MÜSBED 2014;4(3):193-199
DOI: 10.5455/musbed.20140723032043

Olgu Sunumu / Case Report

Clinical, Histological and Radiological Presentation of Root Agenesis in Pseudoxanthoma Elasticum

Mehmet Oğuz Borahan[1], Ömer Birkan Ağralı[2], Leyla Kuru[2], Filiz Namdar Pekiner[1]

[1] Marmara University, Faculty of Dentistry, Department of Oral Diagnosis and Radiology, Istanbul - Turkey
[2]Marmara University, Faculty of Dentistry, Department of Periodontology, Istanbul - Turkey

Yazışma Adresi / Address reprint requests to: Mehmet Oğuz Borahan
Marmara University, Faculty of Dentistry, Department of Oral Diagnosis and Radiology, Nisantasi, Istanbul - Turkey
Elektronik posta adresi / E-mail address: oguzborahan@hotmail.com
Kabul tarihi / Date of acceptance: 23 Temmuz 2014 / July 23, 2014

ÖZET

Pseudoksantoma elastikumda kök agenezisinin klinik, histolojik ve radyolojik olarak incelenmesi

Amaç: Psödoksantoma elastikum (PXE) deri, retina ve kardiyovasküler sistemde elastik liflerin ilerleyen kalsifikasyon ve parçalanması ile karakterize, nadir görülen genetik bir hastalıktır. PXE'nin oftalmik ve dermatolojik belirtileri ve vasküler komplikasyonları heterojendir. Sistemik düzensizliklerin yanı sıra, bir dizi belirtiler bildirilmiştir. Bu olgu raporunun amacı PXE olan bir hastada görülen kök agenezisi sunmaktır.

Vaka Sunumu: PXE tanısı konmuş 22 yaşındaki bayan hasta maloklüzyonu ve estetik şikayet nedenleriyle Marmara Üniversitesi, Diş Hekimliği Fakültesi'ne başvurmuştur. Klinik muayeneye ek olarak, panoramik radyografi ve konik ışınlı bilgisayarlı tomografide kök agenezi görüntülenmiştir. Tedavi planını mekanik periodontal tedavi ve kısa aralıklarla klinik takibi oluşturmuştur.

Sonuç: Radyolojik muayene, dental ve mukozal anomaliler için yararlı ve önemlidir. Sonuç olarak, bu çalışma klinisyenler tarafından dikkate alınması gereken PXE ile birlite kök agenezisi görülen bir hastanın sunumudur.

Anahtar sözcükler: Psödoksantoma elastikum, kök agenezi, konik ışınlı bilgisayarlı tomografi

ABSTRACT

Clinical, histological and radiological presentation of root agenesis in pseudoxanthoma elasticum

Objectives: Pseudoxanthoma elasticum (PXE) is a rare, genetic disorder characterized by progressive calcification and fragmentation of elastic fibers in the skin, retina and cardiovascular system. The ophthalmic and dermatologic expressions of PXE and vascular complications are heterogeneous. In addition to systemic disorders, a number of manifestations have been reported. The aim of this case report is to present, for the first time, root agenesis in a patient with PXE.

Case Report: A 22-year-old girl diagnosed with PXE was referred to the Faculty of Dentistry, Marmara University, with a chief complaint of malocclusion and unaesthetic appearance. In addition to clinical examination, the patient was imaged using panoramic radiography and cone-beam computed tomography, which revealed root agenesis. Treatment plan consisted of mechanical periodontal therapy and recall visits with short intervals.

Conclusion: Radiologic examination is useful and important for dental and mucosal abnormalities. In conclusion, this is the first report of a patient with root agenesis coexisting with PXE which should be taken into account by clinicians.

Key words: Pseudoxanthoma elasticum, root agenesis, cone beam computed tomography

INTRODUCTION

Pseudoxanthoma elasticum (PXE), a genetically determined disorder of elastic fibers, is associated with numerous systemic complications mainly affecting the skin, eyes, and cardiovascular system (1-3). Since 1929, PXE and Groenblad-Strandberg Syndrome have been used synonymously when two Swedish physicians, the ophtalmologist Ester Groenblad and the dermatologist James Strandberg, realized the association between angioid streaks and PXE for the first time and termed the syndrome as Groenblad-Strandberg Syndrome (4,5).

