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Case report

Bilateral retinitis after influenza virus infection in a case report

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ABSTRACT

Purpose: To report 2 years' longitudinal retinal changes using spectral domain optical coherence tomography (SD-OCT) images in a case of retinitis after influenza virus infection.

Observations: A 48-year-old female complained of scotoma in the central visual field after influenza virus infection. Her best visual acuity was 20/16, her fundus examination was normal, and fluorescein angiography demonstrated no evident leakage in either the retina or the optic disc. However, SD-OCT images showed a disrupted, blurred inner-segment ellipsoid zone in the macula of both eyes. Two steroid pulse therapy sessions in the first 3 months showed temporary improvement of the central scotoma. However, atrophy of the photoreceptor layer at the juxta fovea gradually progressed in OCT images during the follow-up period. In contrast, the fovea itself was mostly intact and visual acuity was maintained in the 2-year period.

Conclusions and importance: We experienced a unique case of retinitis after influenza infection, in whom progressive atrophy of the photoreceptor layer was observed in SD-OCT images.

1. Introduction

Several case reports have described ocular manifestations after influenza virus infection; however, the symptoms vary and the pathology is not yet clear. Here, we report a case of retinitis occurring after influenza virus infection, and describe our observations of longitudinal changes in the retinal structure, observed using spectral domain optical coherence tomography (SD-OCT).

2. Case report

A 48-year-old female complained of central scotoma; she had previously been given a clinical diagnosis of influenza A, based on an influenza viral antigen analysis of a throat swab, with a high fever (up to 38.5 °C) a few days earlier.

At the initial visit, her best corrected visual acuity was 20/16 in both eyes. Pupillary response, slit-lamp examination, and a fundus examination yielded normal results. Inflammatory cells were not observed in the anterior chamber and vitreous. Goldman perimeter (GP) evaluation showed central scotoma (Fig. 1A). No abnormal findings were observed in fundus photography (Fig. 2A). Fluorescein angiography (FAG) demonstrated no evident leakage in either the retina or the optic disc (Fig. 2C). Head-MRI showed no evidence of optic neuropathy (data not shown). SD-OCT showed disruption of the ellipsoid zone (EZ) line in the macular area (Fig. 2D). Initially the patient was observed without any treatment because of preserved visual acuity and lack of angiopathy and neuropathy findings.

Two months after the onset, the patient still complained of central scotoma, and an Amsler chart showed focal metamorphopsia signs, corresponding to the scotoma described by GP evaluation (Fig. 1A and B left). SD-OCT showed that a part of the EZ line had disappeared and an edematous cystic lesion with a pale shadow had appeared in the outer nuclear layer (ONL) in the macular area (Fig. 2E). Steroid pulse therapy (methylprednisolone 1000 mg/day) was administered for 3 days, after which her subjective report of central scotoma and Amsler chart examination showed improvement (Fig. 1B right).

Three months after the onset, while decreasing oral prednisolone from 30 mg, her central scotoma had worsened subjectively; this was also supported by the results of Humphrey Field Analyzer (HFA) examination (Fig. 1C). Central scotoma was evaluated using HFA10-2 after 3 months (Fig. 1C–G). SD-OCT showed that, following the edematous change of the ONL, a part of the external limiting membrane

