CASE REPORT

Atypical Vogt-Koyanagi-Harada disease: Diagnostic markers in a case with the unilateral presentation

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ABSTRACT

Vogt-Koyanagi-Harada disease (VKHD) typically presents with bilateral ocular involvement, and unilateral cases are very rare; this may be due to subclinical involvement of the second eye. A 23-year-old female patient presented with blurred vision in her left eye. Fundus and optical coherence tomography (OCT) examination revealed no abnormal findings in the right eye, while choroidal folds extending between the optic disc and macula and increased choroidal thickness were observed in the left eye. Fundus fluorescein angiography (FFA) showed staining only at the left optic disc. In indocyanine green angiography (ICGA), diffuse hypofluorescent dark dots (HDD) were observed in the early phase, and isofluorescent dots in the late phase in both eyes. These findings were interpreted as acute VKHD-related bilateral diffuse choroiditis. Prompt initiation of corticosteroid and immunosuppressive therapy resulted in initial improvement; however, the disease relapsed after the patient discontinued treatment due to gastrointestinal side effects. OCT findings of internal limiting membrane (ILM) undulations in the right eye were interpreted as indicative of inflammation activation. After resuming systemic corticosteroid therapy and adding methotrexate and adalimumab, the patient\'s ocular condition improved, with no further signs of inflammation. This case highlights that unilateral involvement with atypical findings can occur during the acute phase of VKHD, emphasizing the importance of using advanced imaging techniques (OCT, FFA, and ICGA) for early and accurate diagnosis.

Keywords: Choroidal inflammation, internal limiting membrane undulations, Vogt-Koyanagi-Harada disease.

INTRODUCTION

Vogt-Koyanagi-Harada disease (VKHD) is a multisystem disorder characterized by autoimmune granulomatous inflammation, predominantly affecting pigmented groups such as Hispanics, Asians, Middle Easterners, and South Asians, while it is less commonly observed in Sub-Saharan Africans (1). The frequency of the disease in our country varies between 1.2-2.7% and is more common in women between the ages of 20-50 (2-4). It arises due to a T-cell mediated reaction against tyrosinase peptides in the melanin-producing cells located in the uvea, inner ear, meninges, and integumentary system (5). Inflammation primarily begins in the choroidal stroma and may spread to other parts of the eye, including the retina, optic nerve, ciliary body, and sometimes the anterior chamber, depending on the severity of the reaction (6). It can be examined in two main types with different symptoms and findings: acute with first onset and chronic with repeated episodes (7). Prior to the acute stage, neurological and auditory manifestations may emerge, with prodromal symptoms including headache, nausea, dizziness, tinnitus, meningeal irritation, scalp hypersensitivity or orbital

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pain. These symptoms typically last for several days but may not always be present (8,9). This stage might show mild choroidal inflammation that can only be seen with indocyanine green angiography (ICGA) or meningeal inflammation defined by pleocytosis in cerebrospinal fluid analysis (10). In the early stage, the internal limiting membrane (ILM) folds on optical coherence tomography (OCT) can be diagnostic for VKHD (11). While bilateral involvement is seen in the majority of cases at diagnosis, it may take up to two weeks for symptoms to appear in the other eye (12). Multiple choroidal lesions detected by ICGA and choroidal thickening seen on enhanced depth imaging (EDI)-OCT before the development of typical VKHD findings can lead to early diagnosis (13,14). This case report presents a VKHD patient who was initially perceived to have unilateral involvement due to early detection, but was later found to have bilateral involvement upon clinical examination and follow-up.

CASE

A 23-year-old female patient presented in February 2024 with complaints of blurry vision and pain in the left eye persisting for 10 days. The systemic review revealed a history of headaches. She had no known diseases or regularly used medications and had no prior similar complaints. She had not undergone any eye surgery and had no history of eye trauma. Uncorrected visual acuity of the right eye was 20/20 and best corrected visual acuity of the left eye was 20/25 with +2.5 hypermetropic correction. There were no abnormalities in the anterior segment examination. Intraocular pressure was within normal limits. Eye movements and pupillary response were normal. Fundoscopic examination showed a normal optic disc and macula in the right eye, while the left eye had folds extending between the optic disc and macula (Figure 1). EDI OCT revealed a normal macula in the right eye but increased choroidal thickness and subretinal fluid near the optic disc with choroidal undulations in the left eye (Figure 2). Ultrasonography showed mild choroidal thickening and serous detachment, was no sign of a mass (Figure 3). Fundus fluorescein angiography (FFA) showed no abnormal findings in the right eye but staining only in the optic disc of the left eye. In ICGA, diffuse hypofluorescent dark dots (HDD) were observed in the early phase and these became isofluorescent in the late phase in both eyes. These findings were evaluated as bilateral diffuse choroiditis (Figure 4**).** Laboratory evaluations including complete blood count, basic metabolic panel, erythrocyte