PXE possesses both recessive and autosomal dominant pathways and is characterized by severe malformation of elastic and collagen fibers. The abnormalities of both of these fibers are suggested to be responsible for the laxity of the skin in the affected areas (6). The frequency of PXE is not precisely known because of delayed diagnosis, variable manifestations, and its mostly symptom-free condition (3,6). Its estimated prevalence is 1:25 000–100 000 with an almost 2:1 female preponderance (7,8). The prevalence of PXE may be higher than reported in the literature due to the variable expression and penetrance as well as infrequent occurrence of the disease, which may result in insufficient

awareness of medical specialists. Indeed, given the clinical heterogeneity and different modes of inheritance, it has been difficult to diagnose PXE accurately and to calculate correct genetic risks for genetic counseling purposes (2). Although skin lesions at birth have been also noted, the typical age of onset was reported to be between 15 and 25 years (9).

The clinical manifestations of PXE show extensive inter- and intra-familial variability, but typically involve the skin, eye, and cardiovascular system (8). The skin changes are generally diagnosed from 10 to 15 years, and consist of skin papules and cutaneous laxity mainly on the neck, axillae, groin and flexural area (5). The characteristic eye signs of PXE are angioid streaks and recurrent haemorrhages in the retina which can lead to the loss of central vision (7,8). Cardiovascular manifestations are mainly intermittent claudication because of atherosclerosis, early coronary artery disease, and renovascular hypertension which can result in angina pectoris, myocardial infarction, congestive cardiac failure, renal failure, or stroke (2,7). Calcification of the atrial and ventricular endocardium valves can result in mitral valve prolapse and stenosis requiring antibiotic prophylaxis. PXE patients may also experience bleeding complications, especially gastrointestinal haemorrhages, because of the fragility of calcified submucosal vessels. To reduce this risk, platelet inhibitors such as aspirin and non-steroidal anti-inflammatory drugs should be avoided (7,8).

Patients with PXE typically may have a normal life span, but morbidity and mortality depend on the extent of the systemic involvement (8). The disease is progressive and incurable so far. The affected subjects have an increased propensity for ischemic heart disease, cerebrovascular accidents, visual impairment, and cosmetic deterioration of the skin. Life expectancy is reduced when compared with the general population (9)

Utani et al. (10) stated that PXE patients have a low incidence of oral mucosal lesions seen as yellow-white macules. However, Nozzi et al. (11) pointed out that they are common in French PXE patients. In addition to oral mucosal lesions, other signs including oligodontia, amelogenesis imperfecta, multiple dental impactions and highly arched palate of the oral cavity have been reported (6,8,9,11-13), however, this is the first case showing root agenesis of the permanent teeth in PXE. In this study, oral manifestations of a patient having PXE with root agenesis were presented.

CASE REPORT

A 22-year-old girl was referred to the Faculty of Dentistry, Marmara University, with a chief complaint of malocclusion and unaesthetic appearance. Her medical history presented diagnosis of tumoral calcinosis based on skin biopsy, CT, and MRI findings when she has attended to a hospital at the age of 9 years with complaint of papule on right and left scapula, and atelectasis. In 2005, the patient attended to the Dermatology Clinic for the papular lesion on the neck region. Histopathologic examination of the biopsy samples revealed increased number of short, thick, elastic fibers and subnormal epidermis (Figure 1a-b), and the diagnosis was PXE. Opthalmic examination revealed typical angioid