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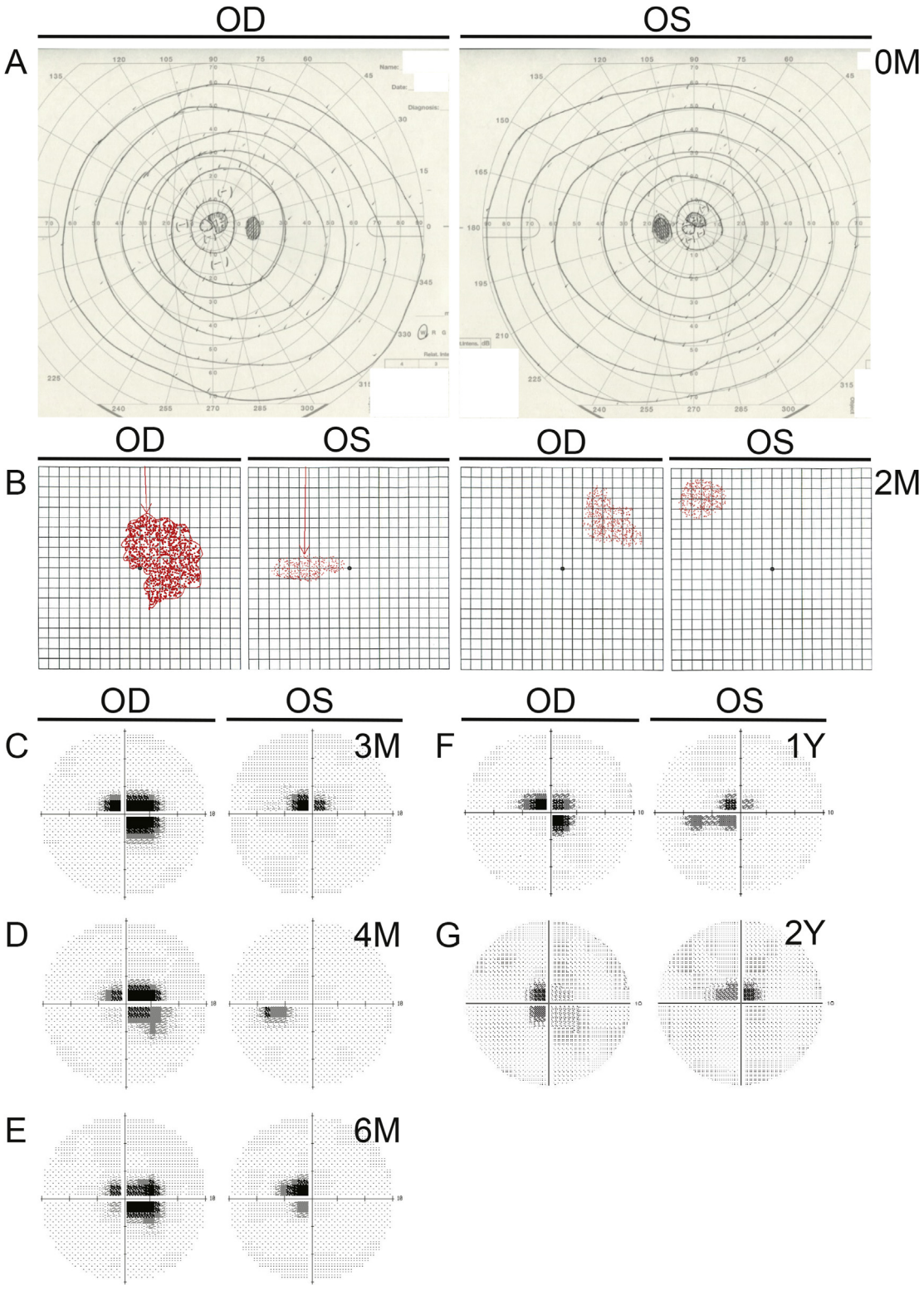

Fig. 1. Change of central scotoma. (A) Goldman perimetry (GP) showing a visual field defect at the initial visit. (B) Amsler chart showing metamorphopsia before (B left) or after (B right) steroid pulse therapy, at 2 months after onset. (C–G) Humphrey Field Analyzer (HFA) 10–2 at 3 (C), 4 (D), 6 (E), 12 (F), and 24 (G) months after onset. In these figures, OD is shown on the left and OS on the right side.

(ELM) line had disappeared, in addition to the EZ line in the macular area (Fig. 2F). Therefore, a second steroid pulse treatment was added, which also yielded improvement of the central scotoma in the left eye in HFA (Fig. 1D).

