Journal of Dental and Oral Health

ISSN: 2369-4475 Review Article

Anemia Fanconi from the Dentist View

This article was published in the following Scient Open Access Journal:
Journal of Dental and Oral Health
Received February 24, 2021; **Accepted** March 03, 2021; **Published** March 08, 2021

Ambarkova Vesna

MSc, DDS,PhD, Senior Research Fellow, University St. Cyril and Methodius, Faculty of Dental Medicine, Department of Paediatric and Preventive Dentistry, Skopje, Republic of North Macedonia

Abstract

Anemia Fanconi (AF) is a rare disease, which bears the name of the famous Swiss paediatrician Guido Fanconi, who first discovered the disease. Congenital abnormalities of the eyes, ears, heart, absent or deformed kidneys, urogenital system are common. There is a delay in physical development. Intelligence in patients with Anema Fanconi is usually normal. The most serious problems with Fanconi anemia are associated with the gradual development of bone marrow disorders. Many patients with Fanconi anemia develop leukemia or myelodysplastic syndrome later, as well as other oncological diseases. Extreme susceptibility to squamous cell carcinoma of the head and neck` and oral cancer is noted within patients with Fanconi anemia. The interdisciplinary team of medical and dental specialists must be included in the medical and dental treatment of patients with Fanconi anemia.

Keywords: Fanconi anemia; Caries experience; Dental caries; Special dental care

Introduction

Anemia Fanconi (AF) is a rare disease, which bears the name of the famous Swiss paediatrician Guido Fanconi, who first discovered the disease [1]. The birth rate of children with AF on average is approximately 1 case per 350,000 newborns. It occurs with the same frequency in both male and female, among all nationalities [1]. Anemia Fanconi as a congenital disorder that is inherited in an autosomal recessive manner. This means that even if the father and mother are carriers of the defective gene (they can be completely clinically healthy), then with each delivery there is a 25% risk for a child to have this disease. Therefore, the incidence of AF is increased in communities of people where marriages are closely related. At least 22 faulty genes are associated with Anemia Fanconi [2].

Signs and symptoms

Congenital aplastic anemia is usually detected at 4 to 12 years of age through pancytopenia. It can occur as isolated anemia or as anemia together with leukopenia or thrombocytopenia. Children with Fanconi anemia often have characteristic external signs. Possible features of known skeletal malformations (for example, thumbs, wrist bones, thighs, spine, ribs), short stature, “bird face” (underdeveloped beard), skin changes - hypopigmented spots, brown colored surfaces or skin covered with coffee. Congenital abnormalities of the eyes, ears, heart, absent or deformed kidneys, urogenital system are common [3,4]. There is a delay in physical development. Intelligence in patients with AF is usually normal. More than 50% of patients have physical abnormalities. These also may include: abnormalities of the brain - small head size, increased fluid in the brain, genital abnormalities [4].

The most serious problems with Fanconi anemia are associated with the gradual development of bone marrow disorders. They usually become noticeable at the age of 5-10 years and then deepen over time, although sometimes the disease is almost asymptomatic for many years. Decreased platelet count leads to increased bleeding (nasal bleeding, bruising “for no reason”), anemia due to decreased red blood cell count leads to weakness and fatigue, and decreased leukocyte count (neutrophil) leads to poor resistance to infections. Many patients develop leukemia or myelodysplastic syndrome [5] later, as well as other oncological diseases [2,6].

Diagnostics

It is possible to suspect Fanconi anemia in a child with some of the external signs

***Corresponding Author:** Vesna Ambarkova PhD,. MSc, DDS, University St. Cyril and Methodius, Faculty of Dental Medicine, Department of Paediatric and Preventive Dentistry, Mother Theresa 17 University Dental Clinic Center Sv.Pantelejmon Skopje 1000, Republic of North Macedonia, Tel ++38970686333, Email: vesna.ambarkova@gmail.com

listed above, combined with changes in clinical blood counts. Other external signs which are worth to be mentioned are hyperreflexia, hypogonadism, microcephaly, microphthalmia, strabismus, ptosis, nystagmus, and ear abnormalities. Macrocytosis, high MCV, high HbF, high erythropoietin can be seen in the blood count of patients with Fanconi anemia. There may be a deficiency of all blood cells, as well as a decrease in the number of platelets or leukocytes. The Diepoxybutane (DEB) test is used to make a diagnosis. The diagnosis can be made by making a karyogram and karyotype, through which the chromosomal defects are detected. Examinations of the bone marrow cell composition (myelogram) are performed for the clarification of the diagnosis. The bone marrow biopsy reveals that it is hypocellular and fatty [1]. In families where there have been cases of childbirth with Fanconi anemia, for all subsequent pregnancies it is recommended a prenatal diagnosis to be done using cordocentesis (taking umbilical cord material) to find out the presence of the disease in the unborn child before birth [7]. Also, examination for Fanconi anemia is recommended in the birth of a child with skeletal abnormalities, especially in the arms.