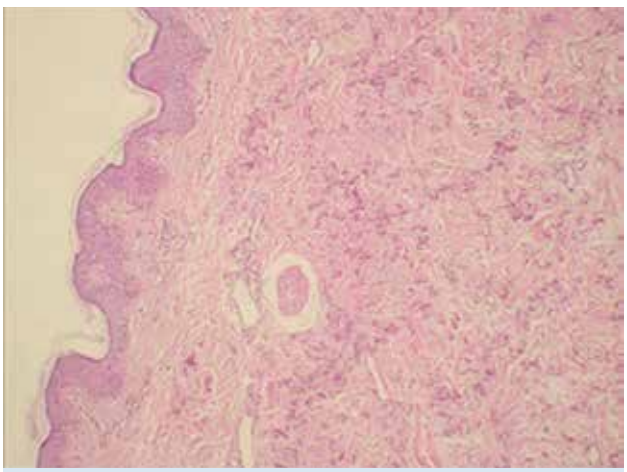

Figure 1a: Degenerated elastic fibers that are shortened, swollen, and become irregular glomus and partial calcification in subepithelial area (HE, x100)

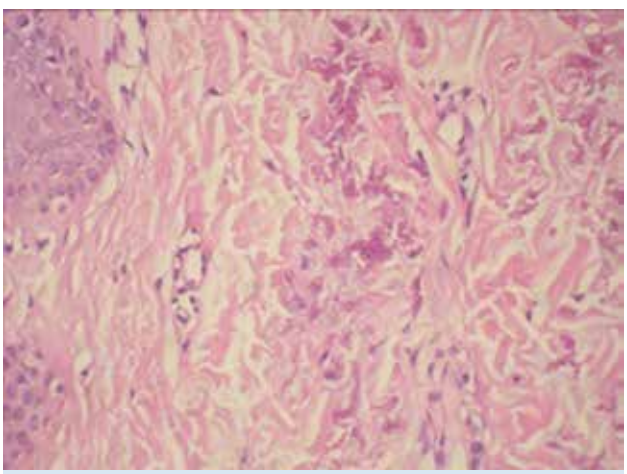

Figure 1b: Degenerated elastic fibers (HE, X400)

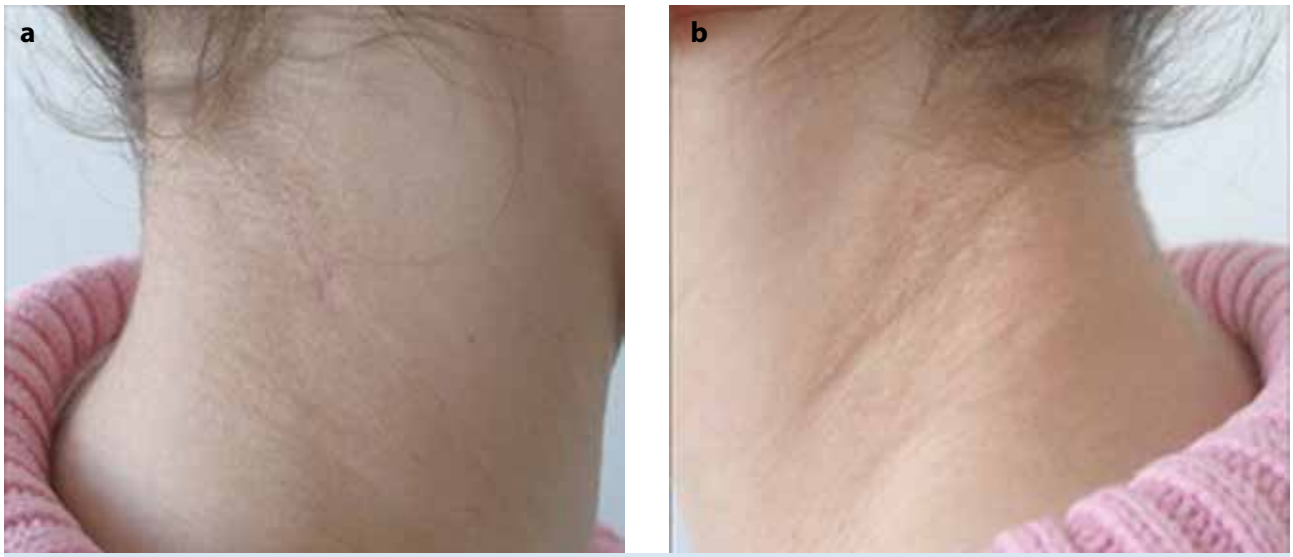

Figure 2a,b: Yellowish, coalescing xanthoma-like papules on both sides of the neck

streaks on both eyes as grey-brown vascular lines which are 4-5 times larger than veins in fundus. The angioid streaks have been reported to be present approximately in 70% of PXE patients.

