Case Report

West Nile Virus Chorioretinitis: First Case with Ocular Involvement in Türkiye

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Abstract

A 59-year-old man who experienced severe visual loss in the right eye for two days following a febrile illness (high fever lasting for 15 days) presented to our center for a second opinion. On examination, his Snellen best corrected visual acuity (BCVA) was 1/10 in the right eye and 9/10 in the left eye. On fundoscopy, we observed a few track-like, cream-colored linear lesions in the superior fundus of the left eye and a small whitish foveal discoloration together with a temporally pallid disc in the right eye. On autofluorescence imaging, there were some scattered hyperautofluorescent patchy areas bilaterally and, most notably, several hyperautofluorescent track-like lines in the left eye. A complete systemic evaluation was carried out and a blood sample was sent via the Provincial Health Directorate for West Nile virus (WNV) polymerase chain reaction and immunoglobulin (Ig) M and G testing. IgM and IgG antibodies were detected by immunofluorescence assay. The diagnosis was bilateral WNV chorioretinopathy. Magnetic resonance imaging of the brain ruled out any central nervous system involvement. A right intravitreal ranibizumab injection was administered for the intraretinal edema. A month later, Snellen BCVA was 2/10 in the right eye 10/10 in the left. Hyperautofluorescent lesions were no longer detectable in either eye but the right optic disc still appeared pallid. Clinicians should suspect WNV horioretinitis in cases presenting with characteristic fundus lesions and a history of febrile illness.

Keywords: Chorioretinitis, fundus autofluorescence, optical coherence tomography, ranibizumab, West Nile virus infection

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Introduction

West Nile virus (WNV) is a single-stranded ribonucleic acid (RNA) flavivirus conveyed mainly by the bite of infected mosquito species of the genera *Culex* and *Aedes*.[1] Though WNV was reported in a Ugandan patient in 1937,[2] the first reports from the western hemisphere about the virus did not appear until the 1999 meningoencephalitis outbreak in the New York City metropolitan area.[3] In 2002, a case of optic neuritis with meningoencephalitis involvement was documented.[4]

WNV infection is asymptomatic in approximately 80% of cases, presents as influenza-like illness in around 20% of cases, and causes meningoencephalitis in less than 1% of cases.[5] Its incubation period is between 3 and 14 days, after which fever, headache, generalized myalgia, asthenia, gastrointestinal symptoms, and maculopapular rash may occur. Neurologic involvement can manifest as meningitis, encephalitis, and meningoencephalitis.[6] The mortality rate is approximately 10% when the central nervous system is involved.[7]

The first case of WNV with chorioretinitis was confirmed by positive immunoglobulin M (IgM) serological test in 2003.[8] WNV-related ocular manifestations described to date include anterior uveitis, vitritis, bilateral multifocal chorioretinitis, non-occlusive or occlusive retinal vasculitis, retinitis, focal lesions without uveitis, macular edema, optic neuritis, neuroretinitis, papilledema, optic atrophy retrogeniculate damage, ocular nerve palsy, and nystagmus.[9,10,11,12,13,14] However, the most common manifestation of ocular WNV infection is chorioretinitis, which is observed in more than 85% of cases presenting with ocular involvement.[12]

We hereby present a case of WNV chorioretinitis diagnosed in Türkiye and share its multimodal imaging features and outcome.

Case Report

A 59-year-old man who experienced severe visual loss in the right eye for two days following a febrile illness (high fever lasting for 15 days) presented to our center for a second opinion. On examination, his Snellen best corrected visual acuity (BCVA) was 1/10 and 9/10 in the right and left eye, respectively. No relative afferent pupillary defect (RAPD) was noted, and his Ishihara color vision test results were 18/21 in the right and 21/21 in the left eye. Slit-lamp examination was unremarkable and intraocular pressure was within normal range bilaterally. On fundoscopy, we observed a few track-like, cream-colored linear lesions in the superior fundus of the left eye and a small whitish foveal discoloration and temporally pallid-looking disc in the right eye (Figure 1a, b). On autofluorescence imaging, there were some scattered hyperautofluorescent patchy areas bilaterally, and most notably, a few track-like linear hyperautofluorescent lesions in the left eye (Figure 1c, d). Optical coherence tomography (OCT) demonstrated some hyperreflective dots in the posterior vitreous, foveal intraretinal cysts, and focal alterations in the retinal pigment epithelium (RPE) and ellipsoid zone (EZ) in the right eye, as well as focal alterations in the RPE and EZ corresponding to the hyperautofluorescent linear changes in the left eye (Figure 1e, f). Fluorescein angiography (FA) showed a few hyperfluorescent lesions at the posterior pole in both eyes, and hyperfluorescent linear lesions extending towards the retinal periphery corresponding to the hyperautofluorescent lines were noted in the left eye (Figures 2a, b and 3a, b). A macular 6x6 mm optical coherence tomography angiography (OCTA) scan exhibited areas of flow void in the right fovea (Figure 2c), whereas OCTA features of the left macula were unremarkable (Figure 3c).