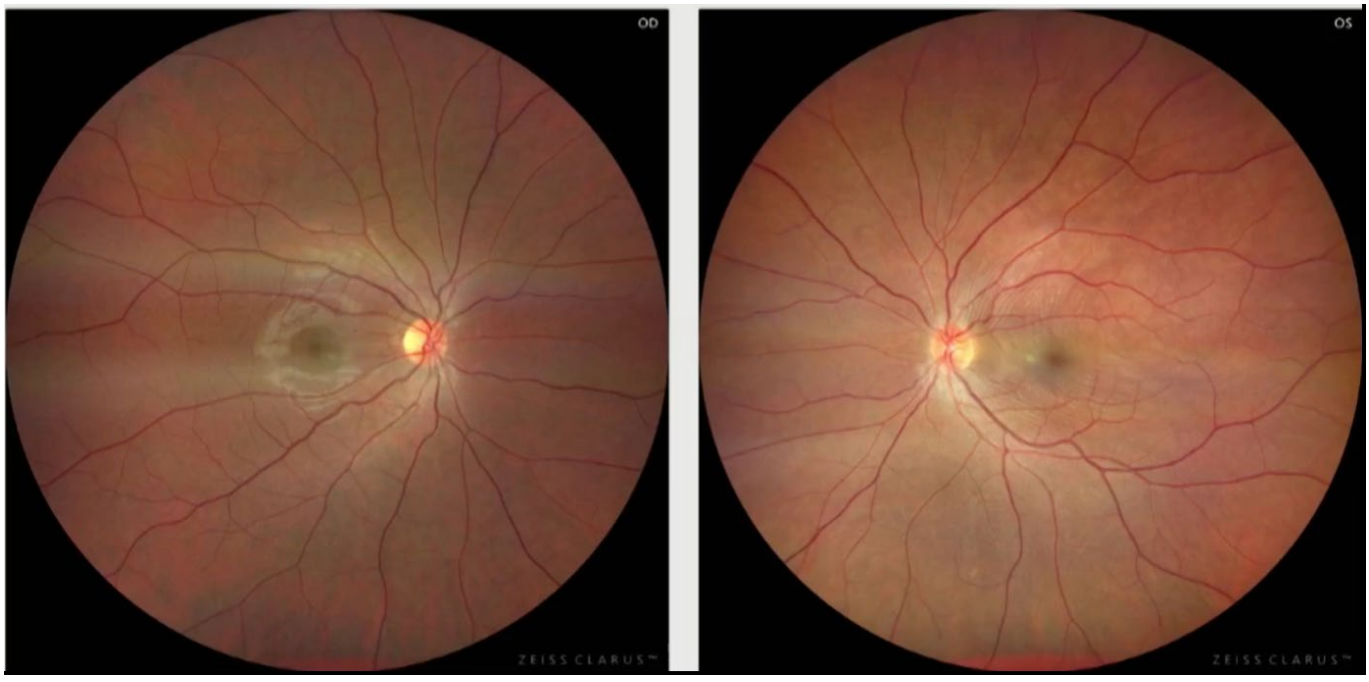

Figure 1: *Fundoscopic examination showed a normal optic disc and macula in the right eye (a), while the left eye had folds extending between the optic disc and macula (b).*

sedimentation rate, C-reactive protein, syphilis antibody, angiotensin-converting enzyme, rheumatoid factor, lysozyme, antinuclear antibody, interferon-gamma release assay, HIV, and Lyme antibody were normal or negative, ruling out infectious and autoimmune diseases. The patient was diagnosed with VKHD. Intravenous pulse methylprednisolone was started as 3x1g, followed by oral methylprednisolone as 1mg/kg. Oral azathioprine and cyclosporine were added as immunosuppressive agents. A month later, uncorrected best visual acuity was 20/20 in both eyes, and the macula appeared normal on fundus examination and OCT. However, it was noted that the patient could not tolerate immunosuppressive treatment due to gastrointestinal (GI) side effects and could not use it regularly. Since no clinical problem was observed, the patient was followed up monthly. Four months after the initial examination, the patient returned with complaints of blurry vision in the right eye. It was noted that the patient had stopped oral steroid therapy three weeks prior. No decrease in visual acuity was observed, but OCT revealed ILM undulations of the right eye (Figure 5). These findings were considered as activation. Oral methylprednisolone was restarted at 1mg/kg, and subcutaneous methotrexate and adalimumab were decided to be added as immunosuppressive treatments.

