Optical coherence tomography angiography features of bilateral retinopathy associated with Chikungunya fever

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A 66-year-old male patient presented with decreased vision in both eyes following episode of Chikungunya fever. Examination revealed bilateral retinal lesions with stippled pigmentary changes at the level of the choriocapillaris, involving the macula in the left eye. The retinopathy consisted of outer retinal disruption and retinochoroidal flow abnormalities detected using with additional imaging, including spectral-domain optical coherence tomography (OCT), autofluorescence, and OCT angiography (OCTA). The index case report describes unique OCTA findings in both eyes of an elderly male secondary to Chikungunya fever. Using the technique of OCTA, insights into the mechanisms of visual damage in viral retinopathies such as Chikungunya fever can be understood.

Key words: Chikungunya, optical coherence tomography angiography, retinopathy

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Chikungunya fever is a debilitating and often fatal vector-borne viral illness transmitted by *Aedes aegypti* and *Aedes albopictus* mosquitoes. The disease is caused by a single-stranded RNA virus belonging to the genus, *Alphavirus* and family, *Togaviridae*. The symptoms of Chikungunya include severe arthralgias, muscle pain, high-grade fever, headache, and skin rash. Although this condition is typically a self-limited illness, it can result in severe arthritis and fever, similar to dengue.[1,2] Chikungunya posterior uveitis presents with retinitis with surrounding retinal edema and opacification. In addition, there can be serous retinal detachment and intraretinal fluid. This condition is an acute disease that affects immunocompetent individuals and can have significant visual morbidity.[3] Optical coherence tomography angiography (OCTA) is a novel modality that allows noninvasive and high-resolution three-dimensional mapping of the retinal and choroidal circulations.[4] Using OCTA, analysis of the retinal microvasculature in the superficial and

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deep retinal plexuses (SCP and DCP), as well as choriocapillaris is possible. In the index case report, the role of OCTA in the analysis of pathological microvascular alterations in a patient with bilateral retinal involvement secondary to Chikungunya fever is highlighted.

Case Report

A 66-year-old Asian Indian male presented with a history of high-grade fever with chills and rigors, severe arthralgia, popular skin rash, and fatigue. He was diagnosed with Chikungunya fever based on IgM-positive results from his serum sample. Investigations revealed erythrocyte sedimentation rate of 34 mm at the end of 1 h, platelet counts of 150,000/mm^3, hemoglobin of 13 g/dL, and total leukocyte count of 12,000/mm^3. The patient received treatment elsewhere for the condition including supportive management by antipyretic agents, fluids, and supportive therapy. For arthritis, the patient was also advised oral hydroxychloroquine. Due to significant fluid loss and severe disease, the patient also developed acute renal failure requiring dialysis. Fifteen days after the onset of fever, the patient developed decreased vision and photophobia in both eyes. However, the visual symptoms were not further evaluated at this time given his systemic comorbidities.

Six weeks after the onset of fever, the patient presented to the Ophthalmology department for further evaluation of decreased vision, which remained persistent. Detailed examination revealed best-corrected visual acuity (BCVA) of 20/60 in the right eye (OD) and 20/30 in the left eye (OS). No relative afferent pupillary defect was apparent. Slit-lamp examination showed the absence of inflammation in the anterior chamber. There was no evidence of vitritis at this time. Intraocular pressure was 12 mmHg in OD and 13 mmHg in OS. The dilated fundus examination of the OD showed the presence of peripapillary areas of depigmented healed retinitis lesions with retinal pigment epithelial (RPE) alterations. Similar lesions were seen near the inferior arcade and temporally. The macula was spared [Fig. 1]. The patient had the presence of a dense nuclear cataract in OD. Autofluorescence imaging (FAF) showed stippled irregular hypoautofluorescence in the nasal peripapillary lesions and hyperautofluorescence in the lesions inferiorly. The OS showed the presence of a healed macular lesion with RPE alterations and hypoautofluorescence on FAF imaging. There was an area of hyperautofluorescence at the superior arcade near the optic nerve head [Fig. 1].

