The blisters and beyond: Adult case of hand, foot, and mouth disease with a surprise twist

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SUMMARY

Hand, foot, and mouth disease (HFMD) is a highly contagious viral illness caused by coxsackievirus. HFMD primarily affects children and is rarely seen in adults. Unilateral acute idiopathic maculopathy (UAIM), a rare inflammatory disorder of the retinal pigment epithelium (RPE), has been associated with HFMD. This case report describes a rare occurrence of UAIM in an adult patient with HFMD. A 36-year-old man with underlying hypertension, presented with sudden onset, painless and non-progressive central vision loss of the right eye. There was a history of self-limiting fever associated with an acute maculopapular rash and blisters over bilateral palms and soles. He had history of contact with his one-year-old son, who was diagnosed with HFMD recently. His visual acuity was counting finger OD and 6/9 OS on presentation at the eye clinic. There was right central scotoma on confrontation test. Fundus examination showed an irregular yellowish-greyish macular lesion. The retinal pigmented epithelium (RPE) was thickened with hyperreflectivity debris on the apical end and disruption of ellipsoid zone subfoveal area on optical coherence tomography (OCT). Fundus fluorescein angiography (FFA) showed early phase of patchy area of irregular hypofluorescent subfoveal area, with surrounding hyperfluorescent at the late phase. He was treated with tapering dose of oral prednisolone for two months. On follow-up, his vision improved to 6/9 with marked resolution of maculopathy. Acute maculopathy is rare in HFMD and challenging to diagnose in adults. Higher index of suspicious and multimodal imaging aids in the diagnosis.

INTRODUCTION

Hand, foot, and mouth disease (HFMD) is a highly contagious viral illness caused by coxsackievirus from the enterovirus family. The species responsible for HFMD belongs to enterovirus species A, with enterovirus A71 accounting for more than 90% of cases. The remaining cases are mainly caused by coxsackievirus A16.[1] HFMD primarily affects children and is rarely seen in adults. Diagnosis of HFMD is mainly based on clinical presentation but involvement of the eye is rare. There have been reports of unilateral acute idiopathic maculopathy (UAIM) associated with HFMD.[2,3] UAIM is a rare inflammatory disease of the retinal pigment epithelium (RPE) that affects healthy young adults, without any preference for sex or race. It is commonly observed on ophthalmic imaging as a disruption of the retinal pigment epithelium (RPE), accompanied by an exudative detachment of the neurosensory retina, affecting central vision. Papillitis, retinal hemorrhages, and mild vitritis, have also been reported.[2]

CASE PRESENTATION

A 36-year-old man with well-controlled hypertension presented with sudden-onset, painless, and non-progressive central vision loss in his right eye for five days. He presented to the emergency department on the first day of symptom onset and was referred to the eye clinic for further assessment following review by the ophthalmology medical officer. Three weeks prior to this, he experienced a self-limiting low-grade fever lasting for five days, accompanied by an acute maculopapular rash and blisters on both palms and soles but no oral ulcers. During this episode, he did not seek medical attention but practised self-isolation. He had history of recent contact with his one-year-old son, who had been diagnosed with HFMD and successfully treated.

At presentation, he was afebrile, with a blood pressure of 110/80mmHg. There were no visible maculopapular rashes, blisters, or oral ulcers. His visual acuity was counting fingers in the right eye (OD) and 6/9 in the left eye (OS), with no relative afferent pupillary defect. A confrontation test revealed a right central scotoma. Anterior segment examination and intraocular pressure in both eyes were within normal limits. Fundus examination of the right eye revealed an irregular yellowish-grey macular lesion (Fig. 1a). The optic disc was pink with well-defined margin and a cup-disc ratio of 0.3. There was no evidence of papillitis, retinitis, macular detachment, retinal hemorrhages, or hypertensive retinopathy. Both anterior and posterior segments of the left eye were unremarkable.

Spectral domain optical coherence tomography (SD-OCT) showed thickening of the retinal pigment epithelium (RPE), hyperreflective debris at the apical end, and disruption of the ellipsoid zone in the subfoveal area (Fig. 2a). This was consistent with RPE inflammation but without evidence of subretinal or intraretinal fluid. Fundus fluorescein angiography (FFA) revealed a patchy area of irregular hypofluorescence in the subfoveal region during the early

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Table I: Summary of reported cases of unilateral acute maculopathy associated with adult onset of hand, foot, and mouth disease.