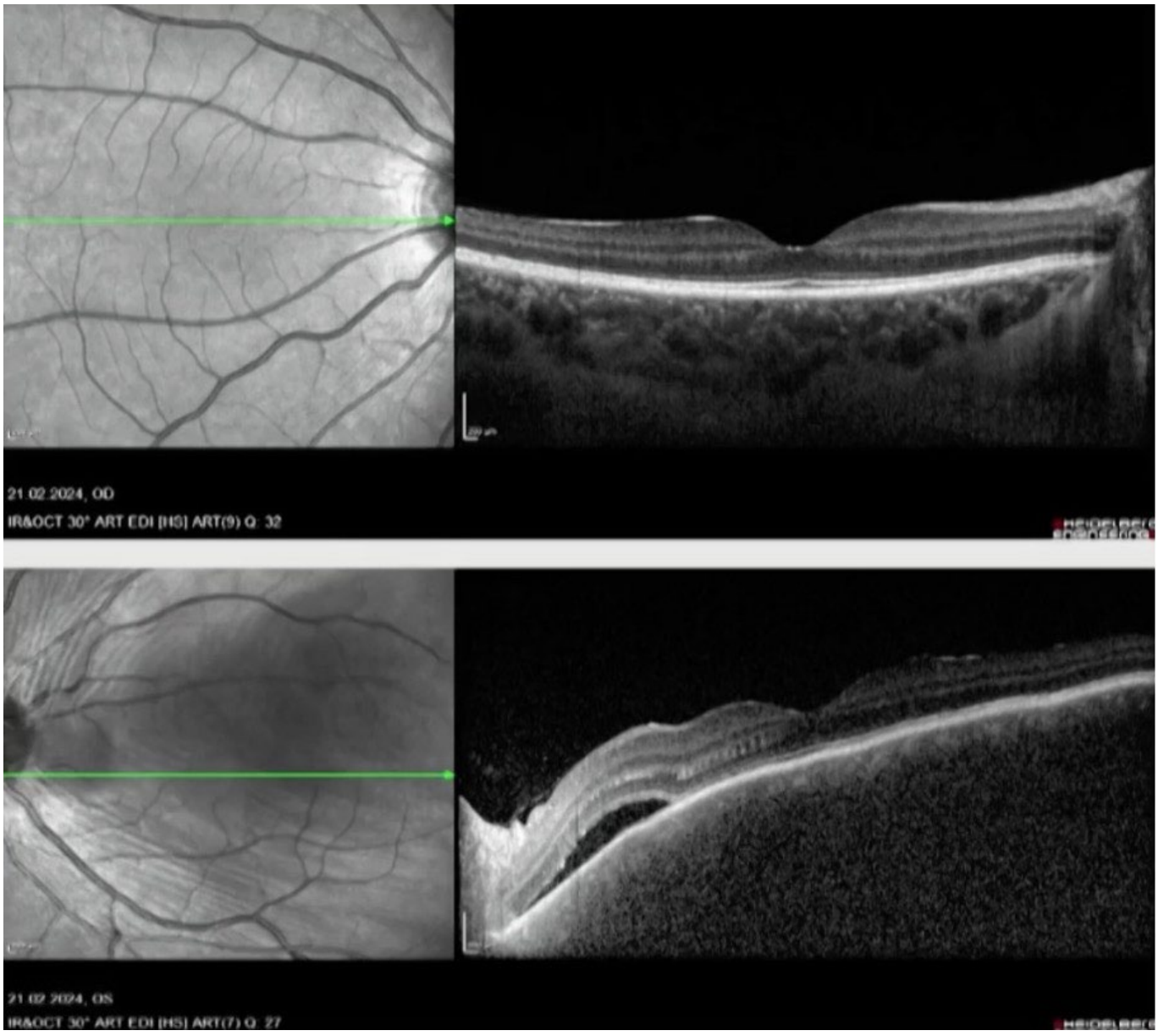

Figure 2: *OCT revealed a normal macula in the right eye but increased choroidal thickness and subretinal fluid near the optic disc with choroidal undulations in the left eye.*