OCT scans through the macula in OD showed a normal foveal contour with relative preservation of all the retinal layers. There were few hyperreflective foci in the inner retinal layers causing subtle back-shadowing on OCT. OCT scan through the macula of OS showed the presence of outer retinal disruption (disruption of the external limiting membrane [ELM], ellipsoid, and myoid zone) and mild RPE elevation and focal thickening [Fig. 2]. OCTA of OD showed an irregular decrease in the SCP and DCP. In addition, the choriocapillaris slab on automatic segmentation revealed few subtle hyporeflective areas suggestive of flow deficit. In OS, the OCTA at the level of SCP and DCP showed a more significant loss of vascular density compared to OD. The choriocapillaris slab in OS showed discrete areas of hyporeflectivity suggestive of flow deficit, more obvious compared to OD [Fig. 3].

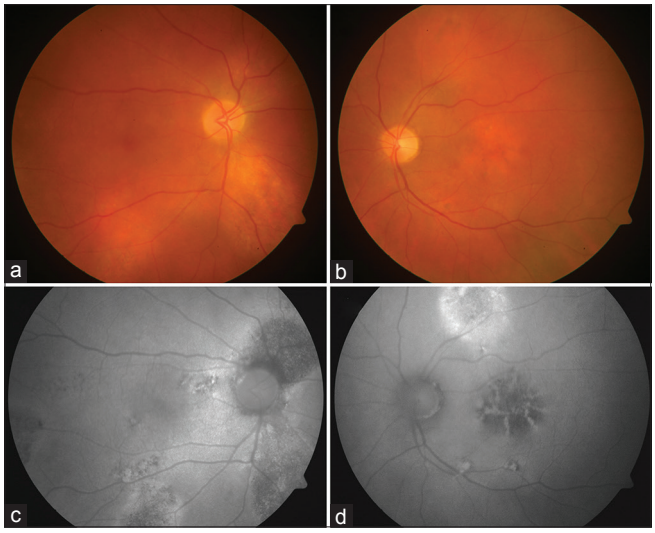

Figure 1: Fundus photographs and autofluorescence of the patient with bilateral retinopathy related to Chikungunya fever in an elderly male. The right eye shows presence of retinal pigment epithelial changes in the nasal peripapillary regions along with resolved disc edema (a). There are similar changes at the level of the outer retinal layers and the retinal pigment epithelium near the inferior arcade. Fundus photograph of the left eye shows presence of retinal pigment epithelial changes and hypopigmented areas suggestive of chorioretinal lesions near the superior arcade and at the center of the macula (b). Autofluorescence imaging of the right eye (c) shows hypoautofluorescence in the nasal peripapillary lesions and stippled irregular hyperautofluorescence in the area temporal to the optic nerve head, inferiorly and near the inferior arcade. Similarly, autofluorescence imaging of the left eye (d) shows hypoautofluorescence with linear streaks of hyperautofluorescence in the macular lesions. The superior arcade lesions are hyperautofluorescent

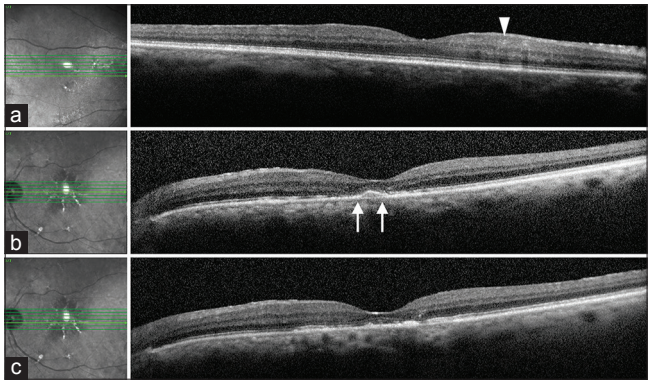

Figure 2: Spectral-domain optical coherence tomography imaging of the right and left eyes of the patient with Chikungunya retinopathy. Spectral-domain optical coherence tomography of the right eye (a) Passing through the macula shows normal foveal contour. There are inner retinal hyperreflective foci (white arrowhead) colocalized to the bright lesions on infrared imaging. Spectral-domain optical coherence tomography of the left eye (b) Shows thinning of the central macula with decrease in thickness of various retinal layers. The retinal pigment epithelial layer shows slight elevation with underlying hyperreflectivity and disruption of external limiting membrane, ellipsoid and myoid zone, and irregular discontinuity of the retinal pigment epithelium (white arrows). Similar changes are seen in the optical coherence tomography B-scan passing just inferior to the fovea. There are outer retinal changes and disruption of various retinal layers (c)