Treatment

Mainly supportive therapy is applied in the treatment of Fanconi anemia, which involves transfusion of filtered erythrocytes and platelets (irradiated, depleted leukocytes). Chelation therapy due to iron load, use of androgen hormones, as well as allogeneic heart transplantation.

On the November 2018 year, at the University Clinic for Hematology the first unrelated transplantation of hematopoietic stem cells was performed in the Republic of North Macedonia. It is one of the most modern and most complex biological interventions that treat the most severe hematological diseases without surgery [8]. This opened the possibility for treatment of patients with Fanconi anemia in our country. Macedonian public health entered the map of world and European medical centers for the treatment of the most serious blood diseases. The Macedonian Bone Marrow Donor Register was established within the Institute of Immunobiology and Human Genetics, within the Medical Faculty and is a member of the World Marrow Donor Association.

Allogeneic bone marrow transplantation is the only chance to achieve normalization of blood formation in patients with AF [9]. In this case, it is highly desirable to perform the transplant while the patient is still young, optimally up to 10 years old. If the patient has healthy siblings who are compatible as potential donors for him, then a transplantation is recommended. Patients with AF are particularly sensitive to chemotherapy (as well as radiotherapy) and should use special conditioning protocols [10].

Prognosis for treatment

The life expectancy of patients with Fanconi anemia depends on how severely the bone marrow function is impaired. Some patients live 30-40 years without treatment, but many die in childhood, either from the disease itself or from cancer that has developed in connection with the disease. That is why it is so important to have an allogeneic bone marrow transplant over time - this is the only chance to restore normal blood formation and increase life expectancy.

Childhood transplants from healthy compatible donor relatives (siblings) lead to success in most FA patients, although such transplants should be screened regularly for early detection of possible malignancies in various organs - the likelihood of their occurrence remains high, even after transplantation [11].

Oral manifestations of the Anemia Fanconi

Calcineurin inhibitors are medications commonly used for long periods in patients undergoing allogeneic hematopoietic stem cell transplant (HSCT). Cases of children with Fanconi anemia who after HSCT manifest similar oral mucosal lesions associated with the use of cyclosporine, phenobarbital and amlodipine, have been described in the literature [12]. Patients with Fanconi anemia have extreme susceptibility to squamous cell carcinoma of the head and neck and anogenital tract [13]. Also many studies have linked Fanconi anemia to oral cancer [6,14,15] and some have assessed the risk of developing oral cancer [16,17].

Lyko K et al. from Brasil conducted comparative study between the 35 patients with Fanconi anemia and 35 healthy control group, investigating the differences between their caries experience, dental care level, and oral hygiene. In their study the patients with Fanconi anemia showed higher decay-missing-filled teeth index values, dental care index, oral hygiene index, but the difference between the groups was not statistical significant [18]. Several clinical case reports of patients with Fanconi anemia of different ages have been described in the literature [19]. The individual approach to dental treatment depends on the state of oral health status and the need for orthodontic treatment [20]. Melanin pigmentation on oral mucosa, traumatic lesions, gingival bleeding, dental biofilm and gingival alterations were the main oral manifestations that were found in the study conducted by de Araujo MR et al. in Brasil [21].

Tekcicek M et al. investigated the 26 children with Fanconi anemia from the central region of Anatolia and find poor oral hygiene and 30% prevalence of dental caries, while radiological examination revealed the presence of microdontia within 44%, congenitally missing teeth within 26%, transposition within 9% and supernumerary teeth within 4% of children [22]. Açikgöz A et al. investigated the oral health, including including oral lesions, gingival and periodontal status within 15 children with Fanconi anemia from Ankara. They thing that the increased tendency toward periodontal disease may be due not only to the anemia, leukopenia, and defective detoxification of oxygen radicals that are characteristic of the Fanconi anemia, but also to medications used during intense immunosuppressive treatment, such as steroids [23].

Conclusion

The interdisciplinary team of medical and dental specialists must be included in the medical and dental treatment of patients with Fanconi anemia. Medical doctors, especially hematologist, nephrologists, dermatovenerologist, ophthalmologist, otorhinolaryngologist, and dentists play an important role in treatment of Fanconi anemia. They have to work together in order to improve oral health-related quality of life of patients with Fanconi anemia. Patients with Fanconi anemia really need special dental care.