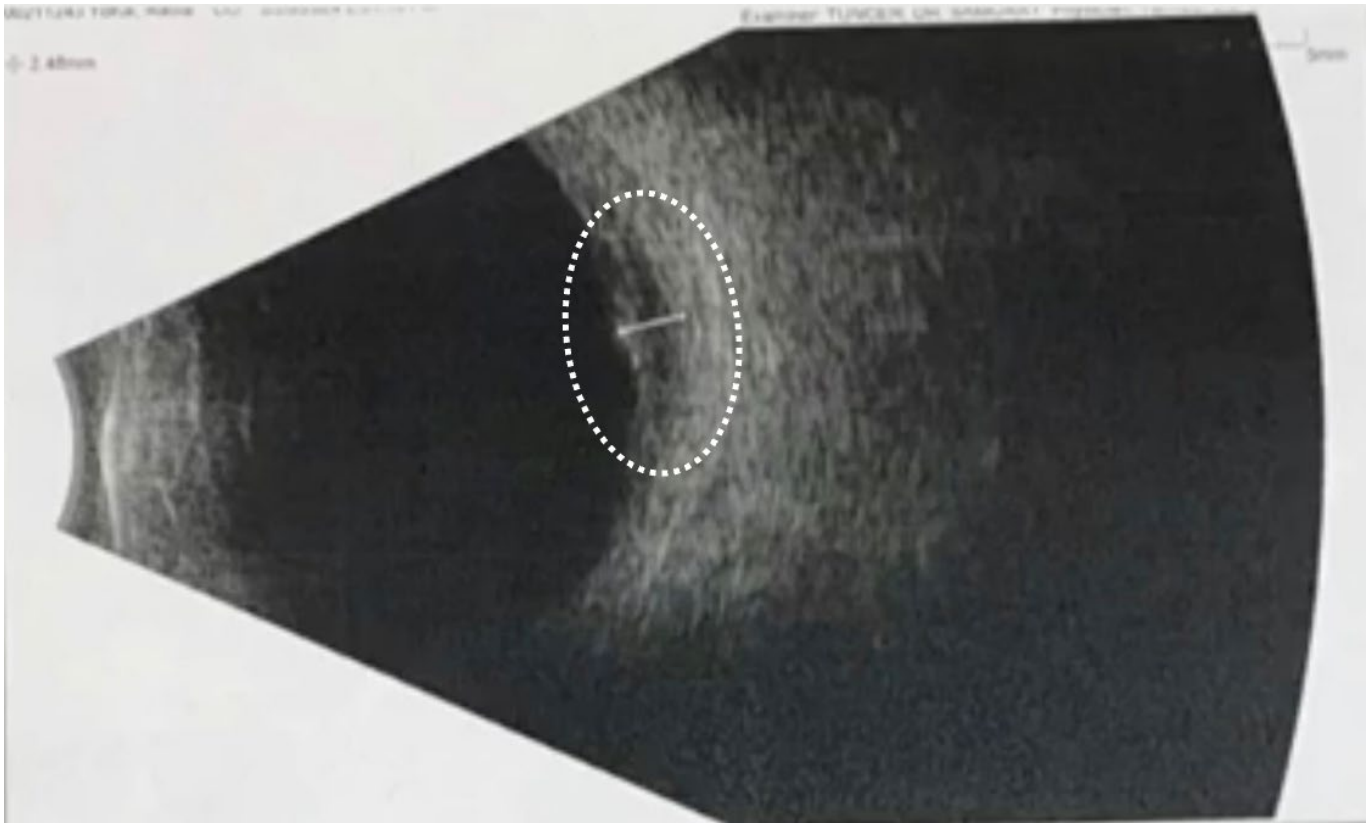

Figure 3: *Ultrasonography showed mild choroidal thickening and serous detachment (dashed ring).*