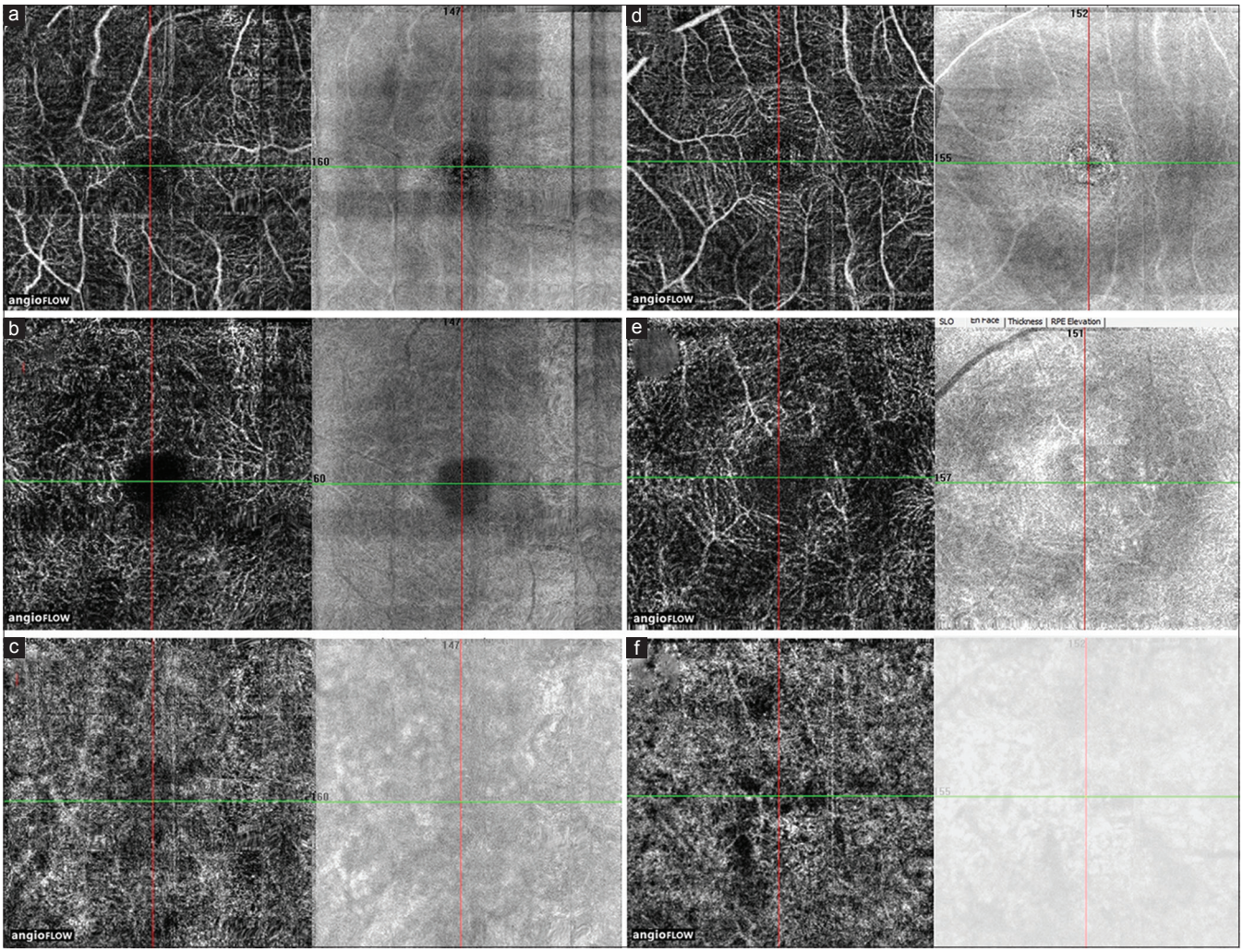

Figure 3: Optical coherence tomography angiography of the right eye (a-c) and left eye (d-f) (en face optical coherence tomography angiography scans along with corresponding structural optical coherence tomography angiography scan). The superficial retinal slabs of the right and left eye (a and d) show irregularly decreased vascularity. The deep retinal slab of the right and left eye (b and e) show areas of decreased vascularity. The deeper retinal layers are more significantly affected compared to the superficial slabs. The choriocapillaris slab (c and f) show focal dark areas of hypo-reflectivity without corresponding signal loss on structural optical coherence tomography angiography suggestive of true choriocapillaris flow deficit

The patient was followed up with no ocular treatment (oral hydroxychloroquine, started 6 weeks ago, was continued), and was afebrile and asymptomatic systemically at this time. Ten weeks after the episode of Chikungunya fever, he was systemically well, and BCVA measured 20/50 in OD and 20/40 in OS. There was no further improvement of BCVA or change in the fundus/OCTA appearance at 4-month follow-up visit.

Discussion

Chikungunya fever-related uveitis can occur during the acute phase of the disease or even weeks or months later. Patients often present with fever, headache, arthralgia, and skin rash a few weeks before the onset of visual symptoms (blurring of vision, diplopia, scotomata, redness, and retroorbital pain).[1-3,5] Involvement of the posterior segment may occur resulting in the development of retinitis lesions. These are usually accompanied by mild vitritis and disc edema.