The patient's history of febrile disease and the bilateral multifocal chorioretinitis suggestive of WNV chorioretinopathy prompted us to look for a possible West Nile fever infection in addition to other infectious causes. A complete physical examination, pertinent laboratory tests, and chest X-ray were carried out at the infectious disease department, and a blood sample was sent via the Provincial Health Directorate for WNV serological evaluation. Antibody serology by immunofluorescence assay showed the presence of IgM and IgG antibodies, but RNA polymerase chain reaction was negative for WNV. Magnetic resonance imaging (MRI) of the brain ruled out central nervous system involvement. After reviewing the current literature and discussing the options with the patient, we administered a single intravitreal 0.5-mg ranibizumab injection to the right eye.

One month after the injection, Snellen BCVA was 2/10 in the right and 10/10 in the left eye. No RAPD was noted and Ishihara color vision was 1/21 in the right and 21/21 in the left eye. Autofluorescence, FA, OCTA, and OCT of the right eye showed that the posterior pole looked almost normal with only temporal optic disc pallor (Figure 4a, b, d, e). The central fixation point was slightly shifted in the right eye (Figure 4c). There was retinal nerve fiber loss in the temporal quadrant (Figure 4f). The left fundus appeared normal on multimodal imaging, and the previously observed hyperautofluorescent lines were no longer visible (Figure 5).

Discussion

WNV infection has been detected previously in Türkiye. Serter[15] reported 29.1% seropositivity in a study conducted in the Aegean part of Türkiye in 1980. Several studies between 2007 and 2010 showed seropositivity rates of 9.4% and 0.56% respectively among blood donors in the South-East and Central Anatolia regions, while 9.2% IgM and 3.4% IgG seropositivity was reported in patients with aseptic/viral meningitis/encephalitis.[16,17,18] In 2010, 47 cases of WNV in humans (median age 58 years, mainly from western provinces) were identified in Türkiye.[19] However, only 12 could be confirmed by the laboratory. Forty of the patients had central

