OLGU SUNUMU CASE REPORT

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Macular Microangiopathy in Fanconi Anemia: A Case Report with Optical Coherence Tomography Angiography Findings

Fankoni Anemisinde Makular Mikroanjiyopati: Optik Koherens Tomografi-Anjiyografi Bulguları ile Bir Olgu Sunumu

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ABSTRACT Fanconi anemia (FA) is a genetic disease in which the bone marrow cannot produce enough blood cells, which is included in the group of hereditary bone marrow failure syndromes. In addition to congenital genitourinary, gastrointestinal, neurodevelopmental, and ophthalmological problems, it may be associated with acquired conditions such as increased cancer risk and retinal occlusive vasculopathy. This article aims to present the macular ischemia findings with multimodal imaging methods in a patient with FA who applied with the complaint of low vision. To our knowledge, this is the first case report showing optical coherence tomography angiography findings in FA.

Keywords: Fanconi anemia; multimodal imaging; optical coherence tomography-angiography; retinal ischemia

ÖZET Fankoni anemisi (FA), kalıtsal kemik iliği yetersizliği sendromları grubuna dâhil olan, kemik iliğinin yeterli miktarda kan hücresi üretemediği genetik bir hastalıktır. Konjenital genitoüriner, gastrointestinal, nörogelişimsel ve oftalmolojik sorunların yanı sıra kanser riskinde artış, retinal oklüziv vaskülopati gibi edinsel durumlarla birliktelik gösterebilmektedir. Bu yazıda, görme azlığı şikâyeti ile başvuran FA tanılı hastada makular iskemi bulgularının multimodal görüntüleme yöntemleri ile sunulması amaçlanmaktadır. Bizim bilgimize göre bu yazı FA'da optik koherens tomografi anjiyografi bulgularını gösteren ilk olgu sunumudur.

Anahtar Kelimeler: Fankoni anemisi; multimodal görüntüleme; optik koherens tomografi-anjiyografi; retinal iskemi

Hereditary bone marrow failure syndromes are a genetic group of diseases in which the bone marrow cannot produce enough blood cells.[1-3] The most common of these diseases are fanconi anemia (FA), dyskeratosis congenita, Shwachman-Diamond syndrome, and Diamond-Blackfan anemia.[4]

FA is genetically and phenotypically heterogeneous. The disease is characterized by progressive bone marrow failure and a high risk of cancer (leukemia, gynecological cancers, etc.). A defect in the repair of deoxyribonucleic acid is involved in the pathogenesis of FA, which is frequently autosomal recessive.[5] Various congenital anomalies, including skeletal system anomalies, dermal pigmentary changes, and genitourinary, gastrointestinal, and neurodevelopmental problems, often accompany FA.[6,7]

Various congenital ocular findings have been described in patients with FA.[8] Depending on the pathophysiology of the disease, different acquired eye diseases may also be present.[9,10]

This article presents the macular ischemia findings obtained via multimodal imaging methods for a patient who presented with low vision and was diagnosed with FA. To our knowledge, this is the first case report describing the findings of optical coherence tomography (OCT) angiography for a case of FA.

CASE REPORT

A 31-year-old female patient was admitted to our clinic due to a bilateral decrease in vision that had worsened over the previous year. She had been diagnosed with FA 19 years previously, she was not re-

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ceiving any treatment for FA at that time, and she had no other systemic diseases. Her hemoglobin level was 9.4 g/dL (normal range: 12-15 g/dL), and her platelet count was 68,000 cells/µL (normal range: 150,00-450,000 cells/µL). A physical examination showed that the patient had short stature (145 cm), small toes, and hyperpigmented lesions in the neck region (Figure 1). Both eyes had microphthalmia; the axial lengths of the right and left eyes were 20.75 mm and 20.34 mm, respectively. The patient's best corrected visual acuity was 0.3 (-1.0, -0.75x10/-1.0x30) bilaterally. Intraocular pressure and an anterior segment examination were normal for both eyes. A fundus examination showed visible choroidal vessels due to regions of chorioretinal atrophy in both eyes. Peripapillary chorioretinal atrophy, irregular enlargement of the foveal margins, and loss of the foveal reflex were observed as well (Figure 2). OCT imaging (OCT Spectralis, Heidelberg Engineering, Germany) showed an enlarged fovea and decreased cupping in both eyes. The outer plexiform layer grew thicker and saw-like in the foveal and perifoveal regions, and the middle retinal layers (inner nuclear, outer plexiform, and outer nuclear layers) were irregular (Figure 3). Fundus fluorescein angiography (FFA) showed peripapillary hyper fluorescence due to window defects in both eyes, enlargement of the foveal avascular zone (FAZ) in the macula, dilated capillaries in the perifoveal area, non-perfusion areas, and capillary leakage (Figure 4). OCT-angiography showed both superficial and deep capillary plexus levels in both eyes, as well as deterioration of the perifoveal anastomotic capillary arcuate, enlargement of the FAZ, capillary non-perfusion areas, and dilated and deformed capillaries. The irregular section of the foveal region was reflected to the OCT in the en-face OCT-angiography images; this revealed flattening and enlargement of the foveal cavity (Figure 5). The FAZ area was 2.129 mm^2 in the right eye and 3.859 mm^2 in the left eye, while the FAZ perimeter was 6.936 mm in the right eye and 8.149 mm in the left eye. The patient's hematologic and ophthalmologic follow-ups are still ongoing.

