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Recurrent aphthous ulcers in Fanconi's anaemia: a case report

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Summary. Fanconi's anaemia (FA) is an autosomal recessive disorder that is clinically characterized by aplastic anaemia, congenital malformations of the renal, cardiac, skeletal and skin structures, and an increased predisposition to malignancies. Patients with FA often present with bleeding and infection, which are symptoms related to thrombocytopenia and neutropenia. There are few reports of the oral manifestations of FA. We describe oral aphthous ulcerations in two siblings with FA. There was a rapid improvement and healing of ulcers after blood transfusions and increased haemoglobin levels. This may support the role of severe anaemia in oral ulcerations.

Introduction

Fanconi's anaemia (FA) is an autosomal recessive disorder that is clinically characterized by aplastic anaemia, congenital malformations of the renal, cardiac, skin and skeletal structures, and an increased predisposition to malignancies. It was first described by Guido Fanconi in 1927 with the presentation of three brothers who had pancytopenia as well as physical abnormalities [1]. The prevalence is one in 360 000 individuals, and physical manifestations may include various malformations such as: short stature; abnormality of the thumbs; microcephaly; *café au lait*, hypopigmented spots; renal malformation; and growth retardation. Some patients with FA have no physical abnormalities [2,3]. The disease often appears in the first decade of life, with a mean age of onset of 6·5 years [4,5]. Patients with FA often present with symptoms related to thrombocytopenia and neutropenia, such as cutaneous bleeding and infections.

The average length of survival is 25 years, but some patients may live until the third or fourth decade of life. The major life-threatening problems are leukaemia and other malignancies [6,7]. These patients are at risk of developing acute myelogenous leukaemia or myelodysplastic syndrome [8,9]. In addition, they may develop non-haematological secondary malignancies with a high incidence of hepatocellular and squamous cell carcinomas (SCCs) [10–12]. The most frequent oropharyngeal tumours are seen on the tongue, gingivae, cricoid, mandible and pharynx. Cases of SCC of the dorsum of the tongue in patients with FA have been reported previously [13–15].

Besides cancer, the oral findings reported in FA include generalized microdontia and aggressive periodontitis [4,12,16]. As in other immune deficiencies, inflammatory lesions are caused by low blood cell counts. A review of previous cases failed to find any mention of oral ulcerations as a feature of FA [4,11–16]. Apthous stomatitis was, however, reported in an patient with FA and periodic fever, apthous stomatitis, pharyngitis, adenitis (PFAPA) syndrome [17]. This paper describes the presence of apthous ulcers in two patients diagnosed with FA, but without PFAPA syndrome.

Case report

Case 1

A 16-year-old girl was referred to the Faculty of Dentistry and Department of Periodontology of the University of Ondokuz Mayis, Kurupelit-Samsun, Turkey, in January 2002 with a main complaint of

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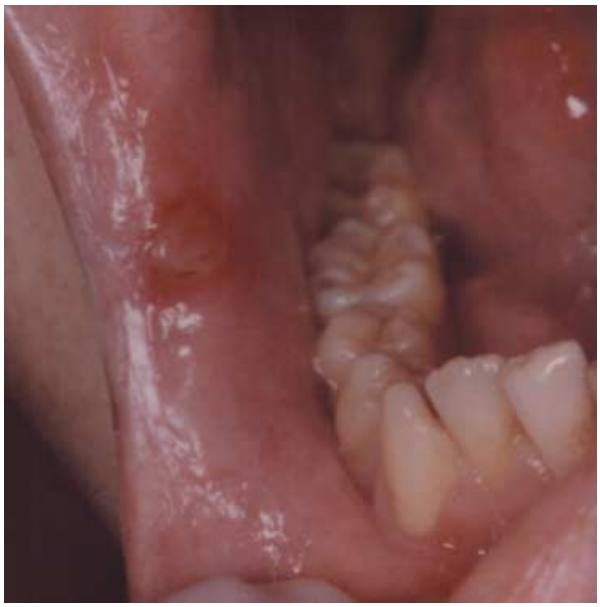

Fig. 1. Case 1: aphthous lesion at the commisura labiorum.