[6] There may be anterior chamber inflammation and macular edema. Similar to other viral retinopathies, severe presentations may include bilateral involvement[7-9] (as in our index case, though rarely reported), exudative retinal detachments, and severe vision-threatening optic neuritis/neuroretinitis.[1-3,5,6] Other manifestations include retinal hemorrhages, retinal edema, and multifocal choroiditis.[7,10] According to a series from South India, and other case reports in literature, the long-term implications of Chikungunya-related posterior segment manifestations are not well known.[3] The fundus and FAF changes were seen in our patient suggest chronicity of the disease. The changes at the level of the RPE and outer retina in our patient, such as the track seen inferior to the disc may be a sequela of choroiditis/exudative detachment that may have occurred in the early/acute phase.

In our study, the retinal lesions that were observed in both the eyes were mainly limited to the outer retinal layers, resulting in disruption of the ELM, ellipsoid and myoid zones (EZ and MZ), and the choriocapillaris [Fig. 2]. In our case, these changes were accompanied by retinovascular alterations in all the retinal layers (superficial and deep) as well as choriocapillaris resulting in flow deficit. As evident on the structural scans, there was no signal loss, suggesting that the hyporeflective areas were truly

representing lack of flow [Fig. 3]. The choriocapillaris flow deficit has not been reported in Chikungunya viral infections previously. However, it is known that Chikungunya-related uveitis can present with choroidal involvement such as bilateral macular choroiditis or multifocal choroiditis.[7] Thus, while retinal involvement may be the most common site of pathology in Chikungunya infections, rare cases may present with choroidal involvement with flow abnormalities, such as the index patient.