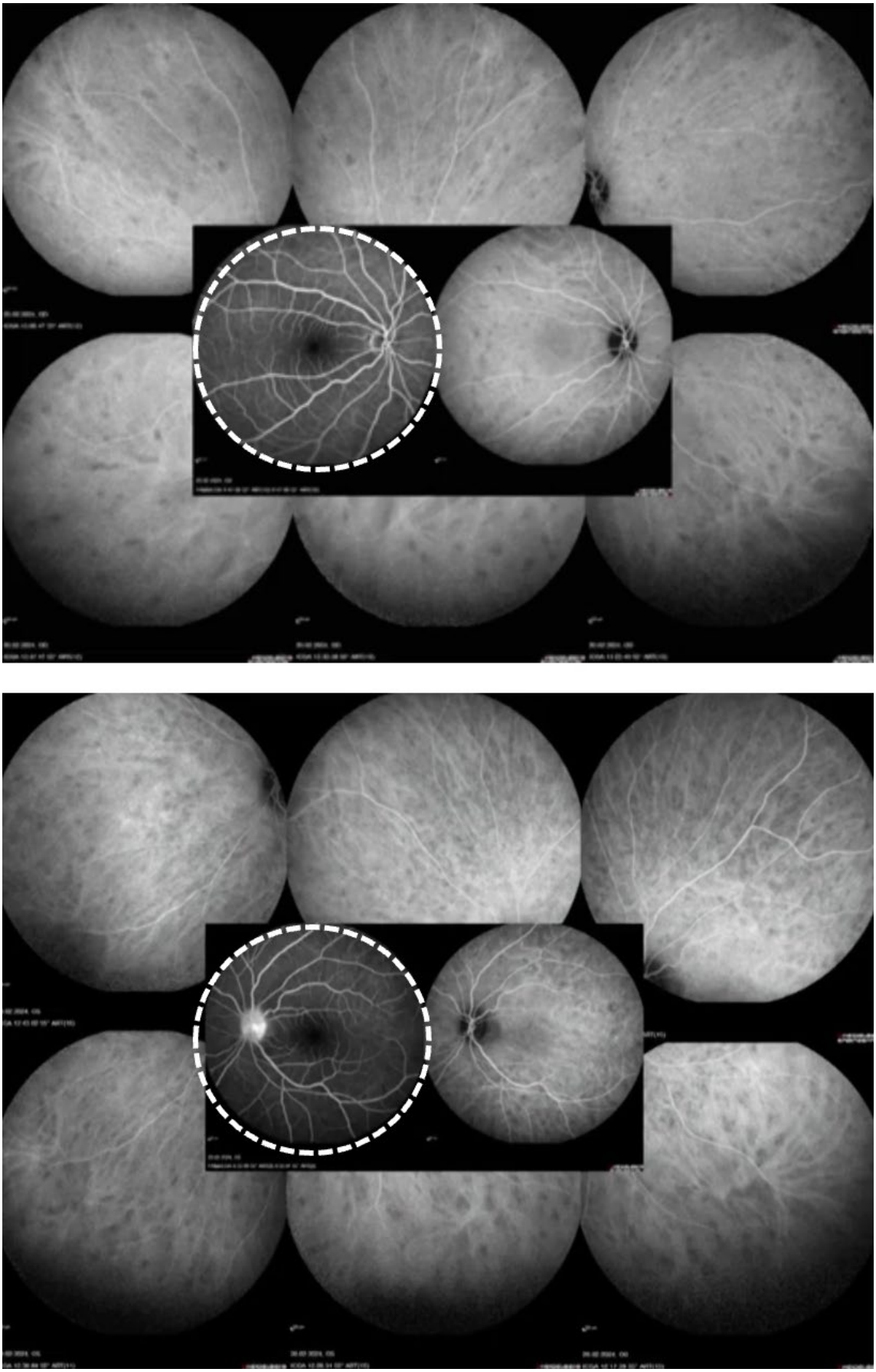

Figure 4: *FFA (White dashed line) showed no abnormal findings in the right eye but staining only in the optic disc of the left eye. ICGA showed diffuse hypofluorescent dark dots (HDD) at the early phase and isofluorescent dots at the late phase in both eyes.*