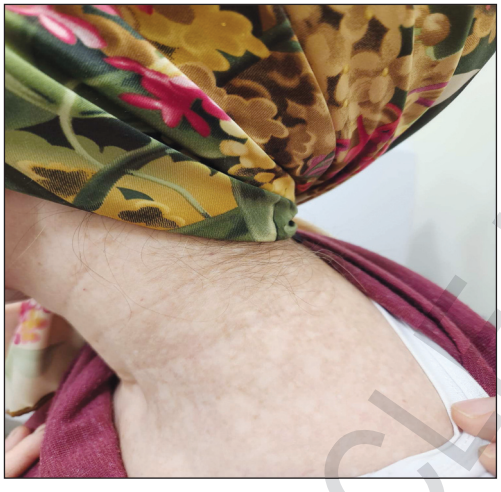

FIGURE 1: Hyperpigmented lesions with lapse involvement are observed in the lateral region of the neck.

An informed consent form was obtained from the patient.

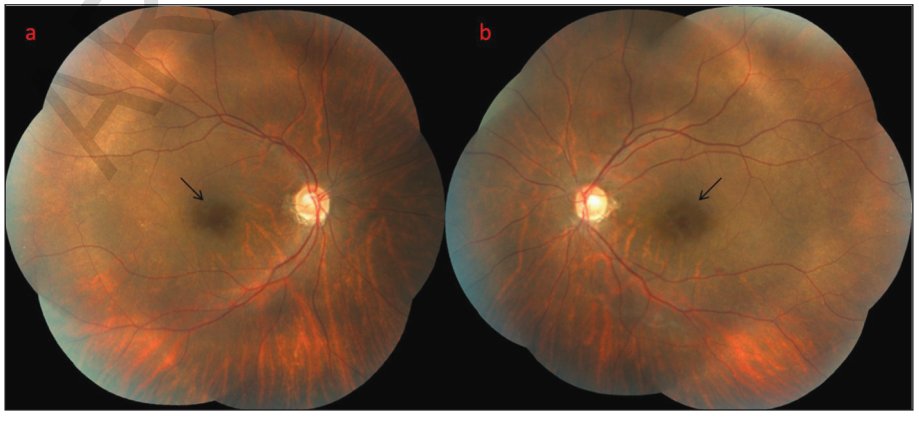

FIGURE 2: Color fundus photograph of both eyes (a and b); choroidal vessels are visible due to chorioretinal atrophy; peripapillary chorioretinal atrophy, irregular enlargement of the foveal margins, and loss of the foveal reflex (black arrow) can also be observed.

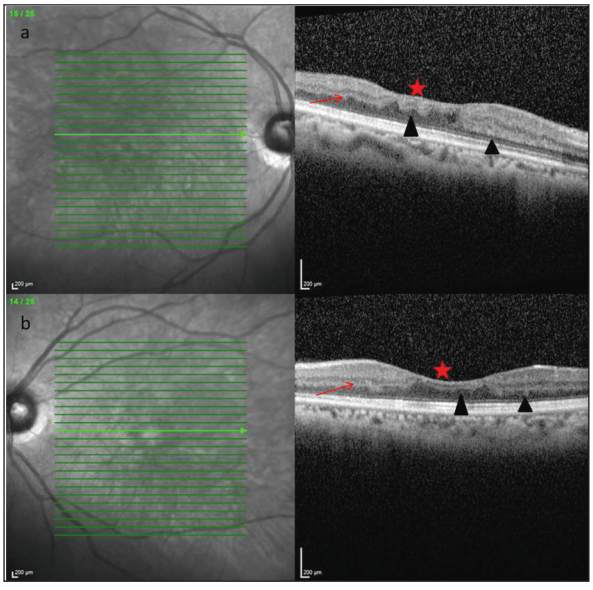

FIGURE 3: Optical coherence tomography imaging of both eyes (a and b) shows foveal enlargement and decreased cupping (red star), thickening and saw-like features of the outer plexiform layer in the foveal and perifoveal regions (black arrowhead), and disorganization of the middle retinal layers (inner nuclear, outer plexiform, and outer nuclear layers) (red arrow).