On extra-oral examination, an average facial proportion and normal temporomandibular joint function were detected. Small, yellowish papules were observed on the skin of neck region on both sides (Figure 2a-b). Although she had no oral mucosal lesions (Figure 3a-e), there were cutaneous deposits of yellow material arranged in linear masses around the lip region extraorally (Figure 4). The intra-oral examination revealed slight gingival inflammation, supra- and sub-gingival dental plaque and calculus deposits, carries on teeth 36, 46 and 26 together with malocclusion. The panoramic radiograph revealed root agenesis (Figure 5). The teeth 37 and 47 were absent without any history of tooth extraction. Teeth number 11, 16, 17, 21, 22 26, 27, 31, 35, 36, 41, 42, 45 and 46 had partial root formation, while teeth number 12, 13, 14, 23, 24, 25, 33, 34, 43 and 44 had no root formation as shown on the dental volumetric tomography (3D Accuitomo; J Morita Mfg Corp, Kyoto, Japan) (Figure 6, 7).

Full mouth periodontal parameters were as follows; plaque index 0.78±0.47, gingival index 0.43±0.52, probing depth 1.44±0.35 mm and mobility 0.11±0.32. The patient received initial periodontal treatment including oral hygiene instructions, scaling and root planning using both hand (Gracey, SG 3/4, 5/6, 7/8, 11/12, 13/14, Minifive, SAS 3/4, Hu-Friedy, USA) and ultrasonic instruments (Cavitron® Bobcat Pro®, Dentsply International Inc, USA). The patient was scheduled a recall program with 6 month intervals.

DISCUSSION

PXE is an inherited connective tissue disorder, characterized by cutaneous, ophthalmological, cardiac and diffuse vascular abnormalities due to progressive calcification of abnormal elastic fibers in the dermis (2). PXE has at least two dominant and two recessive inheritance patterns (3,4). However, the majority of PXE cases are sporadic as shown here (5,14) The present case fits all of the main diagnostic criteria of PXE including characteristic skin lesions exhibiting typical histopathological manifestation and characteristic ocular change as defined by the Consensus Conference of Philadelphia in 1992 14 as category I PXE.

Although most cases of PXE are diagnosed between the ages of 10 to 15 years, cutaneous lesions have been reported in infancy (15,16). Because of subtle and asymptomatic nature of the disorder, there is an average 9-year delay of diagnosis (5,16). Small, yellowish, flat papules develop typically on the neck, and may coalesce to form plaques giving the skin a "gooseflesh" or "plucked chicken" appearance (17). The lesions are asymptomatic but often cause cosmetic concern to the individuals. As the disease progresses, the affected skin may become lax and

