Unilateral hemorrhagic maculopathy: An uncommon manifestation of hand, foot, and mouth disease

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Hand, foot, and mouth disease (HFD) is a common systemic infection occurring in childhood or immunocompromised adults caused by enteroviruses, the most common being coxsackievirus A16 and enterovirus 71. It is characterized by maculopapular eruptions over the hands and feet and ulcerative stomatitis. Ocular involvement is a rare complication and commonly manifests as inflammatory macular pathology. We report a case of HFD in an immunocompetent adult male with unilateral ocular involvement presenting as hemorrhagic maculopathy and its management with complete anatomical and functional recovery.

Key words: Fluorescein angiogram, fundus autofluorescence, hand, foot, and mouth disease, hemorrhagic maculopathy, indocyanine green angiogram, optical coherence tomogram

Hand, foot, and mouth disease (HFD) is a viral infection affecting children and immunocompromised adults and rarely immunocompetent adults.[1] The common causative viruses are enterovirus 71 (E71) and coxsackievirus serotype A16 (CA16) though other serotypes have also been described.[1] The classic clinical presentation is maculopapular or vesicular rash over hands and feet and ulcerative stomatitis but life-threatening systemic complications such as encephalitis, myocarditis, and pulmonary complications are known in susceptible patients. Although the ocular involvement is rare, uveoretinitis,[2] outer retinitis,[3] and exudative maculopathy[4] have been described.

We present a case of a young male with HFD with unilateral hemorrhagic maculopathy (HM) and its management with the recovery of best-corrected visual acuity (VA) and normalization of the retinal anatomy.

Access this article online

Quick Response Code:

Website: www.ijo.in

DOI: 10.4103/0301-4738.195014

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Manuscript received: 13.01.16; Revision accepted: 11.09.16

Case Report

A 21-year-old male presented with a painless decrease in vision of the left eye for 1 day. He had fever along with maculopapular eruption on hands and foot and ulceration on the lower labial mucosa [Fig. 1a-c] for 5 days and he had already been diagnosed by a dermatologist as a case of HFD. On presentation, his VA was 20/20 and 20/30 in the right and left eyes, respectively. Anterior segment evaluation was within normal limits (WNL) in both eyes. Fundus evaluation of right eye was normal, and in the left eye, there were multiple intraretinal hemorrhages (IRHs) within the temporal arcade and serous elevation of the macula [Fig. 1d], rest of the fundus was WNL.

The systemic workup including complete blood counts, peripheral blood smear, and C-reactive protein was WNL and he was negative for human immunodeficiency virus.

The fundus autofluorescence (FAF) showed a generalized reduction of FAF from macula with some areas of dense hypo autofluorescence corresponding to IRH [Fig. 1e], and the optical coherence tomography (OCT) (Heidelberg, Germany, Version 1.9.20.0) showed bifocal serous elevation of the macula [Fig. 1f]. He also underwent a combined fluorescein angiography (FA) and indocyanine green angiography (ICG) which, in the early phase, showed blocked fluorescence in the areas of IRH on FA and "moth-eaten" appearance of the choroidal vasculature (CV) on ICG [Fig. 1g], and in the late phase, FA showed diffuse leak suggestive of a breach in the outer blood-retinal barrier and hypercyanescence on ICG suggestive of the inflammatory pathology of the CV [Fig. 1h], the right eye being normal in all investigations. Based on the clinical findings and other investigations, he was diagnosed as a case of HFD-associated unilateral HM.

The patient was started on oral prednisolone (1 mg/kg body weight) in tapering dose after the clearance from an internist and was reviewed after a week. Next week, his VA had dropped to 20/40 in the left eye and the right eye was normal. His general clinical evaluation showed complete resolution of the maculopapular rash on palms and soles and his oral ulcers had healed. The ocular evaluation showed resolution of the serous detachment and resolving IRH [Fig. 2a]. The FAF showed improvement [Fig. 2b] and OCT showed resolution of serous detachment with debris

Cite this article as: Tandon M, Gupta A, Singh P, Subathra GN. Unilateral hemorrhagic maculopathy: An uncommon manifestation of hand, foot, and mouth disease. Indian J Ophthalmol 2016;64:772-4.