Six months after the onset, oral prednisolone treatment was stopped to avoid systemic complications, and topical betamethasone was started. Central scotoma still remained in the HFA assessment (Fig. 1E). SD-OCT showed expansion of the edematous area in the ONL and absent areas in both the EZ and ELM lines (Fig. 2G). Wide-field fundus autofluorescence (FAF) imaging showed no abnormality (Fig. 2J). Full-field electroretinography showed a normal response of rod and cone photoreceptors (data not shown).

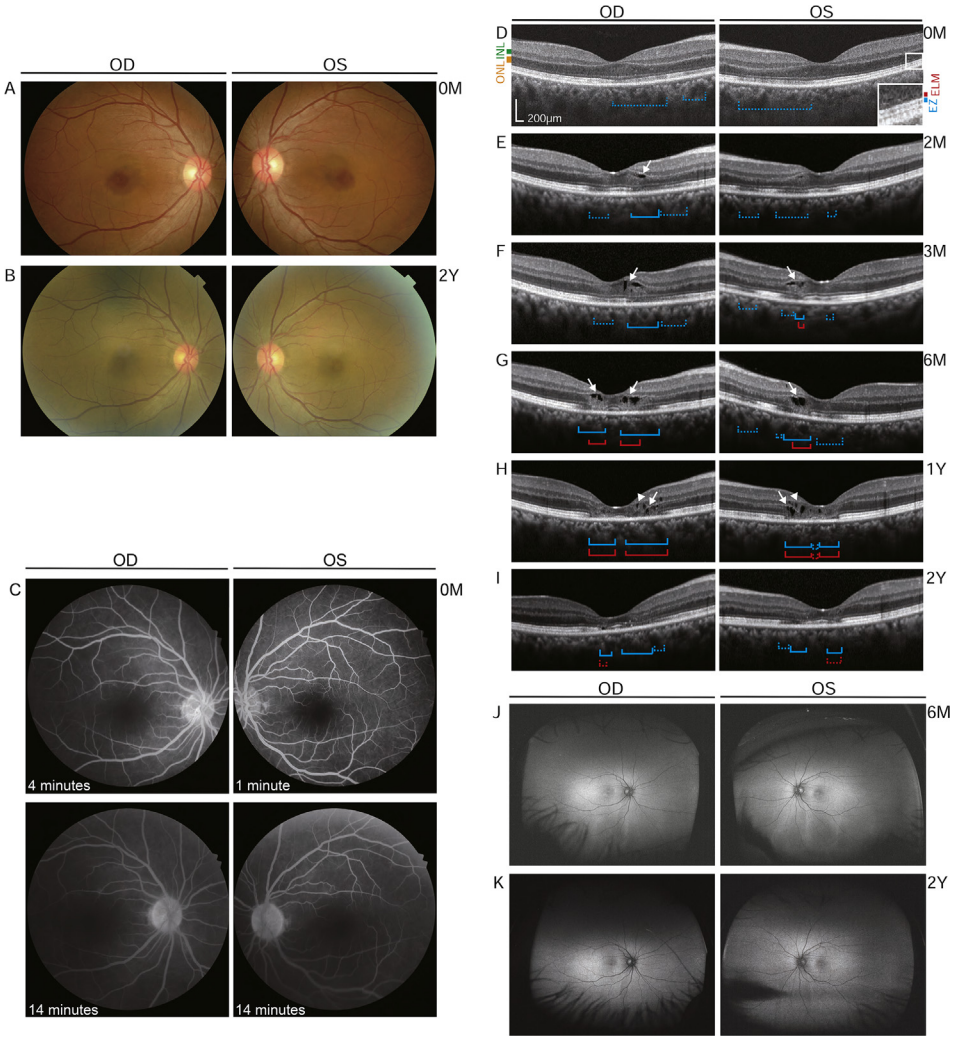

Fig. 2. Change in the fundus lesion. (A and B) Fundus photography at the initial visit (A) and 24 months after the onset (B), showing no abnormal findings. (C) Fluorescein angiography (FAG) at 1 (upper right), 4 (upper left), and 14 (bottom right and left) minutes, showing no evident leakage in either the retina or the optic disc at the initial visit. (D–I) Spectral domain optical coherence tomography (SD-OCT) showing changes in photoreceptor degeneration in the macula at the initial visit (D), 2 (E), 3 (F), 6 (G), 12 (H), and 24 (I) months after the onset. (J and K) Wide-field fundus autofluorescence imaging at 6 (J) and 24 months (K) after the onset, showing no abnormal findings.
In these figures, OD is shown on the left and OS on the right side. (D right) The insets represent the higher magnification of the white boxes. (D–I) Dashed brackets and brackets show disruption and absence of the ellipsoid zone (EZ) (blue) and external limiting membrane (ELM) (red) lines. (E–H) Arrows and arrow heads show edema in the outer nuclear layer (ONL) and inner nuclear layer (INL), respectively. (D) Scale bar, 200 μm (vertical and horizontal, respectively). (D-I) are the same scale. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

One year after onset, SD-OCT showed thinning of the ONL in the macula, an edematous cystic lesion in the inner nuclear layer (INL) and expansion of the absent areas in both the EZ and ELM lines (Fig. 2H). In HFA, the central scotoma was still present, but there was no further deterioration (Fig. 1F).

Two years after onset, the central scotoma was improved in HFA (Fig. 1G). In SD-OCT images, while the thinning of the ONL remained, the edematous cystic lesion had disappeared and the size of the absent areas of the EZ and ELM line were reduced. The fovea seemed to be preserved (Fig. 2I). Even at this time point, no abnormal findings were observed with fundus photography or FAF imaging (Fig. 2B and K). Throughout the follow-up period, visual acuity had been preserved.

3. Discussion