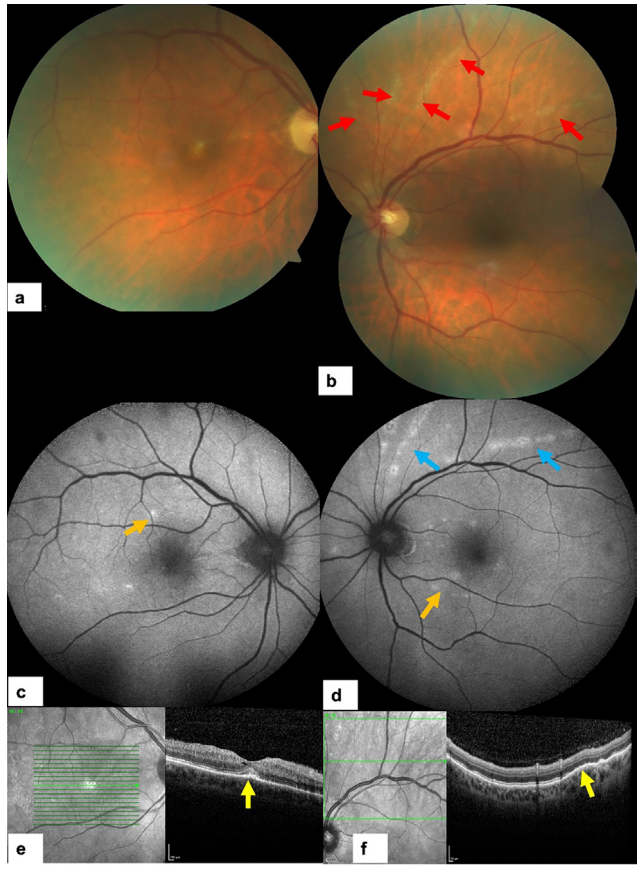

Figure 1. Imaging obtained at first presentation (August 2024): color fundus photographs depicting the small whitish area at the foveal center in the right eye (a) and normal looking macula with path-like cream-colored linear lesions in the superior retina (red arrows) in the left eye (b). Fundus autofluorescence images showing a few hyperfluorescent lesions at the macula (orange arrow) in the right eye (c) and linear hyperautofluorescent lesions extending from posterior pole to periphery (blue arrows) and a few hyperfluorescent lesions at the macula (orange arrow) in the left eye (d). Optical coherence tomography (OCT) of the right eye (e) demonstrating intraretinal cysts, subfoveal hyperreflective material deposition (yellow arrow), a few hyperreflective dots in the posterior vitreous, and foveal retinal pigmented epithelium (RPE) and ellipsoid zone (EZ) alterations. An OCT section taken over the linear lesions in the left eye (f) delineating focally altered RPE and EZ with focal choroidal thickening (yellow arrow)

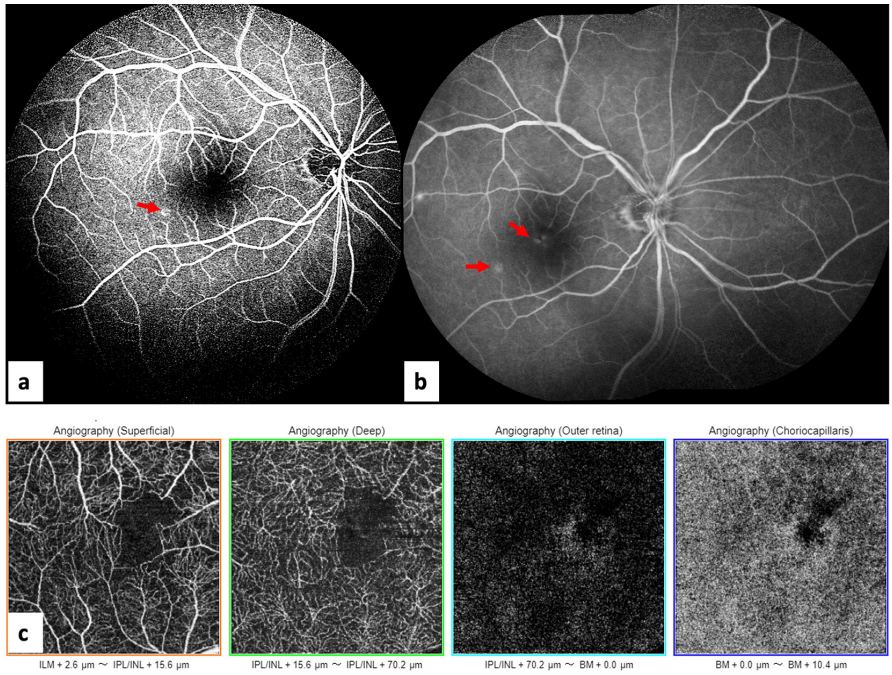

Figure 2. Right eye at first presentation (August 2024): early (a) and late (b) phase fluorescein angiographic images showing central hyperfluorescence together with some hyperfluorescent punctate areas around the macula (red arrows). c) 6x6 mm optical coherence tomography angiographic scans exhibiting a central flow void