DISCUSSION

A range of ocular findings have been found to accompany FA. In a study of 106 patients, Graf et al. report that microphthalmia was the most common congenital ocular finding accompanying FA.[8] However, FA leads primarily to clinical findings due to retinal occlusive vasculopathy.[9,10] Yahia et al. report severe ischemic retinopathy with optic disc neovascularization, vitreous hemorrhage, and neovascular glaucoma in an 11-year-old girl with FA.[9] Denny et al. describe a 21-year-old patient with FA who was evaluated for bilateral retinal hemorrhages and diagnosed via a systemic investigation based on peripheral ischemia, FAZ enlargement, and telangiectatic vessels, which were observed via FFA.[10] In patients with FA, retinopathy develops via the formation of retinal ischemia as a result of the reduced oxygen-carrying capacity of anemic patients and the subsequent stimulation of vascular proliferation.[11] Serum vascular endothelial growth factor levels have been shown to correlate with the degree of anemia and thrombocytopenia in patients with aplastic anemia.[12]

In our case, unlike the cases described above, no signs of peripheral ischemia were observed. Severe macular ischemia was detected via multimodal imaging methods; the patient presented at our clinic due to decreased vision, but a fundus examination revealed no features of ischemic retinopathy. Fluorescein angiography showed enlargement in the FAZ and dilated and leaky vessels at the margin of the FAZ, while OCT images showed irregularity in the middle layers of the foveal and perifoveal regions. The deterioration of the perifoveal anastomotic capillary arcuate at both the superficial and deep capillary plexus levels, as observed via OCT-angiography, and the degree of enlargement of the FAZ indicate the extent of ischemia. The vascular changes observed via OCT-angiography suggest that the structural changes observed via OCT, especially in the middle retinal

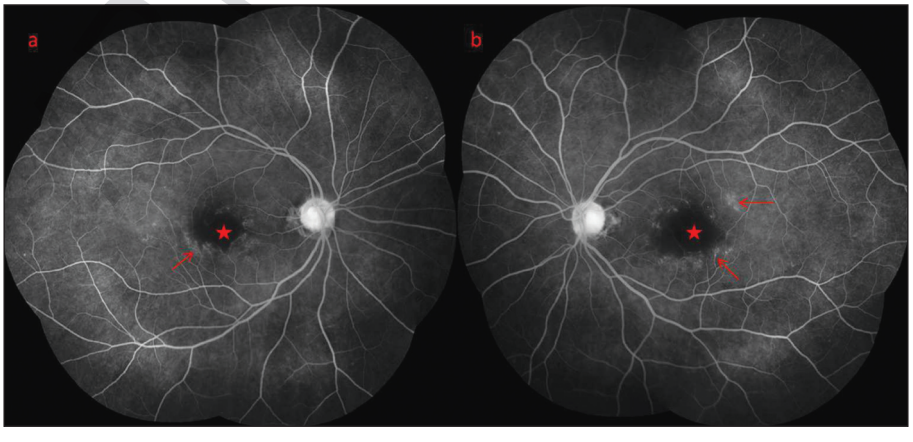

FIGURE 4: Fundus fluorescein angiography shows peripapillary hyperfluorescence due to window defects in both eyes (a and b), enlargement of the foveal avascular zone in the macula (red star), dilated capillaries in the perifoveal area, non-perfusion areas, and capillary leakage (red arrow).