We here presented a unique case of retinitis after influenza infection. Other systemic diseases and viral infections were not found by clinical examination, supporting that the etiology of retinal change was the influenza infection.

Several reports have described a variety of ocular manifestations after influenza infection or influenza vaccination. The typical finding of retinal involvement after influenza infection is retinitis with vascular changes. Mansour et al. reported that the incidence of retinitis after influenza infection was 4.49% in 89 patients in the pandemic of H1N1 influenza in 2009.[1] In literature case reports, Rabon et al. reported bilateral posterior angiopathy with macular edema and multiple cotton wool spots in the inner retina; FAG showed leakage from the perifoveal capillary network.[2] Kovacs et al. suggested that alteration in the inner blood–retina barrier is the origin of dye leakage in retinitis after influenza infection.[3] Cheung et al. reported bilateral vaso-occlusive retinal vasculitis associated with H1N1 influenza A-related encephalitis.[4] The OCT pathology is similar to that of acute macular neuroretinopathy (AMN), which has been described after administration of the flu vaccine.[5] However, the characteristic findings, “darkish brown-red, wedge-shaped dots in the macula pointing the fovea,” were not observed in this case. In addition to AMN, multiple evanescent white dot syndrome, accepted generally as a photoreceptoritis, has reportedly followed administration of the flu vaccine.[6] However, the characteristic findings, such as multiple white dots at the level of the outer retina in fundus photography or multiple hyperfluorescent spots in the early phase in FAG, were not observed in this case.

From this point of view, our case is a unique form of retinitis, as we did not find any exudative and ischemic changes in FAG. Retinitis without any particular fundus finding was also reported by Fukami et al.; however, in their case, granular hyper-fluorescence with multiple dark circular lesions were observed, and the patients had encephalitis related to influenza H3N3.[7]

Moreover, we observed the details of morphological changes in the photoreceptor layer using SD-OCT images. SD-OCT allows clear visualization of retinal structures in vivo, providing pathological information. Photoreceptor damage in the juxta fovea was first detected around the EZ line and gradually expanded to the inner retina, which could indicate that the origin was around the inner segment or outer segment of the photoreceptors. As the degeneration progressed, a part of EZ and