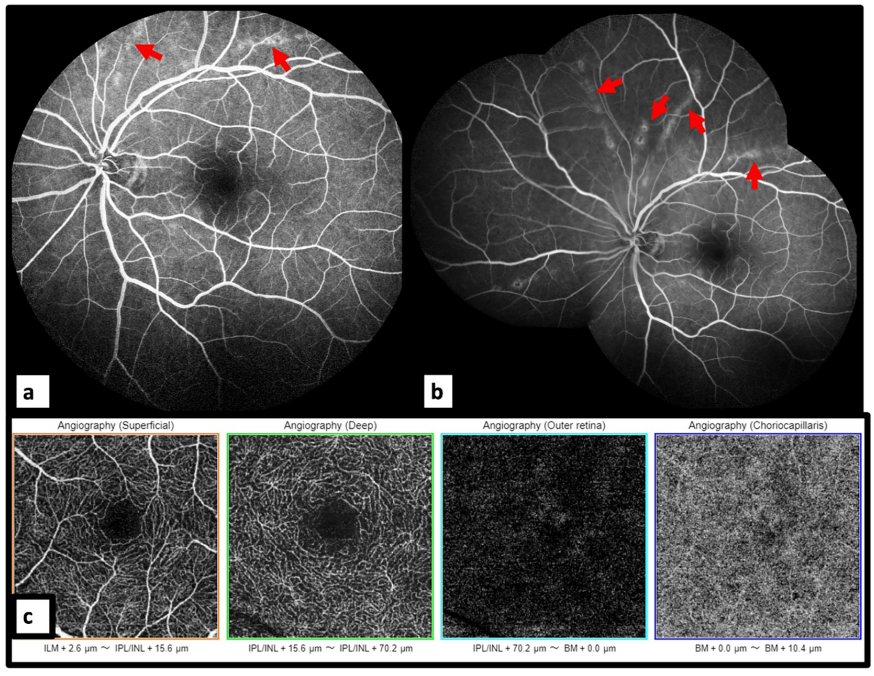

Figure 3. Left eye at first presentation (August 2024): a, b) fluorescein angiographic images showing hyperfluorescent linear lesions (red arrows) extending from the posterior pole to the fundus periphery. c) Normal-looking optical coherence tomography angiography (6x6 mm scans)