One case report describes acute macular neuroretinopathy (AMN) in a patient with Chikungunya fever.[11] AMN is defined as outer retinal ischemia involving the DCP with various features including hyperreflectivity of the outer plexiform layer, outer nuclear layer, and disruption of EZ, ELM, and interdigitation zone.[12] In the published case report, the authors diagnosed AMN but did not note any abnormalities on OCTA, a finding that is not consistent with the diagnosis of AMN. Since the OCTA changes in AMN are quite characteristic, there may have been an error in the interpretation of OCTA in their patient. Alternatively, since the authors used speckle variance OCTA which has slightly less visualization of the contrast and continuity of the vessels compared to split-spectrum OCTA (used for our patient), the DCP ischemia may have been missed.[13] Our patient was on treatment with oral hydroxychloroquine for the past 6 weeks (250 mg/day). The common risk factors for developing retinal toxicity due to hydroxychloroquine include a dose of >6.5 mg/kg/day or a cumulative dose of >1000 gm, being on treatment for >5 years, having preexisting retinopathy and being elderly.[14] Given that our patient did not fit into any of the above criteria, and was on safe dose of hydroxychloroquine for a short period, hydroxychloroquine toxicity was ruled out in our patient.

There are no established treatment guidelines for the management of ocular involvement in patients with Chikungunya fever.[2,3] Antipyretics such as acetaminophen, chloroquine (for arthritis), and hydration are administered for supportive management. While the majority of patients with Chikungunya posterior uveitis are known to recover well with good visual outcome,[3] a subset of patients may have suboptimal visual gain due to permanent retinochoroidal vascular alterations as observed in our case using OCTA.

Conclusion

OCTA may be a good tool to monitor and prognosticate patients with retinopathies related to viral infections such as Chikungunya.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that name, and initial will not be published, and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Lalitha P, Rathinam S, Banushree K, Maheshkumar S, Vijayakumar R, Sathe P, *et al*. Ocular involvement associated with an epidemic outbreak of chikungunya virus infection. Am J Ophthalmol 2007;144:552-6.
2. Mahendradas P, Avadhani K, Shetty R. Chikungunya and the eye: A review. J Ophthalmic Inflamm Infect 2013;3:35.
3. Mahendradas P, Ranganna SK, Shetty R, Balu R, Narayana KM, Babu RB, *et al*. Ocular manifestations associated with chikungunya. Ophthalmology 2008;115:287-91.
4. Agrawal R, Xin W, Keane PA, Chhablani J, Agarwal A. Optical coherence tomography angiography: A non-invasive tool to image end-arterial system. Expert Rev Med Devices 2016;13:519-21.
5. Chhabra M, Mittal V, Bhattacharya D, Rana U, Lal S. Chikungunya fever: A re-emerging viral infection. Indian J Med Microbiol 2008;26:5-12.
6. Rose N, Anoop TM, John AP, Jabbar PK, George KC. Acute optic neuritis following infection with chikungunya virus in Southern rural India. Int J Infect Dis 2011;15:e147-50.
7. Chanana B, Azad RV, Nair S. Bilateral macular choroiditis following Chikungunya virus infection. Eye (Lond) 2007;21:1020-1.
8. Mahesh G, Giridhar A, Shedbele A, Kumar R, Saikumar SJ. A case of bilateral presumed chikungunya neuroretinitis. Indian J Ophthalmol 2009;57:148-50.
9. Murthy KR, Venkataraman N, Satish V, Babu K. Bilateral retinitis following chikun- gunya fever. Indian J Ophthalmol 2008;56:329-31.
10. Nair AG, Biswas J, Bhende MP. A case of bilateral chikungunya neuroretinitis. J Ophthalmic Inflamm Infect 2012;2:39-40.
11. Pang CE, Navajas EV, Warner SJ, Heisler M, Sarunic MV. Acute macular neuroretinopathy associated with chikungunya fever. Ophthalmic Surg Lasers Imaging Retina 2016;47:596-9.
12. Bhavsar KV, Lin S, Rahimy E, Joseph A, Freund KB, Sarraf D, *et al*. Acute macular neuroretinopathy: A comprehensive review of the literature. Surv Ophthalmol 2016;61:538-65.
13. Gorczynska I, Migacz JV, Zawadzki RJ, Capps AG, Werner JS. Comparison of amplitude-decorrelation, speckle-variance and phase-variance OCT angiography methods for imaging the human retina and choroid. Biomed Opt Express 2016;7:911-42.
14. Ding HJ, Denniston AK, Rao VK, Gordon C. Hydroxychloroquine-related retinal toxicity. Rheumatology (Oxford) 2016;55:957-67.