Pseudomembranous conjunctivitis with hand, foot and mouth disease in a pregnant woman: a case report

Yoo Jin Kim and Tae Gi Kim*

Abstract

Background: Hand, foot, and mouth disease (HFMD) is a common systemic infection that is caused by an enterovirus, normally Coxsackie A16. Generally, it affects children or immunocompromised adults. Only a few reports have described pseudomembranous conjunctivitis associated with HFMD. We aim to describe the clinical outcomes and ocular findings of a 37-year-old female with HFMD and concurrent severe pseudomembranous conjunctivitis, who was 28 weeks pregnant.

Case presentation: A female patient who was 28-weeks pregnant was referred for an ophthalmological review due to pain and injection in both eyes. The patient was hospitalized under obstetrics and gynecology and evaluated for Behcet’s disease with oral and perineal ulcers. In an ophthalmic examination, both eyes were observed to have a conjunctival injection. Behcet’s disease-associated conjunctivitis was diagnosed. Topical steroids and antibiotics were administered every 6 h. Two days after her presentation, a maculopapular eruption occurred on her palms. Enterovirus type 71 was detected in a serum virus antibody test, and the patient was diagnosed with HFMD. After 7 days, severe pseudomembranous conjunctivitis and corneal epithelial defects occurred in both eyes. Topical steroids were administered every 3 h, and the pseudomembrane was removed every 2 to 3 days. The pseudomembrane did not occur after 3 weeks, but corneal erosion persisted. After 3 months, the corneal erosion had completely resolved.

Conclusions: HFMD-associated conjunctivitis is a rare complication in adults, however it can appear as a severe pseudomembranous conjunctivitis. In this case, the removal of the pseudomembrane and topical steroids helped improve the symptoms.

Keywords: Hand foot mouth disease, Pseudomembrane, Conjunctivitis, Pregnant
We report the case of a 37-year-old female who was 28 weeks pregnant that was diagnosed with HFMD and concurrent acute pseudomembranous conjunctivitis. Herein, we report the clinical course of this patient, who received topical and systemic treatment.

Case presentation
A 37-year-old female who was 28 weeks pregnant, was referred to our clinic due to a conjunctival injection and eye pain. The patient was admitted to the obstetrics and gynecology department with a perineal ulcer. Vesicular rashes occurred on her tongue and labial mucosa. She was diagnosed with Behcet’s disease and treated conservatively. One week before the onset of her symptoms, she visited a swimming pool. The patient was healthy, with no history of immunosuppression. On admission, the patient had a body temperature of 36.6°C, a pulse of 78 beats per minute, and blood pressure of 111/63 mmHg.

On initial ophthalmological examination, a bilateral bulbar and palpebral conjunctival injection was observed (Fig. 1). A pseudomembrane and follicle were not observed. The patient’s intraocular pressures and anterior segment examination findings were normal in both eyes. Behcet’s disease with ocular involvement was diagnosed. Topical steroids (prednisolone acetate 1%) and antibiotics (tobramycin 0.3%) were administered four times a day. Additionally, ophthalmic ointments (Maxitrol, Alcon) were used before bedtime.

Two days later, a maculopapular eruption began to develop on her palms. HFMD was diagnosed based on the clinical findings and distribution being typical of HFMD (Fig. 2). In order to identify the causative virus of HFMD, serum viral titer tests of Coxsackievirus type A16 and Enterovirus type 71 were performed using neutralizing antibody assays. Serum sample analysis was conducted by an external organization (Green Cross Corporation, Youngin, Korea). As per the results, blood test for Enterovirus type 71 antibody titers were positive (titers 1:64, ≥ 1:8) and coxsackievirus A16 antibody titers were negative (titers 1:4, < 1:8). Other viral tests such as Epstein–Barr virus, cytomegalovirus, and human immunodeficiency viruses showed positive results for IgG and negative results for IgM. In addition, the rapid plasma reagin tests displayed negative results. Therefore, we excluded the possibility of other viral and bacterial infections. Furthermore, autoimmune tests such as antinuclear antibody, antineutrophil cytoplasmic antibody, and anti-cyclic citrullinated peptide also showed negative results.

One week after her presentation, a severe pseudomembrane occurred in the bulbar and palpebral conjunctiva, and a defect of the corneal epithelium was observed (Fig. 3a-c). After administering topical anesthetic drops, most of the pseudomembrane in both eyes was removed using a cotton swab and round-tipped forceps (Fig. 3d). Then, topical steroids (prednisolone acetate 1%) were administered every 3 h. The pseudomembrane was removed every 2 to 3 days for 10 days during a slit-lamp examination.

After 3 weeks, the patient’s conjunctival injection had improved, and a pseudomembrane was not observed. However, punctate corneal erosion was seen in both eyes (Fig. 4). The topical steroids were changed to fluorometholone and were administered every 6 h. Artificial tears and ophthalmic ointment were continuously used. After 2 months, the punctate corneal erosion had improved, and after 3 months, had completely resolved (Fig. 4).