ELM line at the juxta fovea completely atrophied and disappeared, but interestingly, the fovea was preserved, and the central scotoma was improved in HFA at 2 years after the onset. Subsequent cystoid macular edema had been observed, which expanded into the inner retina, and then it gradually reduced longitudinally. In contrast, the retinal pigment epithelium line in SD-OCT images was stable throughout the follow-up period. Normally, the prognosis of visual function in cases with influenza retinitis is considered to be good. On the other hand, severe cases have also been reported, in which vascular occlusion accompanied by encephalitis becomes light perception vision.[4,8] Our patient had preserved visual acuity during the 2-year follow-up period.

The etiology of retinitis is not yet fully understood; however, in several past reports, steroid therapy has been used to treat angiopathy, neuropathy, and retinitis.[4,7,8] Breker et al. considered that retinitis involved production of auto-antibodies in the immune response against the influenza virus, and that these targeted the retina and brain.[8] This could explain the localization of the lesion observed in our patient. In our report, the central scotoma was temporarily improved after steroid pulse therapy. A possible etiology is therefore an auto-immune response that targeted cone photoreceptors, because the lesion was exclusive to the macular area. Antibodies against recoverin, a photoreceptor protein, have been found in patients with cancer-associated retinopathy.[9] However, in our case, anti-recoverin antibodies were not detected in the serum.

4. Conclusion

In this case report of retinitis after influenza infection, we showed mild atrophic progression without any angiopathy, neuropathy, and central nervous system disease; this has not been reported to date. The retinopathy with central scotoma appeared to be caused by influenza infection, and the change in photoreceptor degeneration could be delineated by following its time course in SD-OCT images. Although the occurrence of mild retinitis after influenza infection is not common, we could include this type of retinitis in the differential diagnosis of atypical retinitis.

Patient consent

The patient consented to publication of the case orally.

This report does not contain any personal information that could lead to the identification of the patient.

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Authorship

All authors attest that they meet the current ICMJE criteria for authorship.

Declaration of competing interest

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References

1. Mansour DE, El-Shazly AA, Elawamry AI, Ismail AT. Comparison of ocular findings in patients with H1N1 influenza infection versus patients receiving influenza vaccine during a pandemic. *Ophthalmic Res.* 2012;48(3):134–138.
2. Rabon RJ, Louis GJ, Zegarra H, Gutman FA. Acute bilateral posterior angiopathy with influenza A viral infection. *Am J Ophthalmol.* 1987;103(3 Pt 1):289–293.
3. Kovacs B. Alteration of the blood-retina barriers in cases of viral retinitis. *Int Ophthalmol.* 1985;8(3):159–166.
4. Cheung AY, Anderson B, Stec L, Khandhar P, Williams GA. Bilateral vaso-occlusive retinal vasculitis with H1N1 influenza A infection. *Retin Cases Brief Rep.* 2015;9(2):138–141.
5. De Salvo G, Vaz-Pereira S, Arora R, Lotery AJ. Multicolor imaging in the diagnosis and follow up of type 2 acute macular neuroretinopathy. *Eye.* 2017;31(1):127–131.
6. Abou-Samra A, Tarabishy AB. Multiple evanescent white dot syndrome following intradermal influenza vaccination. *Ocul Immunol Inflamm.* 2019;27(4):528–530.
7. Fukami S, Wakakura M, Inouye J. Influenza retinitis: association with influenza encephalitis. *Ophthalmologica.* 2005;219(2):119–121.
8. Breker DA1, Stacey AW, Srinivasan A, Bursztyn LL, Trobe JD, Johnson MW. Vision loss caused by retinal and lateral geniculate nucleus infarction in H1N1 Influenza. *J Neuro Ophthalmol.* 2015;35(3):265–269.
9. Polans AS, Buczyłko J, Crabb J, Palczewski K. A photoreceptor calcium-binding protein is recognized by autoantibodies obtained from patients with cancer-associated retinopathy. *J Cell Biol.* 1991;112(5):981–989.