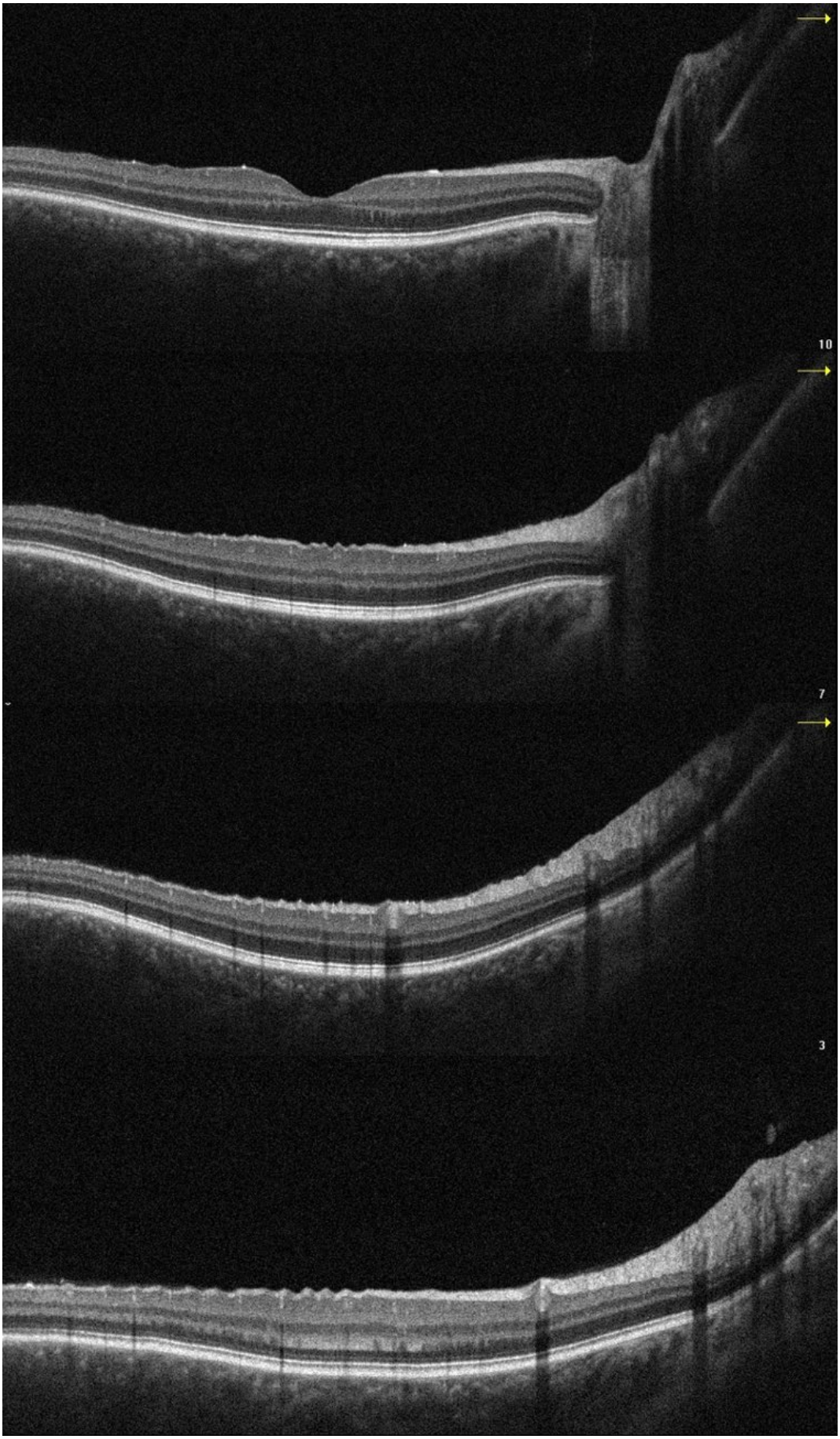

Figure 5: *OCT revealed subtle undulations of ILM in the right eye, suggestive of early inflammatory activity.*

DISCUSSION

It is common to observe simultaneous involvement of both eyes at the time of presentation, while unilateral involvement is quite rare in patients with VKHD. It is known that the fellow eye is affected within two weeks following the involvement of one eye. In our case, while the patient had blurry vision in the left eye, there were no complaints in the other eye. During the prodromal period of VKHD, neurological and auditory-balance symptoms are observed, including headache, orbital pain, neck stiffness, nausea, hearing loss, and tinnitus. This patient had a history of headache and pain around the left orbit ten days before the presentation.

Common ocular findings in the acute phase of the disease, such as exudative retinal detachment, swelling and hyperemia of the optic nerve head, are diagnostic. However, diagnosis of VKHD can be challenging in cases with asymmetric or atypical findings. Today, multimodal imaging techniques including EDI-OCT, FFA, and ICGA provide good support in diagnosis (15). Among atypical presentations, unilateral serous retinal detachment series, unilateral posterior scleritis, and unilateral neuroretinitis are found in the literature (16–18). In our case, fundoscopic examination and OCT imaging revealed unilateral choroidal folds with diffusely increased choroidal thickness, consistent with choroidal infiltration. Ultrasonography showed no choroidal mass lesion. EDI-OCT can be guiding in diagnosis as it shows choroidal thickening secondary to inflammation during the acute phase of the disease. In our case, choroidal thickness measured on EDI-OCT was normal in the right eye but increased in the left eye.

Typical VKH findings on FFA include multiple hyperfluorescent foci indicating a “starry sky” appearance in the early arterial phase, dye pooling in subretinal spaces, and staining of the optic disc in the late phase. In this case, FFA did not show leakage at the posterior pole or retina periphery in either eye, with staining only at the optic disc in the left eye. A study observed the hot disc appearance in 94.4% of acute VKHD patients (19). Chee et al. demonstrated that the presence of pinpoint leakage in the peripapillary region is indicative of the acute phase of the disease and may predict a favorable therapeutic response (20).

In the acute phase of VKH disease, subclinical inflammation in the choroidal stroma is most effectively detected using ICGA. This imaging modality provides critical information for establishing the diagnosis and assessing disease activity during follow-up. (21). In addition, ICGA is important in the differential diagnosis of unilateral cases that may mimic VKHD by causing exudative detachment. Four main ICGA findings include early hyperfluorescent choroidal vessels, hypofluorescent dark dots (HDDs), blurred choroidal vessels, and disc hyperfluorescence (22). In our case, the observation of numerous HDDs on ICGA, which were presumed to be associated with stromal granulomas, provided key diagnostic evidence supporting the diagnosis.