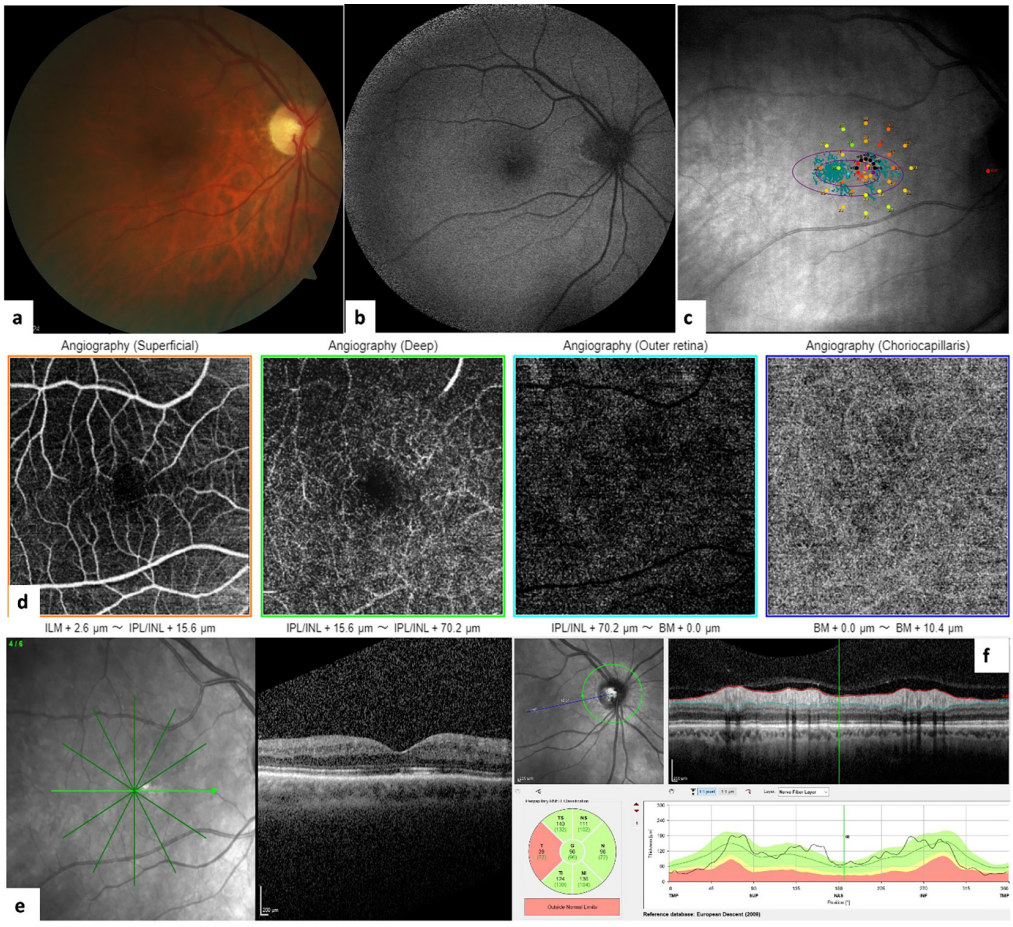

Figure 4. Right eye at last visit (one month after injection): a) almost normal-looking fovea with some temporal optic disc pallor. b) Fundus autofluorescence image exhibiting the disappearance of previously noted hyperautofluorescent lesions. c) Microperimetry depicting the shift of the foveal fixation point. d) Normal optical coherence tomography angiography (6x6 mm scans). e) Optical coherence tomography showing resolution of the intraretinal foveal edema. f) Retinal nerve fiber loss at the temporal quadrant on retinal nerve fiber layer analysis

nervous system manifestations and a total of 10 patients died. However, no case with ocular involvement was noted.[19]

A group of WNV-positive patients in Houston, Texas were followed prospectively for a median of 6.8 years (range, 0.1-11 years) from the time of acute infection, and WNV chorioretinitis occurred in nearly a quarter of them (27/111).[20] Seventeen (49%) of the 35 patients who presented with encephalitis had evidence of WNV chorioretinitis, compared to none (0%) of the 14 meningitis cases, 9 (25%) of 36 uncomplicated fever cases, and 1 (4%) of 26 asymptomatic cases. WNV chorioretinitis was seen more frequently in patients over 60 years of age and patients with diabetes mellitus and signs of encephalitis. Thus, WNV chorioretinitis seemed to be more commonly detected in patients with severe neurological sequelae. Very recently, Ruiz-Lozano et al.[21] reported a case of ocular WNV infection and performed a review of the relevant literature through October 2023. They included only cases with ocular involvement and serologic and/or cerebrospinal fluid confirmation. Overall, 111 eyes of 60 patients were taken into consideration. The median time from the viral prodrome to onset of ocular symptoms was 7 days, and neurologic involvement was noted in 47 patients (78%). Posterior segment findings were observed in 107 eyes (96%), including characteristic multifocal chorioretinal lesions in 86% of eyes. Topical and systemic treatment was administered for 35% and 28% of the eyes, respectively.[21] Our patient had no neurologic manifestations, as evidenced by normal MRI, but had apparent bilateral chorioretinitis.

Multimodal imaging has a crucial role in establishing the diagnosis of WNV chorioretinitis.[14,21,22,23,24] Chorioretinal lesions in acute cases are classically described as deep, round, cream-colored lesions.[9,22,23] Typical fundus autofluorescence imaging shows characteristic lesions such as multiple well-delineated, mixed hypo- or hyper-autofluorescent punctate chorioretinal lesions or a linear pattern that helps the clinicians to distinguish WNV from other forms of chorioretinitis.[22] These curvilinear