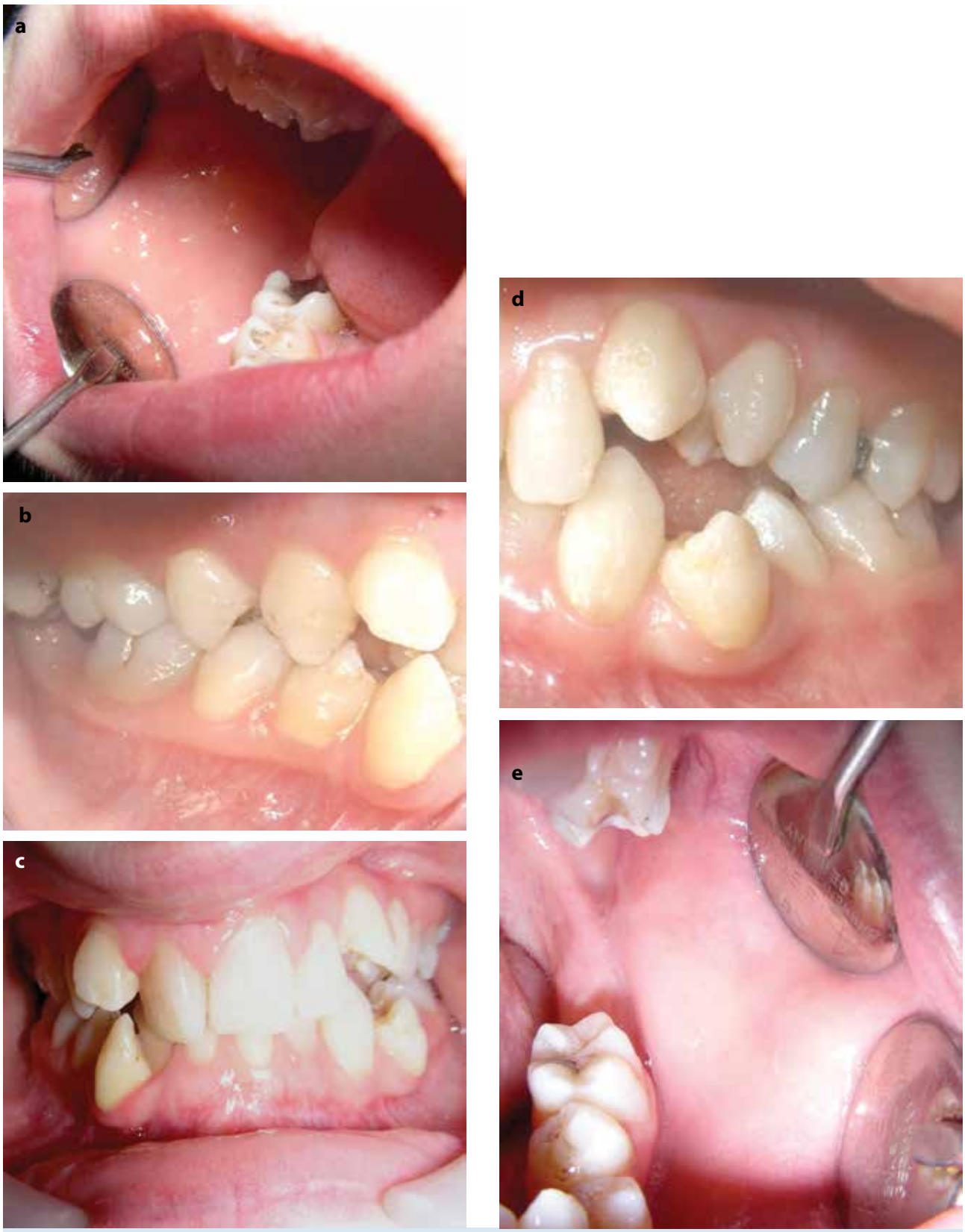

Figure 3a-e: Intraoral view of the patient without mucosal lesions

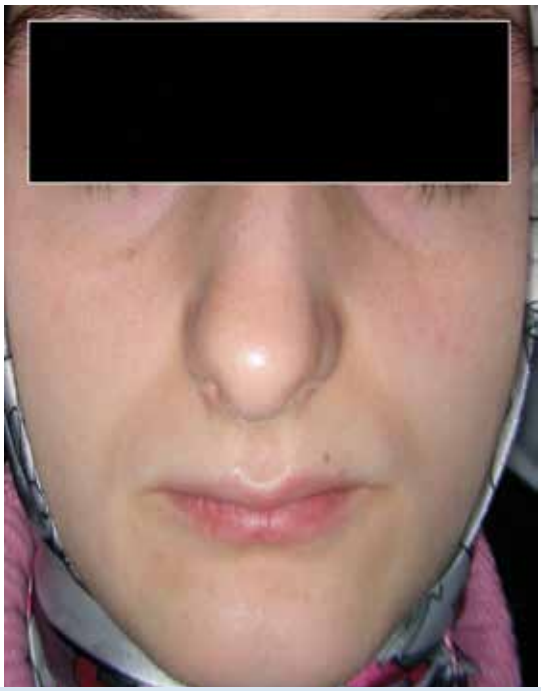

Figure 4: Cutaneous deposits of yellow material arranged in linear masses around the lip region

wrinkled, hanging in folds. Generalised severe laxity of the skin is rare (7).