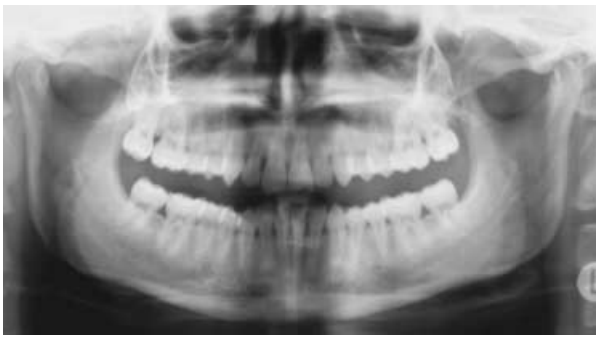

Fig. 2. Orthopantomograph of case 1.

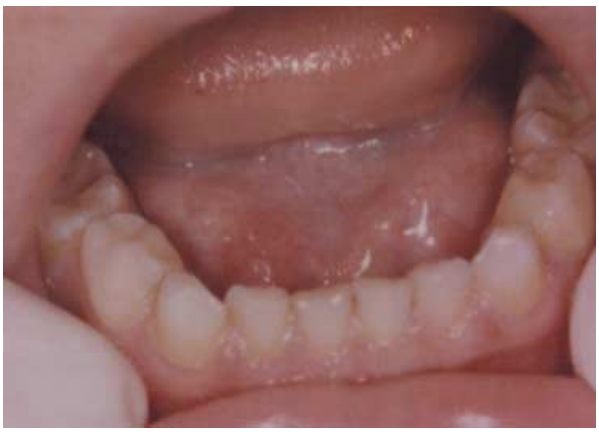

Fig. 3. Case 2: aphthous lesion on the mouth floor.

lesions in her mouth. The diagnosis of FA was made at the age of 2·5 years. The subject had a long history of recurrent mouth ulcers in various regions of the oral mucosa which healed in about 2 weeks. The family history revealed the death of the first child in the family at the age of 7 years as a result of anaemia; a 15-year-old brother was healthy and another 7-year-old brother was under treatment for the same disease. Their parents were consanguineous. Oral and periodontal examination revealed painful aphthous ulcerations greater than one centimetre in diameter on the tongue, the buccal mucosa, soft palate and labial commissures (Fig. 1). The subject also had plaque-induced gingivitis. There were no abnormal radiographic findings (Fig. 2). Physical examination revealed normal intelligence, small stature, pale and hyperpigmented skin, and that the right thumb was hypoplastic.

The subject's blood counts prior to transfusion were: haemoglobin (Hb), 58 g/L; platelet (PLT), 60×10^9/L; and white blood cell (WBC), $1{\cdot}8 \times 10^9$/L (with 72% lymphocytes and 28% neutrophils on peripheral blood smear). Erythrocyte suspension (red blood cells) was transfused because of her severe anaemia and she had required monthly (when necessary) blood transfusion intermittently for the past 3 years. Some 2 months after her last blood transfusion (at the end of February 2002), no aphthous lesions were observed, but there were ragades. The subject's blood counts at this time were: Hb, 110 g/L; PLT, 73×10^9/L; and WBC, $2{\cdot}0 \times 10^9$/L. One month later (3 months after the last blood transfusion), aphthous lesions had recurred and her blood counts were: Hb, 79 g/L; PLT, 53×10^9/L; and WBC, $1{\cdot}6 \times 10^9$/L. The subject's Hb level was brought up to normal after erythrocyte transfusion and the lesions healed uneventfully again.

Case 2

The 7-year-old brother of the case described above had a diagnosis of FA at the age of 7 months. His physical examination revealed short stature, skin pallor, multiple *café au lait* spots, ecchymoses in the infra-orbital area and lips, and the absence of the first metacarpal bone on the left. Intra-oral examination revealed a single aphthous ulcer in the floor of the mouth (Fig. 3). Periodontal examination and radiography were normal. The subject's current blood counts were: Hb, 99 g/L; PLT, 21×10^9/L; and WBC, $4{\cdot}3 \times 10^9$/L (with 88% lymphocytes and 12% neutrophils on peripheral blood smear). He received instructions for oral hygiene since his

ulcers were lower in number and frequency compared to his sister.