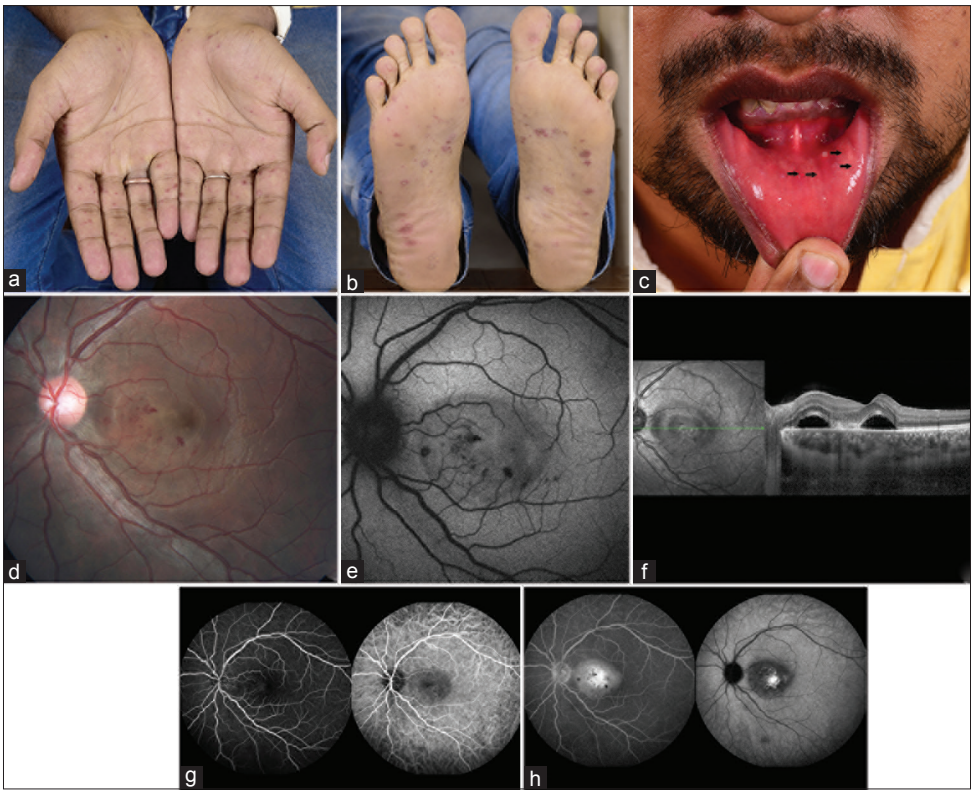

Figure 1: (a and b) Maculopapular eruptions over palms and foot. (c) Ulcerative stomatitis (black arrowheads). (d) Fundus photo showing intraretinal hemorrhages and serous elevation of the macula. (e) Fundus autofluorescence shows generalized reduction at macula and some dense areas of hypo-autofluorescence corresponding to intraretinal hemorrhage. (f) Optical coherence tomography showing bifocal serous elevation of the macula. (g and h) Combined fluorescein angiography and indocyanine green angiography in the early and late phase, respectively. Early phase fluorescein angiography showing blocked fluorescence corresponding to intraretinal hemorrhage and indocyanine green angiography showing "moth-eaten appearance." Late-phase fluorescein angiography shows diffuse leak and indocyanine green angiography showing diffuse hypercyanescence

collection at the inner segment-outer segment junction (IS/OS) with intact external limiting membrane [Fig. 2c]. His next follow-up at 1 month showed improvement in VA (20/20) and anatomical improvement corroborated by fundus evaluation, FAF and OCT [Fig. 2d-f]. His last follow-up at 2 months showed VA in both eyes 20/20, and he was symptomatically normal. The anterior segment was WNL, and the fundus showed normal foveal reflex in both eyes. The FAF was nearly normal with some stippling, probably due to recovering retinal pigment epithelial function, and the foveal contour on OCT was normalized with the reformation of IS/OS junction [Fig. 2g-i].

Discussion

HFD commonly affects children and immunocompromised adults, and only a few cases of immunocompetent adults have been described in literature.[5] The mechanism of eye involvement has been proposed to be either direct viral infection by hematogenous spread or autoimmune process. The ocular involvement was first described by Yannuzzi *et al*. as unilateral acute idiopathic maculopathy (UAIM) in nine patients with preceding viral prodrome.[6] The condition is associated with CA16 or E71 infection, but a number of other serotypes have also been described. Systemic disease caused by E71 is more severe than CA16.[1] Jung *et al*. reported that the most common association of UAIM was viral fever as a prodromal symptom (50%) and HFD was in 25% cases with a positive titer of coxsackievirus in 50% cases.[7] They also described the "moth-eaten" appearance of CV on ICG, but late leak or areas of hypercyanescence was not seen in any patient, which is in contrast to our case where the leak in the late phase was present. The neurosensory detachment is a common finding and has been described in the reported literature.

The use of systemic steroids in HFD is a controversial issue as the spontaneous resolution of the disease has been reported in about 3 months.[4,8] Two reports on the use of steroids in HFD have been described previously.[9,10] In this case, we used steroids, and the patient had anatomical and functional normalization within 2 months which goes in conjunction with the previous reports of steroid usage, and the recovery was faster. The difference between this case and a previous case[9] where steroids were used is that in our case, there was complete recovery of retinal architecture as shown by normalization of OCT and reformation of IS/OS junction. The present case and the previous two cases did not have any ocular or systemic side effect with steroids usage.