Lin et al. found ILM undulations with exudative retinal detachment in 52% of acute VKHD patients (23). Almalki et al. demonstrated that ILM undulations preceded exudative retinal detachment in a case, emphasizing that ILM undulations alone could be an early sign of acute VKHD (11). In our case, the development of blurry vision in the right eye four months after diagnosis was accompanied by ILM undulations on OCT. These findings were considered as inflammation activation.

Prompt and effective treatment in VKHD affects the disease course. The first 4 weeks after the onset of the disease are described as a therapeutic window (24). Even when treatment begins early, corticosteroid monotherapy can lead to granulomatous anterior uveitis, sunset glow fundus, subretinal fibrosis, alopecia, poliosis, and vitiligo in chronic VKHD (25–27). Combining corticosteroids with immunosuppressive drugs can largely prevent progression to the chronic stage and the emergence of extraocular manifestations by controlling choroidal inflammation. (28). In our case, after the diagnosis, systemic corticosteroid treatment was started along with oral cyclosporine and azathioprine as immunosuppressive agents. Follow-ups indicated improvement in choroidal inflammation findings. However, clinical activation was observed after the patient stopped immunosuppressive treatment early due to gastrointestinal side effects and corticosteroid treatment was stopped early. Thereupon, corticosteroid dose was started at 1 mg/kg, and it was decided to add subcutaneous methotrexate and adalimumab as immunosuppressive agents. The patient had no ocular or systemic complaints or findings at the last examination.

CONCLUSION

While acute VKH disease is known to typically present with bilateral involvement, it can occasionally be confused with unilateral cases due to subclinical involvement in one eye. Therefore, prodromal symptoms should be carefully questioned, early OCT findings should be considered, and imaging techniques like FFA and ICGA should be utilized if there is any suspicion. Early diagnosis and prompt, effective treatment are crucial for managing the disease and preventing progression to the chronic stage, thereby achieving complete remission. Delays in treatment can lead to irreversible and severe visual loss.

DECLARATION OF CONFLICTING INTERESTS

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Informed consent

The patient has provided informed consent for publication of this case.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

REFERENCES

1. Rubsamen PE, Gass JD. Vogt-Koyanagi-Harada syndrome. Clinical course, therapy, and long-term visual outcome. Arch Ophthalmol. 1991;109(5):682–7.
2. Ozdal P, Ozdamar Y, Yazici A, Teke MY, Ozturk F. Vogt-Koyanagi-Harada disease: Clinical and demographic characteristics of patients in a specialized eye hospital in Turkey. Ocul Immunol Inflamm 2014; 22(4):277-86.
3. Yalçındağ FN, Özdal PC, Özyazgan Y, Batıoğlu F, Tugal-Tutkun I; BUST Study Group. Demographic and clinical characteristics of uveitis in Turkey: The First National Registry Report. Ocul Immunol Inflamm. 2018;26(1): 17-26.
4. Tugal-Tutkun I, Ozyazgan Y, Akova YA, Sullu Y, Akyol N, Soylu M, et al. The spectrum of Vogt-Koyanagi-Harada disease in Turkey: VKH in Turkey. Int Ophthalmol. 2007; 27(2-3): 117–23.
5. Gocho K, Kondo I, Yamaki K. Identification of autoreactive T cells in Vogt-Koyanagi-Harada disease. Investig Ophthalmol Vis Sci. 2001;42:2004–9.
6. Herbort Jr CP, Abu El Asrar AM, Yamamoto JH, Pavésio CE, Gupta V, Khairallah M, et al. Reappraisal of the management of Vogt–Koyanagi–Harada disease: Sunset glow fundus is no more a fatality. Int Ophthalmol. 2017;37:1383–95.
7. Lodhi SAK, Lokabhi Reddy JM, Peram V. Clinical spectrum and management options in Vogt–Koyanagi–Harada disease. Clin Ophthalmol. 2017;11:1399–406.
8. Kosma KK, Kararizou E, Markou I, Eforakopoulou E, Kararizos G, Mitsonis C, et al. Headache as a first manifestation of Vogt-Koyanagi-Harada disease. Med Princ Pract Int J Kuwait Univ Heal Sci Cent. 2008;17:253–4.
9. Moorthy RS, Inomata H, Rao NA. Vogt-Koyanagi-Harada syndrome. Surv Ophthalmol. 1995;39:265–92.
10. Herbort CP, Tugal-Tutkun I, Abu-El-Asrar A, Gupta A, Takeuchi M, Fardeau C, et al. Precise, simplified diagnostic criteria and optimised management of initial-onset Vogt–Koyanagi–Harada disease: an updated review. Eye. 2022;36:29–43.
11 Almalki K, Alsulaiman SM, Abouammoh MA. Internal limiting membrane folds as a presenting sign in acute initial-onset Vogt-Koyanagi-Harada disease: A case report. Ocul Immunol Inflamm. 2022;30:641–5.
12. Roe RH, Rathinam SR, Wong RW, McDonald HR, Jumper JM, Cunningham ETJ. Delayed fellow eye involvement in patients with Vogt-Koyanagi-Harada disease. Br J Ophthalmol. 2009;93:701–2.
13. Abouammoh MA, Gupta V, Hemachandran S, Herbort CP, Abu El-Asrar AM. Indocyanine green angiographic findings in initial-onset acute Vogt-Koyanagi-Harada disease. Acta Ophthalmol. 2016;94:573–8.
14. Yang P, Zhong Y, Du L, Chi W, Chen L, Zhang R, et al. Development and evaluation of diagnostic criteria for Vogt-Koyanagi-Harada disease. JAMA Ophthalmol. 2018 Sep;136:1025–31.
15. Silpa-Archa S, Silpa-Archa N, Preble JM, Foster CS. Vogt-Koyanagi-Harada syndrome: Perspectives for immunogenetics, multimodal imaging, and therapeutic options. Autoimmun Rev. 2016;15:809–19.