Discussion and conclusions
HFMD can be associated with conjunctivitis, as reported in a few cases in the literature [11]. Diagnosing HFMD mainly relies on pathognomic clinical findings and can be supported by laboratory tests such as a serum antibody titer or polymerase chain reaction (PCR) [12]. In this case, a PCR was not performed. However, enterovirus type 71 was detected in a serum virus antibody test. Therefore, the patient was diagnosed with HFMD-associated pseudomembranous conjunctivitis due to the characteristic distribution of the lesions [13]. To the best
of our knowledge, there are, to date, no reports that de-
scribe the clinical course of patients with HFMD-
associated pseudomembranous conjunctivitis.

The underlying pathological mechanisms of HFMD-
associated pseudomembranous conjunctivitis remain un-
clear but may be explained by direct viral infection of
the conjunctiva through hematogenous spread or due to
an autoimmune response. Ocular complications were
first described in 1991 by Yannuzzi et al., who focused
on unilateral acute idiopathic maculopathy [14]. This
condition is associated with Coxsackievirus 16 or an En-
terovirus 71 infection, but a number of other serotypes
have also been described. Systemic disease caused by En-
terovirus 71 is more severe than Coxsackievirus 16 [1].
In the present case, the patient was positive for Enter-
ovirus 71, and therefore was more likely to have more se-
vere ocular complications.

Enterovirus 71 can be found in the saliva, sputum, nasal
mucus, and stools. The virus quickly spreads through
close contact between individuals, droplets in the air, or
by touching contaminated objects. Less commonly,
HFMD can be transmitted by swallowing water in a swim-
mimg pool that has been contaminated with a stool con-
taining the virus [15–17]. In this case, the patient was
likely infected by contaminated water, as the symptoms
appeared 7 days after going to a swimming pool.

Herpangina symptoms, including oral ulcers, are
caused by viral particles traveling to secondary sites of
replication after viremia. Conjunctival inflammation and
pseudomembranes can also be estimated as a result of
viral replication. Pseudomembranous conjunctivitis is
caused by inflammation of the conjunctiva and is char-
acterized by mucopurulent discharge and pseudomem-
brane formation, which is mainly composed of mucus
and fibrin [18, 19]. Management is aimed at reducing
ocular inflammation with topical steroids and hydrating
the ocular surface with artificial tears and lubricants. Re-
moving the pseudomembrane can help improve symp-
toms and wound healing. Conjunctival goblet cell loss
occurs in ocular surface inflammatory diseases, and this
can cause long-term symptoms of dry eye disease [20].
Similarly, in this case, corneal punctate erosion im-
proved after 3 months of treatment. Therefore, when an
ocular complication occurs due to HFMD, it is necessary
to evaluate and treat long-term dry eye disease.

Specifically, the patient, in this case, was pregnant. In
rare cases, HFMD can result in serious infections regard-
less of pregnancy. According to Giachè et al., 41 % of
HFMD-infected pregnant females were symptomatic,
and only 15.5 % developed mucosal ulceration, such as
oral aphthae [21]. These findings suggest that HFMD in
pregnancy is usually asymptomatic or mild. Therefore, it
can be assumed that it is very rare that a serious muco-
cutaneous lesion occurred, as in this case.

An important differential diagnosis of HFMD is ery-
thema multiforme major. Erythema multiforme major is
an acute, self-limiting mucocutaneous disease charac-
terized by the abrupt onset of red papules that evolve to
target or bull’s eye-like lesions on the dorsal and acral surfaces of the hands and feet as well as the extensor surfaces of the extremities [22]. In this case, the patient was positive for Enterovirus A71. Additionally, the eruption was limited to her palms, and the lesion was not shaped like a target. Therefore, the patient is more likely to have had ocular complications associated with HFMD.

In conclusion, we have described the clinical features of HFMD-associated pseudomembranous conjunctivitis. Although HFMD is most common in infants and children, our case highlights that ocular complications may occur in adults and present with severe pseudomembranous conjunctivitis. Clinicians should be aware of the possibility of HFMD in adult patients with pseudomembranous conjunctivitis.

**Abbreviation**
HFMD: Hand, foot and mouth disease

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**Authors’ contributions**
TGK, and YJK reviewed and interpreted the patient data. TGK was major contributors in writing the manuscript. All authors read and approved the final manuscript.

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**Availability of data and materials**
Not applicable.

**Declarations**

**Ethics approval and consent to participate**
This study adhered to the tenets of the Declaration of Helsinki. Ethics Committee approval was not required for this case report.

**Consent for publication**
We obtained written consent to publish from the patient for publication of this case report and any accompanying images.

**Competing interests**
The authors declare that they have no competing interests.
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