Reference	Number of case(s)	Age	Sex	Duration of onset (Days)	Eye	Initial VA (Snellen chart)	Final VA (Snellen chart)	OCT finding	Treatment
Yen et al., 2023[3]	1	23	M	5	OS	6/48	6/60	Heterogeneous hyperreflective thickening of the outer retina and RPE in the foveal region with loss of ellipsoid zone	Nil
Duman et al., 2016[4]	1	24	M	3	OS	6/60	6/6	Disruption of the IS-OS junction and hyperreflective debris at the apical end of RPE	Nil
Yannuzzi et al., 1991[5]	9	15-45	4 M 5 F	2-5	NR	6/18- CF	6/6- 6/60	Subfoveal NSR detachment with thickened RPE	Nil *
Miguel et al., 2011[6]	1	25	M	NR	OD	6/6 †	6/5	Thickened RPE and hyperreflective RPE lesion protruding into IS-OS junction	Oral corticosteroid
Agrawal et al., 2015[7]	1	35	F	1	OD	6/24	6/6	Dumb-bell-shaped lesion with disruption of the IS-OS junction and hyperreflective debris at the apical end of RPE	Oral corticosteroid
Demirel et al., 2014[8]	1	30	M	3	OD	6/15	6/7.5	Subfoveal NSR detachment with with mild intraretinal cystic changes. Disruption of IS-OS junction and RPE layer	Nil
Jung et al., 2012[9]	1	27	F	1	OD	6/60	6/6	Subfoveal NSR detachment with disruption of IS-OS junction and hyperreflective debris at the apical end of RPE	Nil
Hughes et al., 2012[10]	1	19	F	3	OD	CF	6/6	Subfoveal NSR detachment with disruption of IS-OS junction and hyperreflective in the subretinal space with irregularity of the RPE	Nil
Our case	1	36	M	5	OD	CF	6/9	Disruption of the ellipsoid zone and hyperreflective debris at the apical end of thickened RPE	Oral corticosteroid

NR: Not reported, NSR: Neurosensory retina, CF: Counting finger.
* One patient was treated with oral corticosteroid and a nearly instant recovery in vision was observed.
† Good VA due to very early stage of the disease, absence of serous macular detachment and slight eccentricity of the RPE lesion.

phase (Fig. 3a), with surrounding hyperfluorescence in the late phase, suggesting the potential of exudative detachment (Fig. 3b). However, no microbiological confirmation of coxsackievirus was sought from vitreous or aqueous samples. A clinical diagnosis of unilateral acute idiopathic maculopathy (UAIM) associated with HFMD was established. The patient was treated with a tapering dose of oral prednisolone (1 mg/kg) over two months due to poor visual acuity at presentation. After one month of steroid therapy, his vision improved to 6/9. There was marked improvement in macular lesion (Fig. 1b) and resolution of maculopathy on OCT findings (Fig. 2b). The left eye remained unaffected throughout the follow-up period.

DISCUSSION

Coxsackievirus is a human enterovirus that spreads primarily via oral ingestion of virus shed from the gastrointestinal or upper respiratory tract of infected hosts, or through vesicular fluid and oral secretions. The virus is most contagious during the first week of illness, with symptoms typically manifesting several days after exposure. Once ingested, the virus multiplies in the lymphoid tissues of the lower intestine and pharynx, subsequently spreading to regional lymph nodes. Although rare, viral dissemination to various organs — including the eyes, heart, liver, skin and central nervous system — may result in encephalitis, polio-like syndrome, acute transverse myelitis, Guillain-Barre syndrome, benign intracranial hypertension, and acute cerebellar ataxia.

Most patients with HFMD experience a mild illness and recover within seven to ten days without complications. Classic HFMD is characterized by low-grade fever, malaise, a maculopapular rash or blisters on the hands, soles, and buttocks, and painful ulcerative lesions in the throat, mouth, and tongue. While fever typically resolves within two days, rashes and sores may take up to a week to heal. Notably, many patients with HFMD present with only one or two of these symptoms as in this case.[1]

Unilateral acute idiopathic maculopathy (UAIM) is an inflammatory maculopathy involving the outer retina, retinal pigment epithelium (RPE), and choroid without specific aetiology. Studies have demonstrated that Coxsackievirus B3 can directly infect the RPE in vitro, with its proteins triggering host immune responses.[3,4] Immune-mediated damage is another proposed mechanism underlying the pathogenesis of UAIM.[4] UAIM typically presents with sudden central vision loss, often preceded by a

