CASE REPORT

DOI: 10.5336/caserep.2022-91849

Evaluation of Intraoral Lesions of a Patient with Fanconi Anemia: A Rare Case Report

Zeliha Merve SEMERCİ[a], Hümeyra TERCANLI ALKIŞ[a], Sevcihan GÜNEN YILMAZ[a]

[a]Departmant of Oral and Maxillofacial Radiology, Akdeniz University Faculty of Dentistry, Antalya, Türkiye

This original article presented in "5th International Health Sciences and Life Congress" as poster presentation, March 10-12, 2022, Burdur, Türkiye.

ABSTRACT Fanconi anemia (FA) is a rare autosomal recessive inherited syndrome characterized by chromosomal instability, aplastic anemia and cancer predisposition, accompanied by congenital anomalies. In these patients, the probability of tumor development in the head and neck region is higher than in the normal population. A patient with fanconi aplastic anemia was admitted to our clinic due to painful lesions in the oral cavity. A brush biopsy was taken from the relevant lesions and sent for histopathological examination. No atypical cells were found in the biopsy result, and the patient was called for regular dental check-ups due to the increased risk of malignancy. In this case report, it is aimed to examine the findings of a patient with FA and the necessity of monitoring the intraoral lesions in terms of malignancy risk, in the light of the literature.

Keywords: Fanconi anemia; squamous cell carcinoma; mouth neoplasms

Fanconi aplastic anemia (FA) is a rare aplastic anemia characterized by congenital malformations. Its estimated prevalence is 1:130,000.[1,2] It results from loss of function of at least one gene of the FA/BRCA pathway required for DNA repair. In these patients, there is a marked progressive bone marrow depression with pancytopenia, especially predisposition to urogenital, head and neck malignancies.[3] The physical phenotype of FA patients is extremely heterogeneous; approximately 60% of patients have at least one physical finding. The most common findings are short stature, hyper-hypopigmented areas, radial bone abnormalities including thumb abnormalities, microcephaly, microphthalmia, structural kidney abnormalities, and hypogonadism.[4] Not all patients have malformations or pancytopenia at birth. The first clinical sign may be hematological malignancies or other complications.[5,6] Solid tumors are most commonly seen in the anogenital region, head and neck region and are 500-700 times more common in patients who have undergone hematopoietic stem cell transplantation (HSCT) compared to the normal population.[7,8]

This case report was aimed to examine the oral lesions and histopathological evaluation of a patient with painful intraoral lesions, who was diagnosed with FA at the age of 2 years and underwent bone marrow transplantation, in terms of malignancy risk.

CASE REPORT

A 19-year-old female patient, was admitted to our clinic because of painful sores in the oral region. Informed consent was obtained from the patient.

From the patient's anamnesis, it was learned that the patient was diagnosed with FA at the age of 2 (in 2005) and had a bone marrow transplant at the age of 10 (in 2013). She was born as a result of consanguineous marriage. Extraoral examination revealed a developmental disorder and thumb anomaly (Figure 1).

Correspondence: Zeliha Merve SEMERCİ
Departmant of Oral and Maxillofacial Radiology, Akdeniz University Faculty of Dentistry, Antalya, Türkiye
E-mail: merveertugrul@outlook.com

Peer review under responsibility of Turkiye Klinikleri Journal of Case Reports.

Received: 09 Jun 2022 ***Received in revised form:*** 21 Sep 2022 ***Accepted:*** 14 Oct 2022 ***Available online:*** 24 Oct 2022

FIGURE 1: The patient's thumb anomalies.

In her detailed anamnesis, it was learned that she had bilateral cheek biting habits.

As a result of the clinical examination of the patient, a tendency to hemorrhage, ulcerations, gingivitis, rotated teeth, apthous-like lesions due to trauma were observed in the posterolateral and anterior regions of the tongue. It was learned that apthous-like lesions were painful and the patient had been aware of these lesions for one month. It was learned that the patient did not use any medication other than vitamin D supplementation.