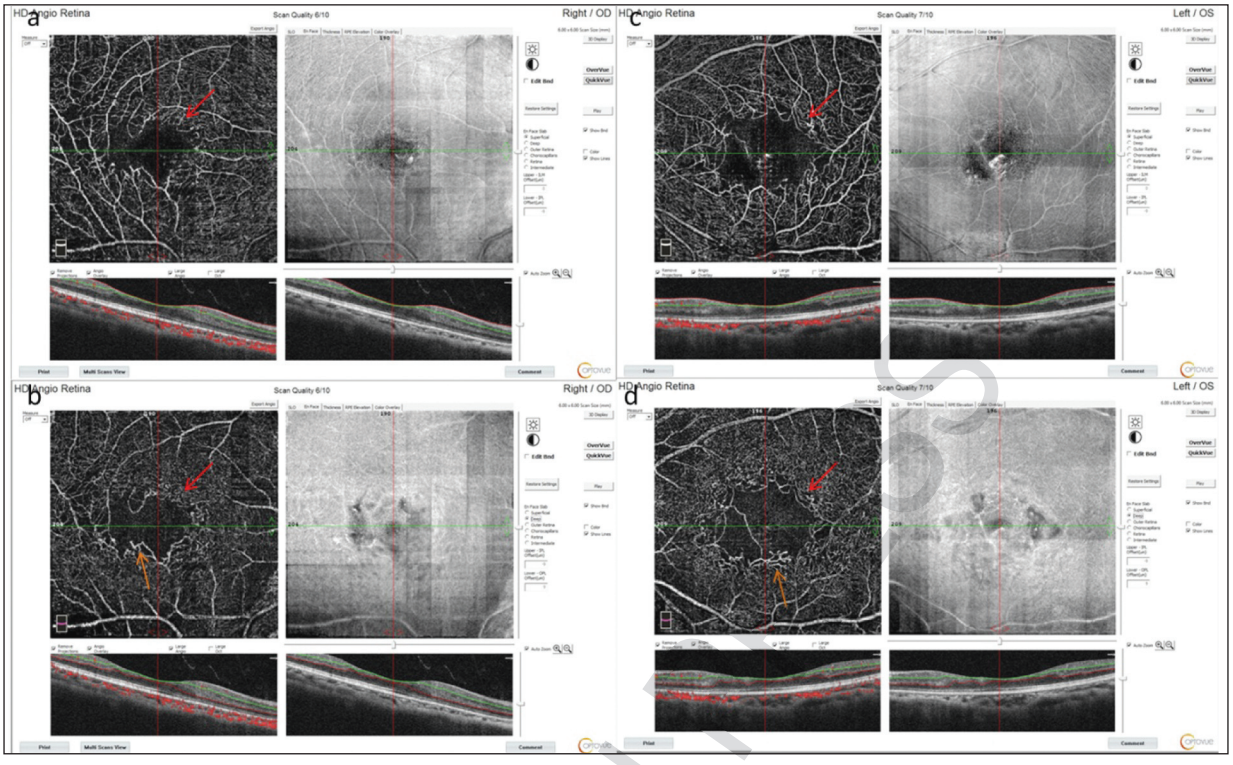

FIGURE 5: OCT-angiography of both eyes at the superficial (a and c) and deep capillary plexus (b and d) levels shows disruption of the perifoveal anastomotic capillary arcuate (red arrow) as well as foveal avascular zone enlargement, capillary non-perfusion areas, and dilated and deconstructed capillaries (orange arrow). The foveal region has an irregular appearance in all en-face OCT-angiography images; this appears as flattening and enlargement of the foveal depression in OCT images.
OCT: Optical coherence tomography.

layers, may be due to chronic ischemia. OCT-angiography provides a quantitative evaluation of the vascular perfusion of different retinal layers. Photoreceptor axons that are rich in mitochondria form the outer plexiform layer, and their nutrition depends largely on the deep capillary plexus. However, the photoreceptor inner and outer segments receive 90% of their vascular support from the choriocapillaris. In this case, the outer plexiform layer forms a border between the 2 circulations; this border is much more susceptible to ischemia.

The FAZ is the region of the human retina with the highest cone photoreceptor density and the highest level of oxygen consumption. Although a relationship between FAZ size and visual function has not been demonstrated in healthy eyes, the same is not true for vascular diseases of the retina. In eyes with diabetic retinopathy and retinal vein occlusion, widening of the FAZ has been shown to correlate with decreased visual acuity.[13] The reason for our patient's decrease in bilateral visual acuity seems to be FAZ enlargement due to occlusive retinopathy, which in this case accompanies FA and macular microangiopathy.

In conclusion, the decreased oxygen-carrying capacity of patients with FA may disrupt the ischemia perfusion balance and cause FAZ enlargement and retinal microangiopathy. Multimodal imaging methods, including OCT-angiography, play a key role in diagnosing this condition, which may cause permanent vision loss.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or mem-

bers of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Eyüpcan Şensoy;* ***Design:*** *Eyüpcan Şensoy;* ***Control/Supervision:*** *Eyüpcan Şensoy, Berrak Şekeryapan Gediz;* ***Data Collection and/or Processing:*** *Eyüpcan Şensoy, Berrak Şekeryapan Gediz, Burcu Kazancı;* ***Analysis and/or Interpretation:*** *Eyüpcan Şensoy;* ***Literature Review:*** *Eyüpcan Şensoy, Berrak Şekeryapan Gediz;* ***Writing the Article:*** *Eyüpcan Şensoy;* ***Critical Review:*** *Eyüpcan Şensoy, Berrak Şekeryapan Gediz;* ***References and Fundings:*** *Eyüpcan Şensoy;* ***Materials:*** *Eyüpcan Şensoy, Berrak Şekeryapan Gediz, Burcu Kazancı.*

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