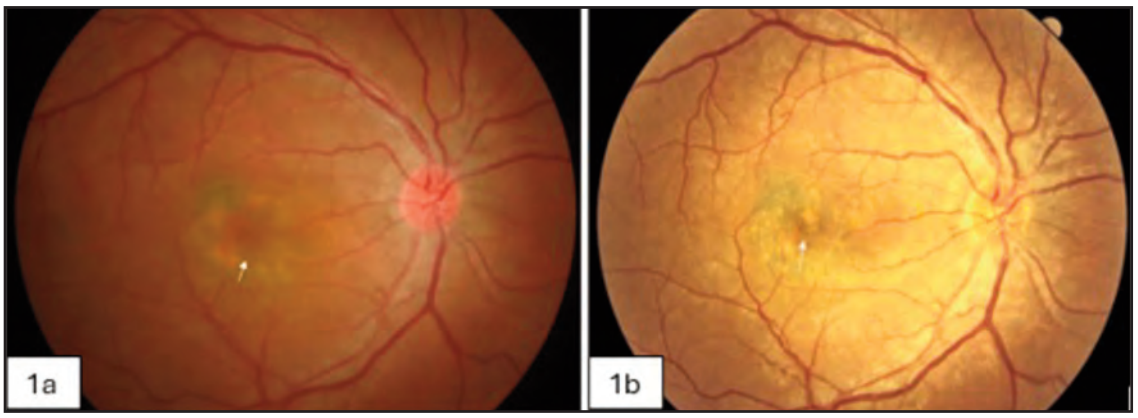

Fig. 1: 1a show irregular yellowish-greyish macular lesion (arrow). 1b show yellowish-greyish macular lesion (arrow) become smaller and more discrete at 12th week

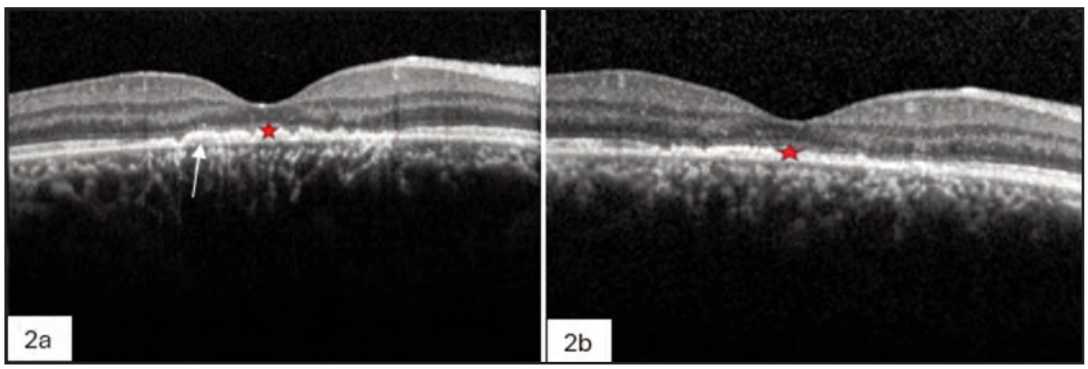

Fig. 2: 2a show thickened RPE with hyperreflectivity debris (arrow) on the apical end of and disruption of ellipsoid zone at the subfoveal area (star). 2b show reduced thickening of RPE and more prominent ellipsoid zone (star) at 12th week