The occurrence of HM in association with HFD in an immunocompetent adult is an uncommon event, and spontaneous resolution of the disease is known but the use

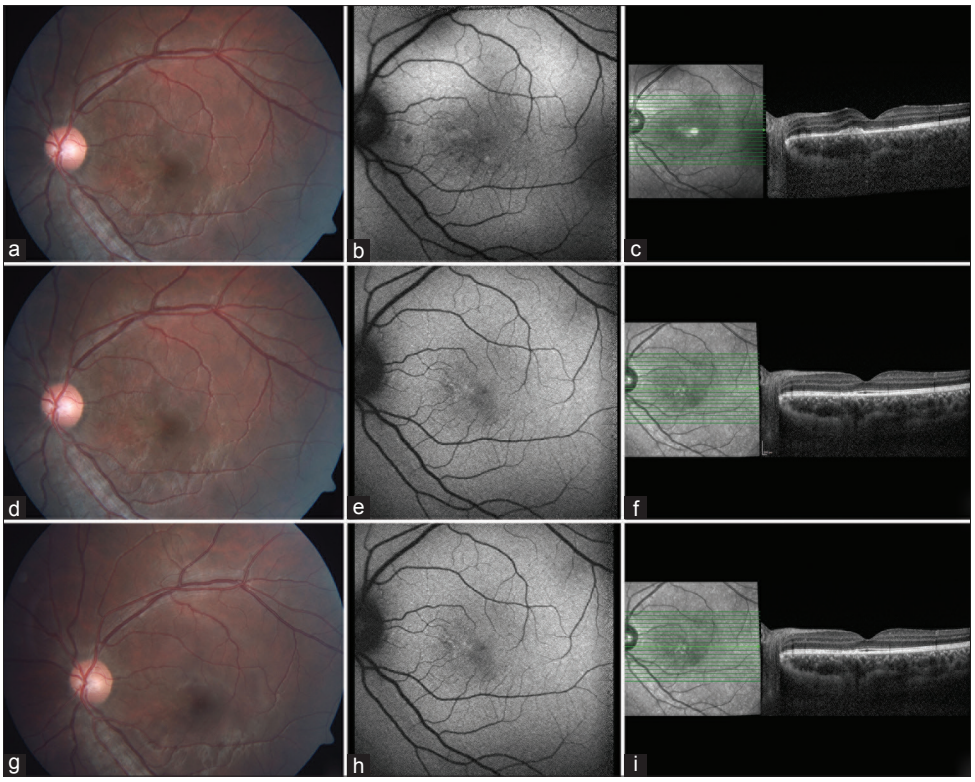

Figure 2: (a) Fundus photo showing resolution of serous detachment and resolving intraretinal hemorrhage. (b) Fundus autofluorescence showing reduction of the area of hypo-autofluorescence and resolving intraretinal hemorrhage. (c) Optical coherence tomography showing complete resolution of serous detachment at macula with intact external limiting membrane and debris at inner segment/outer segment junction. (d) Fundus photo showing resolving intraretinal hemorrhage. (e) Fundus autofluorescence showing improvement at 1 month. (f) Optical coherence tomography showing reformation of the inner segment/outer segment junction and resolution of the debris. (g) Fundus photo showing resolved hemorrhagic maculopathy. (h) Normalizing macular fundus autofluorescence with some stippling. (i) Normalized foveal contour with resolved debris at inner segment/outer segment junction

of steroids can shorten the duration of ocular morbidity, and faster visual rehabilitation can be achieved.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Tsao KC, Chang PY, Ning HC, Sun CF, Lin TY, Chang LY, *et al.* Use of molecular assay in diagnosis of hand, foot and mouth disease caused by enterovirus 71 or coxsackievirus A 16. J Virol Methods 2002;102:9-14.
2. Takeuchi M, Sakai J, Usui M. Coxsackievirus B4 associated uveoretinitis in an adult. Br J Ophthalmol 2003;87:501-2.
3. Haamann P, Kessel L, Larsen M. Monofocal outer retinitis associated with hand, foot, and mouth disease caused by coxsackievirus. Am J Ophthalmol 2000;129:552-3.
4. Vaz-Pereira S, Macedo M, De Salvo G, Pal B. Multimodal imaging of exudative maculopathy associated with hand-foot-mouth disease. Ophthalmic Surg Lasers Imaging Retina 2014;45:e14-7.
5. Shin JU, Oh SH, Lee JH. A case of hand-foot-mouth disease in an immunocompetent adult. Ann Dermatol 2010;22:216-8.
6. Yannuzzi LA, Jampol LM, Rabb MF, Sorenson JA, Beyrer C, Wilcox LM Jr. Unilateral acute idiopathic maculopathy. Arch Ophthalmol 1991;109:1411-6.
7. Jung CS, Payne JF, Bergstrom CS, Cribbs BE, Yan J, Hubbard GB 3rd, *et al.* Multimodality diagnostic imaging in unilateral acute idiopathic maculopathy. Arch Ophthalmol 2012;130:50-6.
8. Duman R, Duman N, Kutluksaman B, Çetinkaya E, Inan S, Inan ÜÜ. A review of unilateral acute idiopatic maculopathy related to hand-foot-mouth disease with a representative case. Int Ophthalmol 2016;36:445-52.
9. Agrawal R, Bhan K, Balaggan K, Lee RW, Pavesio CE, Addison PK. Unilateral acute maculopathy associated with adult onset hand, foot and mouth disease: Case report and review of literature. J Ophthalmic Inflamm Infect 2015;5:2.
10. Kadrmas EF, Buzney SM. Coxsackievirus B4 as a cause of adult chorioretinitis. Am J Ophthalmol 1999;127:347-9.