Widespread erosive lesion due to trauma on the left cheek, white hyperkeratotic areas with leukoplakia appearance on the dorsum of the tongue, and lesions due to biting on the bilateral posterolateral parts of the tongue were observed (Figure 2a,b). Vitamin-D deficiency was detected in the patient's blood values (Table 1). The patient was told that the habit of biting the cheek triggered the lesions and that she should quit this habit. She was called for control 2 weeks later. Although the lesions regressed 2 weeks later, due to the increased risk of squamous cell carcinoma (SCC) in FA patients, a brush biopsy was taken from the posterior region of the dorsum of the tongue and left cheek, and they were referred to pathology (Figure 3a,b). Oral brush biopsy is a non-invasive diagnostic method. It may be useful in the early diagnosis of mucosal lesions. However, in lesions with high suspicion of malignancy, incisional biopsy for histopathological evaluation is mandatory.[9] In this patient, brush biopsy was preferred because it was determined that the aphthous-like ulcers were due to trauma and the lesions regressed as a result of periodic follow-ups. Benign oral epithelial cells were observed in the pathology report and no atypical cells were detected. A month later, the patient's lesions regressed again and the patient's regular follow-up continues.

DISCUSSION

FA is a rare autosomal recessive syndrome defined by chromosomal instability, aplastic anemia, and predisposition to cancer, accompanied by congenital anomalies. It is often seen in the first decade of life, especially around 8 years of age. It occurs with the same frequency in both males and females, among all nationalities.[9]

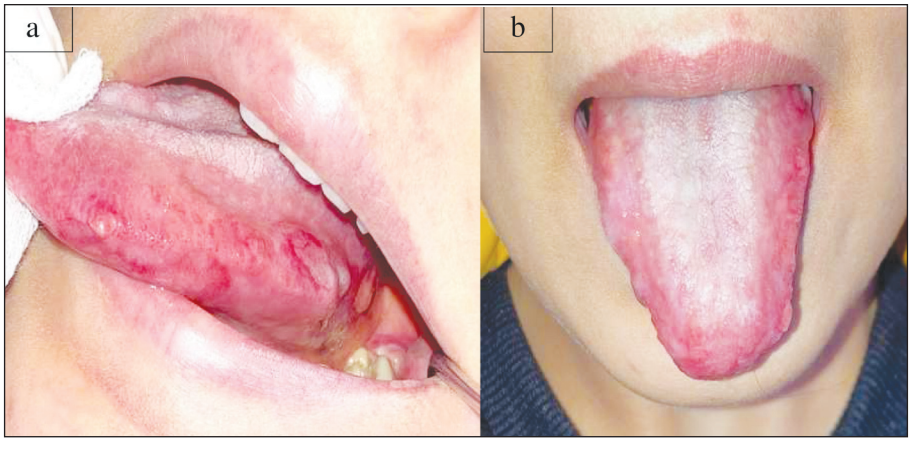

FIGURE 2: a, b) Ulcerative lesions due to trauma on the posterolateral and anterior areas of the tongue.

TABLE 1: Blood levels taken from the subject.

Tests applied	Result	Unit of	Reference
Hemoglobin	13.4	g/dL	12-16
Hematocrit	40.2	%	35-52
Leukocyte	7.11	Th/mm^3	4.37-9.68
Folate	10.30	g/dL	4.8-37.3
Erythrocyte	4.55	Million/mm^3	4-6
Ferritine	77.70	g/dL	13-150
Vitamin B_{12}	300.00	g/dL	197-771
25-OH Vit D3	10.10 *L	g/dL	30-100

In patients with FA, the risk of developing head and neck cancer, especially SCC, is between 200 and 1000 times.[10] In addition, the low overall survival rate of patients with SCC and FA reinforces the need for early detection of SCC.[1,2,11] Since the tendency to malignancy increases in these patients; regular dental examination is much more important than the normal population, as infections originating from the oral region can affectthe systemic condition.