The histology of PXE present characteristic manifestations. In skin lesions swollen, clumped, and fragmented elastic fibres and calcium deposits have been found in the mid and deep reticular dermis (18). Similar changes occur in elastic fibres of the blood vessels, Bruch's membrane of the eye, endocardium, and other organs. Transepidermal elimination of altered calcified elastic fibres may be occasionally seen (14). In our patient, when she was 14 years old, widespread of short, thick, elastic fibers with partial calcification and subnormal epidermis were detected on the biopsy specimens from neck region and, therefore the diagnosis was considered as PXE.

The characteristic eye signs of PXE are angioid streaks, which are irregular, reddish-brown, or grey lines that radiate from the optic disc (5). Angioid streaks appear to be present in at least 85% of patients with PXE and the typical age of onset is between 15 and 25 years (16). They result from degeneration and calcification of the elastic fibres of the

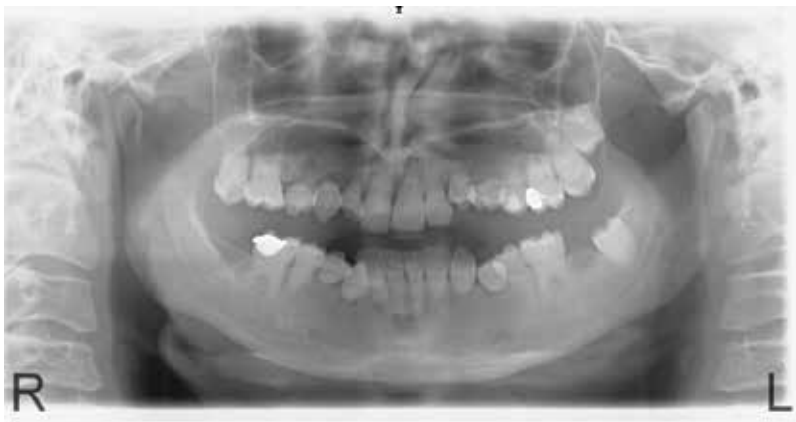

Figure 5: Root agenesis on panoramic radiograph

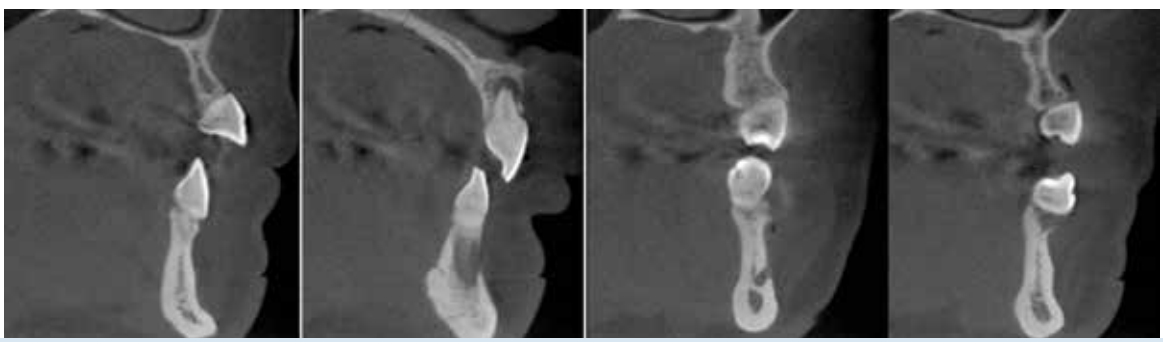

Figure 6: Cross-sectional view of the teeth on dental volumetric tomography

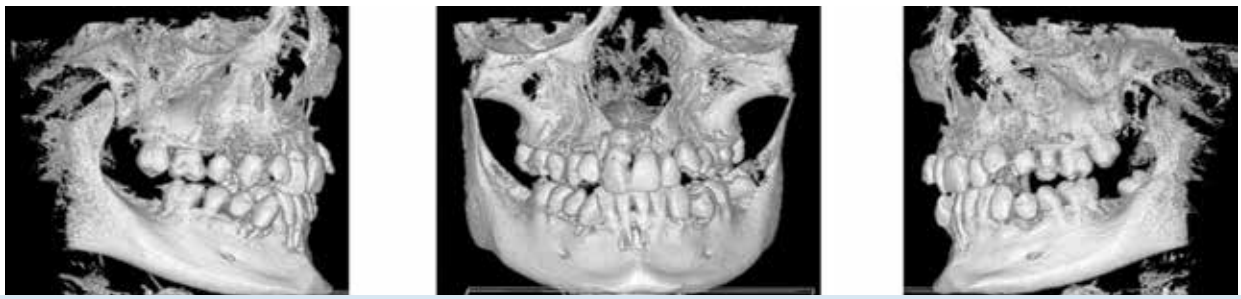

Figure 7: Appearance of three dimensional view of the patient

retina leading to breaks in the Bruch's membrane. Retinal haemorrhages, neovascularisation, and scarring may occur and can lead to loss of central vision (7). Our patient had also typical ocular manifestations of angioid streaks. Cardiological and gastric examinations revealed no problems. It should be kept in mind, however, that some disturbances regarding these systems may occur later in life (8). Lebwohl et al. (14) stated that, there may be weakness or absence of pulses in the arms and legs, accompanied by variable degrees of intermittent claudication at the third decade. Therefore, our patient was assigned for regular medical follow-up for early detection of any possible system involvement in the future.