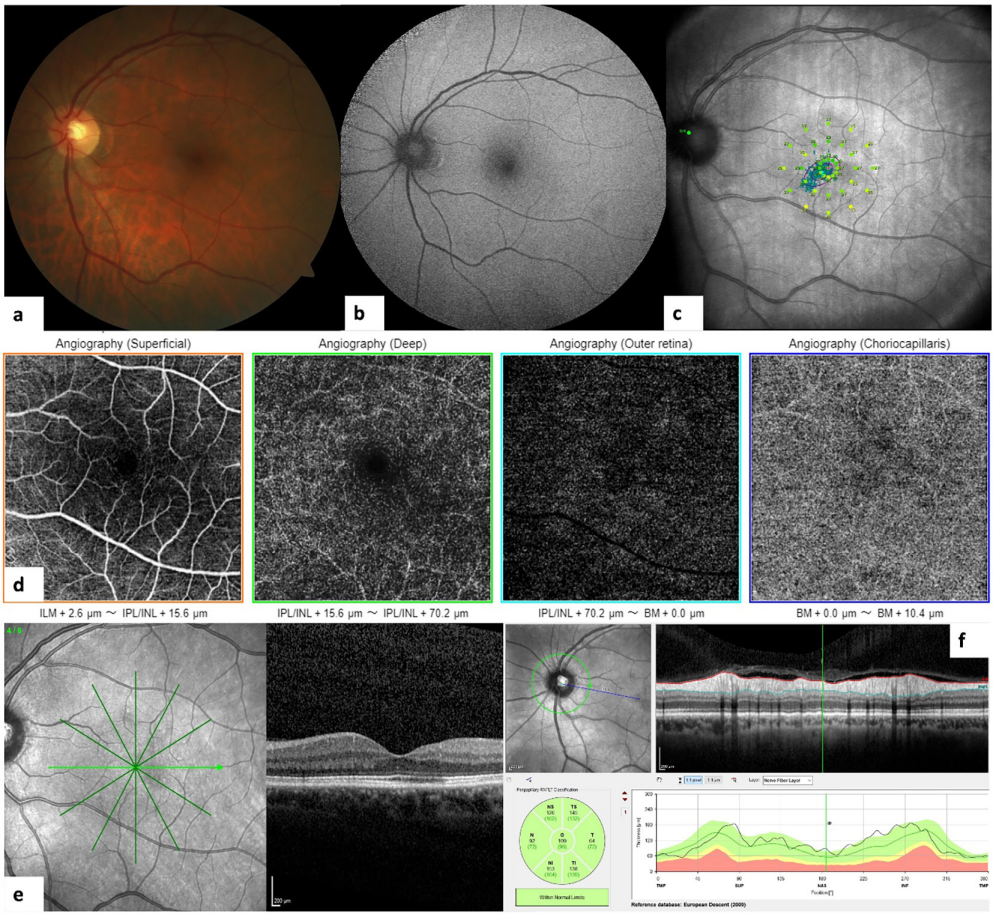

Figure 5. Left eye at last visit: a) normal fundus appearance. b) Disappearance of hyperfluorescent linear lesions previously noticed on fundus autofluorescent images at presentation. c) Normal fixation pattern on microperimetry. d) Unremarkable optical coherence tomography angiography appearance (6x6 mm scans). e) Normal foveal contour on optical coherence tomography. f) Normal nerve fiber layer thickness analysis

retinal lesions are thought to be related to spread of virus from the central nervous system to the retina via the optic nerve.[25] Hematogenous spread may also occur via the choroidal circulation.[26,27] FA usually shows pathognomonic target-like lesions (central hypofluorescence with a hyperfluorescent rim) extending curvilinearly from the optic nerve head.[25] OCT reveals deeper lesions that do not involve the inner retinal layers and nerve fiber layer and may show signs of macular edema.[23,26,27,28,29] The autofluorescence images obtained in the present case encouraged us to investigate the possibility of WNV infection.

Optic neuritis or chorioretinitis in a patient with possible meningoencephalitis during mosquito season should raise suspicion of WNV infection.[30] Diagnosis of WNV-associated ocular lesions is based on ophthalmological examination, detection of specific IgM antibodies, and exclusion of other more common forms of uveitis.[13,14] While treatment is mainly supportive, topical and systemic steroids may be employed for the ophthalmic findings, but there is no clear data regarding their efficacy.[31] Except for the most severe cases requiring hospitalization, WNV chorioretinitis is considered a self-limiting pathology with partial visual recovery unless secondary inflammatory choroidal neovascularization (CNV) occurs.[26]

Macular edema may also occur due to increased vascular permeability resulting from WNV chorioretinitis and retinal vasculitis.[32] The utilization of intravitreal anti-vascular endothelial growth factor agents was reported in patients with WNV infection developing macular edema[32] and CNV.[5,26] In our case, a single intravitreal ranibizumab injection was administered to alleviate the right macular edema. A month later, partial resolution of macular edema was noted on OCT. However, associated probable optic nerve damage limited visual improvement. No additional injection was given.

To the best of our knowledge, the present case is the first documented case in Türkiye of WNV-associated ocular involvement consisting of bilateral chorioretinitis with unilateral foveal edema and optic nerve damage following an acute WNV infection. Clinicians in endemic regions should be alert to the classic fundus features of WNV chorioretinopathy to establish the correct diagnosis even in the absence of neurological involvement.

Ethics

Informed Consent: The patient's consent has been obtained.

Declarations

Authorship Contributions

Surgical and Medical Practices: Ö.Ö., A.A., Z.A., A.N., A.O.S., Concept: Ö.Ö., A.O.S., Design: Ö.Ö., A.O.S., Data Collection or Processing: Ö.Ö., A.A., Z.A., A.N., A.O.S., Analysis or Interpretation: Ö.Ö., A.O.S., Literature Search: Ö.Ö., A.O.S., Writing: Ö.Ö., A.O.S.

Conflict of Interest: No conflict of interest was declared by the authors.

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