According to the literature, it has been reported that the risk of developing SCC over the age of 40 is 20%. It is known that an increased risk of SCC is associated with chromosomal instability. The increased incidence of SCC in patients who have undergone HSCT is explained by the exposure to radiotherapy and chemotherapy during the transplant process.[12]

Carcinomas occur in early age (20-40 years) and are associated with an increased sensitivity to radiotherapy, and they are especially localized in the oral cavity and the tongue is the most frequently affected organ.[11] Due to the defect in DNA repair in these patients, there is sensitivity to chemotherapy and radiotherapy, therefore surgical resection of the tumor is recommended. Radiotherapy or chemotherapy can be applied in coordination with surgery in large tumors whose diagnosis is delayed or difficult to surgery.[13] HSCT is the only way to correct the hematological disorder in FA cases. Graft versus host disease (GVHD) is one of the most important complications of allogeneic transplantation. In its simplest terms, it occurs as a result of foreign recognition of donor T cells to acceptor antigens. Tissue damage associated with GVHD is more severe in these patients due to the defect in the cell repair mechanism.[14]

In addition to the existing increased tumor risk, there is a higher risk of solid tumor development in patients who have successfully undergone HSCT. Rosenberg et al. compared 145 transplanted patients with FA with 117 non-transplanted patients in terms of the risk of developing SCC and reported that the risk of developing SCC increased 4.4 times in the transplant group, depending on age. The risk of developing SCC 15 years after transplantation has been reported to be 10.1% per year, which is dramatically higher than the general population.[15]

In this case report, the oral findings of a patient with FA, a rare hereditary anomaly, were presented and follow-up appointment scheduled every 3 months

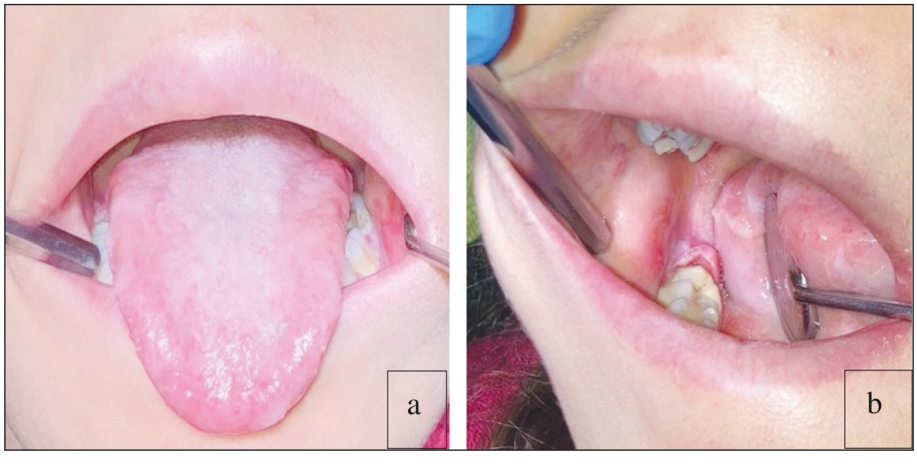

FIGURE 3: a, b) Regression in oral lesions.

in terms of increased risk of oral malignancy. Although the lesions in the case were thought to be of traumatic origin, a brush biopsy was taken from the patient because of the above-mentioned malignancy tendency and the patient's age was close to the age of onset of carcinomas. In our patient, benign epithelial cells were observed as a result of brush biopsy pathology, and the lesions regressed after a 1-month follow-up. The patient was informedand called for regular control in terms of intraoral lesions.