Lebwohl et al. (19) also stated that two thirds of patients under the age of 30 with PXE had creases at the mental region. They suggested that, considering the elastic tissue content of the skin and the mucosa of the lip and chin, patients with PXE might have morphological changes on lower face development (19). Oral manifestations including yellowish intramucosal nodules on the mucosal surface of the lips, buccal mucosa, soft or hard palate, and tonsillar areas were previously reported (8). Highly arched palate has been reported by Pyeritz et al. (20). Nadeu et al. (21) reported temporomandibular disorder in a 46-year-old-female patient with PXE. On the contrary, our patient had normal face height and morphology, no mental creases, no oral mucosal lesions and no temporomandibular dysfunction. Morrier et al. (7) reported a 10-year-old girl with PXE having amelogenesis imperfecta with a reduction of enamel thickness on the crown of all erupted and unerupted teeth, agenesis of the maxillary right second premolar, delayed eruption of mandibular first premolars, and the presence of large calcifications in all tooth pulp chambers. Sayın et al. (6) presented oligodontia in a patient with PXE who had no maxillary premolars and molars on both sides. They stated that because PXE is a syndrome involving the connective tissues, tooth agenesis may be the result of a defect of the connective tissue forming the teeth or may be independent from PXE. In this case report, root agenesis along with two missing teeth are assumed to be the result of connective tissue defect, in agreement with Sayın et al. (6). To our knowledge, this is the first report of a patient with root agenesis coexisting with PXE in medical and dental literature.

In conclusion, PXE, a disorder affecting the skin, eyes, and cardiovascular system, presents a number of oral manifestations and, therefore, clinicans must be aware of the presence of dental and mucosal abnormalities and radiological examinations play an important role in dental practice for patients with PXE.

Acknowledgements

This study was presented as a poster presentation in 40th Turkish Society of Periodontology, İzmir, TURKEY, 14-16 May 2010 and derived from the study presented as a poster in 17th International Congress of Dentomaxillofacial Radiology on 28 June-2 July 2009, Amsterdam, The Netherlands and supported by Marmara University Scientific Research Project Council (Project no: SAG-D-300409-0105).

