and intraoral features as guidelines. A diagnostic model was 3D printed.

Crown preparation was done on all first molars. Digitally, the bite height was increased, and metal-ceramic crowns were made and luted (Fig. 5-6). A wax-up prototypes were 3D printed from castable wax. Silicon impression was taken from the lower and upper jaw, and a silicon key was made and used to build up the lingual wall of the anterior teeth with composite (3M Filtek Z250) and adhesive system (3M Adper Single Bond 2). The sharp edges at the transition of the hypoplasia were beveled, and the rest of the crown was built up with layering technique. Then finished and polished with rubber polishers (Fig. 7). Once the composite restorations were placed, esthetics were greatly improved, and the patient was very happy with the result.

Fig. 5. Intraoral view of the upper jaw with the luted metal ceramic crown on first molars.



Fig. 6. Intraoral view of the lower jaw with luted metal ceramic crown on first molars.



Fig. 7. Intraoral view of the restored anterior teeth.



DISCUSSION

Oral candidiasis is usually the first observed manifestation of APECED. Candidal infection of the mouth manifesting as recurrent thrush and chronic hyperplastic candidiasis is often the initial presenting feature, and clinical features of any associated endocrinopathy may not manifest for 10-15 years; occasionally, however, the sequence is reversed, or candida infection is completely absent [10]. This was also the case with our patient, where we did not detect a candidal infection during treatment, but she reported multiple recurrences in the past. Clinically both “acute” and “chronic” forms of candidiasis could be observed. Periodic examinations revealed a change in the clinical picture, with practically the only constant feature being angular cheilitis, which we also observed.

Clinical variability and the lack of a clear correlation between genotype and phenotype is associated with additional mechanisms involved in a complex interplay between genetic, epigenetic, immunological and/or environmental factors [13, 14].

McGovern E, et al. [15] found a strong association between oral chronic mucocutaneous candidiasis and enamel defects, suggesting that fungal infection may be a major factor or a disease marker that interferes with the delicate process of amelogenesis itself.

Defects in dental development affect a large proportion of patients with APECED and, together with candidiasis, characterize the main oral manifestations of the disease. Tooth enamel is very sensitive to genetic, nutritional, metabolic, infectious and immune diseases. Unlike bone, it permanently remembers systemic and/or local stresses. Enamel defects are considered to be the most distinctive ectodermal manifestations of APECED. Perheentupa J. [16] reported that enamel defects were present in 75% of a cohort of 89 Finnish patients with the disease. Similarly, McGovern E, et al. [15] reported that 12 of 16 patients (75%) with APECED showed enamel defects. However, their etiology remains unclear. Hypoparathyroidism has been cited as one of the main causes of enamel hypoplasia. Changes in mineral levels in the body have been shown to lead to disturbances in the apposition and mineralization of hard dental tissues in both human and animal teeth.

In our case, the child was diagnosed with HPT at the age of 6, which is well after the beginning of mineralization and crown formation of the anterior teeth and first molars. The absence of more than ½ of the enamel indicates a prolonged disturbance in amelogenesis and the presence of stress factors during most of the period of development of the dental crown. The same levels of enamel loss in individual groups of teeth correspond to certain periods of its formation. In their study, McGovern E, et al. [15] found that incisors, premolars and second molars are most often affected, and according to Perniola R, et al. [9], it's the canine teeth. Besides the presence of enamel defects, McGovern E, et al. [15] found a higher rate of caries, enamel erosion and periodontal disease compared to control patients. We observed equally severe le-

sions in incisors and canines, mild involvement of premolars and molars, and no changes in second molars. Brenchley L, et al. [17] described a similar loss of enamel in combination with chalky white and yellow horizontal grooves and pits on the enamel surfaces, as well as taurodontism, without carious lesions and oral candidiasis. In our patient, the teeth were free of carious destruction but with hyperesthesia as a result of enamel loss. Dental hyperesthesia, as well as discomfort in the oral cavity caused by oral candidiasis, are challenges in maintaining good oral hygiene, which could also explain the increased prevalence of periodontal diseases in patients with APECED. In our case, we observed a moderate degree of gingivitis.

Describing two cases of APECED, Welbury R, et al. [18] concluded that enamel hypoplasia can develop both before and after the onset of clinical hypocalcemia, even when there is adequate replacement therapy and biochemical evidence of normal serum calcium levels. Graham A, et al. [10] and Brad GF, et al. [11] have also reported cases of enamel hypoplasia in patients with APECED. Generalized enamel hypoplasia is a relatively common finding in APECED and could be a sign for diagnosis. According to Bello MO, et al. [19], enamel hypoplasia could not always be present. Serum calcium levels are hypothesized to be low enough to cause defects in enamel mineralization but not low enough to affect neuromuscular excitability. Although endocrine-renal mechanisms can maintain serum Ca and P within normal limits, it should be noted that the changes in their levels leads to enamel defects. There is also the autoimmune theory that enamel hypoplasia is independent of hypoparathyroidism and is caused by an autoimmune attack on the enamel organ [1]. Pavliè A, et al. [20] found it likely that ameloblasts or their

proteins would likewise become the target of auto-antibodies. According to them, this would lead to changes in the amount and composition of the organic enamel matrix, the former causing hypoplasia and the latter causing abnormalities in its pattern, primary mineralization and maturation.

Late tooth eruption, hypodontia, and incomplete root formation are other findings observed in APECED.

Although the oral manifestations of the disease take place as secondary priority, they require careful and specialized care. The lack of a sufficient amount of enamel, as well as the presence of damaged enamel, requires an individual judgment in the restorative approach. Enamel hypoplasia, as well as reduced bite leading to a reduced lower facial section and highly pronounced nasolabial folds, necessitated the fabrication of crowns on the first molars and the raising of the bite. Due to the dentinal hypersensitivity, the well-defined border of hypoplasia in the frontal teeth, as well as preserved gingival 1/3 of the enamel, led us to fabricate direct composite restorations through a microinvasive approach and preserve the maximum volume of HDT.

CONCLUSION

Autoimmune polyendocrinopathy candidiasis ectodermal dystrophy (APECED) is a rare but well-defined disorder. Very often, the first clinical signs are present in the oral cavity, and dentists are the first to detect them and refer the patient to the appropriate specialist for the diagnosis of APECED. Considering the amount of healthy hard dental tissues, the presence of dental hypersensitivity and the age of the patient, we preferred a minimally invasive approach to restore dental anatomy, function and aesthetics.

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Address for correspondence:

Kremena Markova
 Department of Operative Dentistry and Endodontics, Faculty of Dental Medicine, Medical University of Plovdiv;
 3, Hristo Botev Blvd., Plovdiv, Bulgaria
 E-mail: kremenadrangova@gmail.com,