In conclusion, considering the risk of head and neck malignancies to settle in the oral cavity in patients with FA, painful intraoral lesions and periodontal pathologies detected in these patients should be taken into account, regular dental check-ups should be recommended, and patients should be informed about the importance of early diagnosis. A multidisciplinary team of medical and dental specialists should be included in the medical and dental treatment of patients with FA.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

All authors contributed equally while this study preparing.

REFERENCES

1. Pizzo PA. The pancytopenias. Chapter 475. In: Berhman RE, Kliegman RM, Arvin AM , eds. Nelson Textbook of Pediatric. 15th ed. Philadelphia: WB Saunders Company; 1996. p.1412-4.
2. Rosenberg PS, Tamary H, Alter BP. How high are carrier frequencies of rare recessive syndromes? Contemporary estimates for Fanconi Anemia in the United States and Israel. Am J Med Genet A. 2011;155A(8):1877-83. [Crossref] [PubMed] [PMC]
3. Moreno OM, Paredes AC, Suarez-Obando F, Rojas A. An update on Fanconi anemia: clinical, cytogenetic and molecular approaches (Review). Biomed Rep. 2021;15(3):74. [Crossref] [PubMed] [PMC]
4. Shimamura A, Alter BP. Pathophysiology and management of inherited bone marrow failure syndromes. Blood Rev. 2010;24(3):101-22. [Crossref] [PubMed] [PMC]
5. Mehta PA, Tolar J. Fanconi Anemia. In: GeneReviews®. Adam MP, Ardinger HH, Pagon RA, et al, eds. Seattle, WA: University of Washington; 2002.
6. Krausz C, Riera-Escamilla A, Chianese C, Moreno-Mendoza D, Ars E, Rajmil O, et al. From exome analysis in idiopathic azoospermia to the identification of a high-risk subgroup for occult Fanconi anemia. Genet Med. 2019;21(1):189-94. [Crossref] [PubMed]
7. Alter BP, Giri N. Thinking of VACTERL-H? Rule out Fanconi Anemia according to PHENOS. Am J Med Genet A. 2016;170(6):1520-4. [Crossref] [PubMed]
8. Sadık E, Toraman Alkurt MT. Oral mukozanın şüpheli lezyonlarının teşhisinde kullanılan yardımcı yöntemler [Adjunctive techniques for examination of suspicious lesions of oral mucosa]. Gazi Üniversitesi Diş Hekimliği Fakültesi Dergisi. 2012;29(3):201-8. [Link]
9. Ambarkova V. Oral and dental manifestations of fanconi anemia. Galician Medical Journal. 2021;28(3):E202132. [Crossref]
10. Amenábar JM, Torres-Pereira CC, Tang KD, Punyadeera C. Two enemies, one fight: An update of oral cancer in patients with Fanconi anemia. Cancer. 2019;125(22):3936-46. [Crossref] [PubMed]
11. Furquim CP, Pivovar A, Amenábar JM, Bonfim C, Torres-Pereira CC. Oral cancer in Fanconi anemia: Review of 121 cases. Crit Rev Oncol Hematol. 2018;125:35-40. [Crossref] [PubMed]
12. Rosenberg PS, Greene MH, Alter BP. Cancer incidence in persons with Fanconi anemia. Blood. 2003;101(3):822-6. [Crossref] [PubMed]
13. Kutler DI, Patel KR, Auerbach AD, Kennedy J, Lach FP, Sanborn E, et al. Natural history and management of Fanconi anemia patients with head and neck cancer: a 10-year follow-up. Laryngoscope. 2016;126(4):870-9. [Crossref] [PubMed] [PMC]
14. Yeşilipek MA. Hematopoetic stem cell transplantation in children. Turk Pediatri Ars. 2014;49(2):91-8. [Crossref] [PubMed] [PMC]
15. Rosenberg PS, Socié G, Alter BP, Gluckman E. Risk of head and neck squamous cell cancer and death in patients with Fanconi anemia who did and did not receive transplants. Blood. 2005;105(1):67-73. [Crossref] [PubMed]