Discussion

Blood diseases do not appear to cause gingival or oral mucosal disease themselves, but they do accelerate tissue changes and tissue response to dental plaque. Although FA is a common form of inherited bone-marrow disorder, there are few reports of oral findings in FA. Opinya *et al*. first reported a 24-year-old male with severe horizontal alveolar bone loss, black pigmentation on the oral mucosa and palate, a furred and bluish tongue, extreme tooth mobility, gingival recession, suppuration from periodontal pockets deeper than 10 mm, and bleeding on probing [16]. Engel *et al*. reported a 30-year-old, fully edentulous woman with FA undergoing bone grafting and implant surgery, but did not provide detailed information about her periodontal status [12]. The relationship between FA and aggressive periodontitis was first reported in a study by Nowzari *et al*. [3]. Batirbaygil *et al*. reported the case of a 15-year-old boy with generalized hypoplasia of the teeth, and anomalies in the shape and size of his teeth [18]. Yalman *et al*. [19] compared the dental caries, micro-organisms related to these caries, salivary status and periodontal health of patients with FA who were treated with bone-marrow transplantation (BMT) and those who received no transplant. The above authors reported that plaque index, gingival index, periodontal pocket depths and bleeding on probing scores were significantly higher in cases who had not received BMT. This can partly be related to the regular dental care provided as part of BMT services [19]. On the other hand, aphthous lesions in FA have only been reported as a feature in PFAPA [17]. Our cases are of interest because they show aphthous lesions without PFAPA syndrome and spontaneous healing of ulcers following erythrocyte (red blood cell) transfusions.

The aetiology and pathogenesis of aphthous ulcerations in FA are not clear. Nevertheless, both patients had reduced neutrophil counts and anaemia. One explanation might be decreased immunity. It may indicate some sort of breakdown in the cellular immunity of the patient at the time of occurrence of aphthous lesions. These two cases suggest that aphthous ulcerations may be more common in patients with FA. There is a need for closer collaboration between medical and dental colleagues in the correct management of these patients. Better understanding of the aetiology of aphthous ulcerations in FA is still needed.

Résumé. L'anémie de Fanconi (FA) est une maladie autosomique récessive caractérisée cliniquement par une anémie aplasique, des malformations congénitales au niveau rénal, cardiaque, squelettaire, cutané ainsi qu'une prédisposition accrue aux cancers. Les patients avec FA sont souvent victimes de saignements et d'infections, symptômes liés à la thrombocytopénie et la neutropénie. Il ya très peu de cas décrits concernant les manifestations buccales de FA. Nous décrivons des ulcérations buccales aphteuses chez deux enfants apparentés atteints de FA. Des transfusions sanguines et des niveaux plus élevés d'hémoglobine ont permis une amélioration rapide et une guérison des ulcères. Ceci peut supporter l'idée du rôle de l'anémie sévère dans les ulcérations buccales.

Zusammenfassung. Fanconi Anämie ist eine autosomal rezessive Erkrankung die sich äußert in Anämie, angeborenen Fehlbildungen von Niere, Herz, Skelett, Haut sowie einer Prädisposition zur Entwicklung von Malignomen. Patienten mit Fanconi Anämie müssen häufig wegen Blutungen oder Infektionen behandelt werden als Folge von Thrombopenie und Neutropenie. Es gibt nur wenige Berichte über orale Manifestationen der FA. Wir beschreiben aphthöse Ulzerationen bei zwei Geschwistern mit Fanconi Anämie. Unter erhöhten Hämoglobinspiegeln nach Transfusion kam es zur raschen Abheilung dieser Ulzerationen.

Dies könnte auf eine Rolle der Anämie bei der Entstehung der Ulzerationen hinweisen.

Resumen. La anemia de Fanconi (AF) es un desorden autosómico recesivo caracterizado clínicamente por anemia aplásica, malformaciones congénitas renales, cardíacas, esqueléticas, dermatológicas y una mayor predisposición a malignizaciones. Los pacientes con AF presentan con frecuencia sangrado e infección, síntomas relacionados con la trombocitopenia y la neutropenia. Hay pocos informes sobre las manifestaciones orales de la AF. Nosotros describimos ulceraciones aftosas orales en dos hermanos con AF. Hubo una mejoría rápida y curación de las úlceras después de las transfusiones de sangre y la elevación de los niveles de hemoglobina. Esto puede apoyar el papel de la anemia severa en las úlceras orales.

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