REFERENCES

1. Gorlin RJ, Cohen MM, Levin LS. Syndromes of the head and neck. 3rd ed. Oxford: Oxford University Press; 1990.
2. Hu X, Plomp AS, van Soest S, Wijnholds J, de Jong PT, Bergen AA. Pseudoxanthoma elasticum: a clinical, histopathological, and molecular update. Surv Ophthalmol. 2003; 48: 424-438.
3. Miki K, Yuri T, Takeda N, Takehana K, Iwasaka T, Tsubura A. An autopsy case of pseudoxanthoma elasticum: histochemical characteristics. Med Mol Morphol. 2007; 40: 172-177.
4. Viljoen D. Pseudoxanthoma elasticum (Groenblad-Strandberg syndrome). J Genet Med. 1988; 25: 488-490.
5. Finger RP, Charbel Issa P, Ladewig MS, Götting C, Szliska C, Scholl HP et al. Pseudoxanthoma elasticum: genetics, clinical manifestations and therapeutic approaches. Surv Ophthalmol. 2009; 54: 272-285.
6. Sayin MO, Atilla AO, Esenlik E, Ozen T, Karahan N. Oligodontia in pseudoxanthoma elasticum. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2007; 103: e60-64.
7. Morrier JJ, Romeas A, Lacan E, Farges JC. A clinical and histological study of dental defects in a 10-year-old girl with pseudoxanthoma elasticum and amelogenesis imperfecta. Int J Paediatr Dent. 2008; 18: 389-395.
8. Laube S, Moss C. Pseudoxanthoma elasticum. Arch Dis Child. 2006; 90: 754–756.
9. Moreira AP, Feijó FS, Neffá Pinto JM, Martinelli IL, Rochael MC. Pseudoxanthoma Elasticum. Dermatol Online J. 2009; 15: 7.
10. Utani A, Tanioka M, Yamamoto Y, Taki R, Araki E, Tamura H, Miyachi Y. Relationship between the distribution of pseudoxanthoma elasticum skin and mucous membrane lesions and cardiovascular involvement. J Dermatol. 2010; 37: 130-136.
11. Nozzi L, Grenier de Cardenal D, El Alamy F, Duyninh T, Martin L. Prevalence of involvement of the oral mucosa and periodontal tissue in pseudoxanthoma elasticum. Ann Dermatol Venereol. 2008; 135: 183-186.
12. Pope FM. Autosomal dominant pseudoxanthoma elasticum. J Med Genet. 1974; 11: 152-157.
13. Velázquez-Cayón RT, Torres-Lagares D, Yáñez-Vico RM, Cárabe-Fernández A, Benítez-Rodríguez J, Serrera-Figallo MA, Gutiérrez-Pérez JL. Dental impactions related to pseudoxanthoma elasticum. J Oral Maxillofac Surg. 2012; 70: e214-216.
14. Lebwohl M, Neldner K, Pope FM, De Paepe A, Christiano AM, Boyd CD, Uitto J, McKusick VA. Classification of pseudoxanthoma elasticum: report of a consensus conference. J Am Acad Dermatol. 1994; 30:103-107.
15. Sherer DW, Bercovitch L, Lebwohl M. Pseudoxanthoma elasticum: significance of limited phenotypic expression in parents of affected offspring. J Am Acad Dermatol. 2001; 44: 534–537.
16. Hacker SM, Ramos-Caro FA, Beers BB, Flowers FP. Juvenile pseudoxanthoma elasticum: recognition and management. Pediatr Dermatol. 1993; 10: 19-25.
17. Galadari H, Lebwohl M. Pseudoxanthoma elasticum: Temporary treatment of chin folds and lines with injectable collagen. J Am Acad Dermatol. 2003; 49: 265-266.
18. Miraglia E, Visconti B, Bruni C, Calvieri C, Guistini S. Pseudoxanthoma elasticum (PXE): 25 case reports and follow up. Prevent Res. 2012; 2: 254-260.
19. Lebwohl M, Lebwohl E, Bercovitch L. Prominent mental (chin) crease: a new sign of pseudoxanthoma elasticum. J Am Acad Dermatol. 2003; 48: 620-622.
20. Pyeritz RE, Weiss JL, Renie WA, Fine SL. Pseudoxanthoma elasticum and mitral-valve prolapse. N Engl J Med. 1982; 307: 1451-1452.
21. Nadeau C, Kuperstein AS, Mupparapu M, Stoopler ET. Temporomandibular disorder in a patient with pseudoxanthoma elasticum: a case report and review. Spec Care Dentist. 2013; 33: 255-259.