References

1. Deaconu A, Vodă D, Bulucea D. Fanconi Anemia — Case Report of Rare Aplastic Anemia at Child. *Acta Medica Marisiensis.* 2014;60(3):125-12
2. Nepal M, Che R, Zhang J, Ma C, Fei P. Fanconi Anemia Signaling and Cancer. *Trends Cancer.* 2017;Dec;3(12):840-856.
3. Yang X, Zhang X, Jiao J, et al. Rare variants in FANCA induce premature ovarian insufficiency. *Hum Genet.* 2019;138(11-12):1227-1236.
4. van den Hondel D, Wijers CH, van Bever Y, et al. Patients with anorectal malformation and upper limb anomalies: genetic evaluation is warranted. *Eur J Pediatr.* 2016;175(4):489-97.
5. Savage SA, Walsh MF. Myelodysplastic Syndrome, Acute Myeloid Leukemia, and Cancer Surveillance in Fanconi Anemia. *Hematol Oncol Clin North Am.* 2018;32(4):657-668.
6. Furquim CP, Pivovar A, Amenábar JM, et al. Oral cancer in Fanconi anemia: Review of 121 cases. *Crit Rev Oncol Hematol.* 2018 May;125:35-40.
7. Lee HJ, Park S, Kang HJ, et al. A case report of Fanconi anemia diagnosed by genetic testing followed by prenatal diagnosis. *Ann Lab Med.* 2012;32(5):380-4.
8. Panovska-Stavridis I, Pivkova-Veljanovska A, Ridova N, et al. Molecular Monitoring in Acute Myeloid Leukemia Patients Undergoing Matched Unrelated Donor - Hematopoietic Stem Cell Transplantation: Single Center Experience. *Pril (Makedon Akad Nauk Umet Odd Med Nauki).* 2020;41(3):5-12.
9. Ebens CL, MacMillan ML, Wagner JE. Hematopoietic cell transplantation in Fanconi anemia: current evidence, challenges and recommendations. *Expert Rev Hematol.* 2017;10(1):81-97.
10. Mehta PA, Davies SM, Leemhuis T, et al. Radiation-free, alternative-donor HCT for Fanconi anemia patients: results from a prospective multi-institutional study. *Blood.* 2017;129(16):2308-2315.
11. Abram TJ, Pickering CR, Lang AK, et al. Risk Stratification of Oral Potentially Malignant Disorders in Fanconi Anemia Patients Using Autofluorescence Imaging and Cytology-On-A Chip Assay. *Transl Oncol.* 2018;11(2):477-486.
12. Ballardin BS, Mobile RZ, Coracin FL, et al. A case series of medication-related fibrovascular hyperplasia following hematopoietic stem cell transplantation for Fanconi anemia. *Pediatr Transplant.* 2020;00:e13947.
13. Toptan T, Brusadelli MG, Turpin B, et al. Limited detection of human polyoma viruses in Fanconi anemia related squamous cell carcinoma. *PLoS ONE*. 2018;13(12):e0209235.
14. Pivovar A, Furquim CP, Bonfim C, et al. Mouth examination performance by children's parents and by adolescents in Fanconi anemia. *Pediatr Blood Cancer.* 2017;64(11).
15. Ambarkova V. Oral Cancer. *Ann Dentist Oral Disord* 2019:110.
16. Furquim CP, Soares GM, Ribeiro LL, et al. The Salivary Microbiome and Oral Cancer Risk: a Pilot Study in Fanconi Anemia. *J Dent Res.* 2017;96(3):292-299.
17. Velleuer, E., Ralf Dietrich, N. Pomjanski, et al. Diagnostic accuracy of brush biopsy–based cytology for the early detection of oral cancer and precursors in Fanconi anemia. *Cancer Cytopathology*. 128 (2020): n. pag.
18. Lyko K, Lemes AL, Bonfim C, et al. Oral health status in children and adolescents with Fanconi anemia. *Spec Care Dentist.* 2016;;36(2):71-4.
19. Kaul R, Jain P, Saha S, et al. Fanconi anemia in pediatric dentistry: Case report and review of literature. *SRM J Res Dent Sci.* 2017;8:92-6.
20. Miranda F, Garib D, de Lima Netto BA, et al. Orthodontic intervention in Fanconi's anemia: A case report. *Spec Care Dentist.* 2020;40(4):382-389.
21. de Araujo MR, de Oliveira Ribas M, Koubik AC, et al. Fanconi's anemia: clinical and radiographic oral manifestations. *Oral Dis.* 2007;13(3):291-5.
22. Tekcicek M, Tavil B, Cakar A, et al. Oral and dental findings in children with Fanconi anemia. *Pediatr Dent.* 2007;29(3):248-52.
23. Açikgöz A, Ozden FO, Fisgin T, et al. Oral and dental findings in Fanconi's anemia. *Pediatr Hematol Oncol.* 2005;22(6):531-9.