16. Usui Y, Goto H, Sakai J, Takeuchi M, Usui M, Rao NA. Presumed Vogt-Koyanagi-Harada disease with unilateral ocular involvement: report of three cases. Graefe's Arch Clin Exp Ophthalmol. 2009;247:1127–32.

17. Kouda N. Early manifestation of Vogt-Koyanagi-Harada Disease as unilateral posterior scleritis. Jpn J Ophthalmol. 2002;46:590–3.

18. Pellegrini F, Interlandi E, Prosdocimo G. Vogt-Koyanagi-Harada disease presenting as unilateral neuroretinits. Neuro-Ophthalmology. 2018;42:11–6.

19. Arellanes-García L, Hernández-Barrios M, Fromow-Guerra J, Cervantes-Fanning P. Fluorescein fundus angiographic findings in Vogt-Koyanagi-Harada syndrome. Int Ophthalmol. 2007;27:155–61.

20. Chee SP, Jap A, Cheung CM. The prognostic value of angiography in Vogt-Koyanagi-Harada disease. Am J Ophthalmol. 2010;150(6): 888-93.

21. Çakar Özdal P. Vogt-Koyanagi-Harada Hastalığı. Güncel Retina. 2021; 5(1): 56-64.

22. Miyanaga M, Kawaguchi T, Miyata K, Horie S, Mochizuki M, Herbort CP. Indocyanine green angiography findings in initial acute pretreatment Vogt-Koyanagi-Harada disease in Japanese patients. Jpn J Ophthalmol. 2010;54:377–82.

23. Lin D, Chen W, Zhang G, Huang H, Zhou Z, Cen L, et al. Comparison of the optical coherence tomographic characters between acute Vogt-Koyanagi-Harada disease and acute central serous chorioretinopathy. BMC Ophthalmol. 2014;14:87.

24. Urzua CA, Herbort CP, Takeuchi M, Schlaen A, Concha-del-Rio LE, Usui Y, et al. Vogt-Koyanagi-Harada disease: the step-by-step approach to a better understanding of clinicopathology, immunopathology, diagnosis, and management: a brief review. J Ophthalmic Inflamm Infect. 2022;12:17.

25. Usui Y, Goto H, Sakai J, Takeuchi M, Usui M, Rao NA. Presumed Vogt-Koyanagi-Harada disease with unilateral ocular involvement: report of three cases. Graefe's Arch Clin Exp Ophthalmol 2009;24:1127–32.

26. Keino H, Goto H, Usui M. Sunset glow fundus in Vogt-Koyanagi-Harada disease with or without chronic ocular inflammation. Graefe's Arch Clin Exp Ophthalmol. 2002;240:878–82.

27. Sakata VM, da Silva FT, Hirata CE, Marin MLC, Rodrigues H, Kalil J, et al. High rate of clinical recurrence in patients with Vogt-Koyanagi-Harada disease treated with early high-dose corticosteroids. Graefe's Arch Clin Exp Ophthalmol. 2015;253:785–90.

28. Papasavvas I, Tugal-Tutkun I, Herbort CP. Vogt-Koyanagi-Harada is a curable autoimmune disease: Early diagnosis and immediate dual steroidal and non-steroidal immunosuppression are crucial prerequisites. J Curr Ophthalmol. 2020;32:310–4.