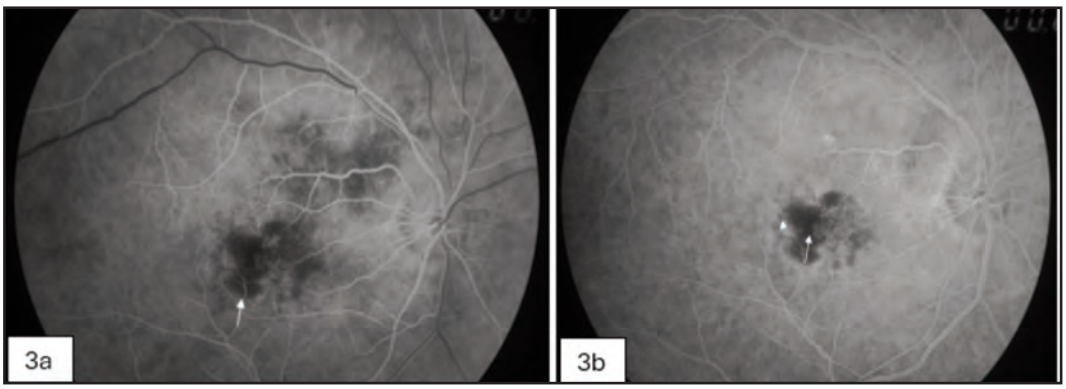

Fig. 3: 3a show early irregular patchy area of hypofluorescent (arrow) at the subfoveal area (16 second). 3b show late irregular hypoflorescent area (arrow) surrounding the hyperfluorescent area (arrow head) (23 second)

prodromal illness. Most patients experience significant visual recovery within several weeks. UAIM was first described by Yannuzzi et al. in 1991. He described nine patients with sudden, unilateral severe visual loss, macular serous detachment, and central scotoma.[5] Seven of these patients had a brief viral or flu-like illness preceding their ophthalmic symptoms.

There was reported case of UAIM without an initial systemic illness, during pregnancy and post vaccination such as COVID-19 vaccination.[6] This clinical variability makes the diagnosis of UAIM challenging. The important differentials include central serous chorioretinopathy (CSCR), Vogt–Koyanagi–Harada disease and placoid syphilitic retinitis, which can usually be differentiated from UAIM by their characteristic pattern in FFA.

To date, a total of 17 cases of UAIM associated with HFMD have been reported including the present report (Table I). These cases involved young adults aged 15–45 years, with a slight male predominance (male-to-female ratio of 9:8). Similar to the present case, visual symptoms were acute,

lasting between one to five days with involvement of unilateral macular. It is hypothesised that the clinical manifestations of HFMD-related UAIM depend on the disease stage. In the early phase, subfoveal neurosensory retinal detachment results in visual disturbance. Over time, the detachment resolves, leaving thickened RPE and ellipsoid zone disruption, which gradually normalise as the disease progresses. Reduction in hyperreflective debris and improvement in visual acuity further support this proposed progression. Other reported findings include intraretinal hemorrhages, papillitis, and vitreous cells.

Changes of the macula in UIAM can be monitored by fundus photographs and other imaging modalities in ophthalmology including OCT, FFA, fundus autofluorescence (FAF) and indocyanine green angiography (ICGA). Agrawal et al. described FAF findings, noting a complex heterogeneous pattern of hyper- and hypo-autofluorescence with clear demarcation lines. As the disease resolved and visual acuity improved, FAF showed increased hypo-autofluorescence, indicating RPE loss. ICGA revealed irregular heterogeneous patches of hypofluorescence corresponding to the macular lesions. However, such retinal alterations are not unique to Coxsackievirus; similar findings have been reported in association with other viral pathogens, including Dengue virus.[7]

In the present case, HFMD was diagnosed clinically. The definitive diagnosis can be done by serological detecting the presence of coxsackievirus but not essential in the management of HFMD. UAIM shares some clinical features with CSCR, making it an important differential diagnosis in cases of subfoveal detachment with fever and flu-like symptoms. Most reported cases of CSCR and UAIM resolve spontaneously within three to 12 weeks of follow-up.

The prognosis of UAIM is generally favourable, with most cases resolving spontaneously without treatment within weeks to months. Treatment is usually initiated if the presenting visual acuity is poor and extensive maculopathy as demonstrated in Table I. Although rare, extensive maculopathy may cause permanent foveal atrophy with residual central scotoma, and in some cases complicated by choroidal neovascularization and macular scarring, resulting in long-term visual impairment. Oral prednisolone may expedite recovery in patients with significant visual loss. In our patient, corticosteroid therapy was tapered over two months, with final visual acuity improving to 6/9 after 12 weeks of follow-up.[2,4]

In summary, HFMD-associated UAIM is a self-limiting condition with good visual recovery. Early recognition of ocular involvement and timely referral from primary care are essential, as vision-threatening differential diagnoses cannot be reliably excluded at initial presentation. This case illustrates that Coxsackievirus, beyond its well-known manifestations in hand, foot, and mouth disease, can also affect the eyes. Prompt ophthalmic assessment is therefore essential, as it enables appropriate management and supports favorable visual recovery.

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