

Case report

Orf virus infection after Eid al-Adha

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ABSTRACT

Human orf, also called ecthyma contagiosum, is a zoonotic infection that causes self-resolving skin lesions after contact with infected livestock. We present the case of a 45-year-old Moroccan-born man who developed multiple painful erythematous, violaceous plaques on his hands after butchering a sheep to celebrate the Muslim holiday Eid al-Adha. The diagnosis of orf virus infection was established based on exposure history, histopathology, and classic skin lesions. Although orf virus infection is traditionally seen in individuals with frequent animal contact such as farmers and veterinarians, clinicians evaluating suspicious lesions in patients without occupational risk factors should consider additional cultural practices that may expose the patient to orf virus.

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Introduction

Human orf, also known as human ecthyma contagiosum, is a zoonotic disease caused by orf virus most commonly acquired through contact with infected livestock such as goats or sheep. Orf virus is a DNA virus from the *Poxviridae* family that infects epidermal keratinocytes through disruptions in the skin barrier (e.g. cuts, burns). The resulting characteristic skin lesions manifest sequentially as different morphologies based on stage of the infection with maculopapular, targetoid, nodular, papillomatous, and crusted lesions occurring prior to resolution [1]. Infected animals generally develop lesions on the lips and corners of the mouth, but lesions may also appear on the throat, vulva, and teats. The skin lesions of ecthyma contagiosum shed orf virus into the environment and can result in animal-to-animal or animal-to-human transmission.

Humans can also become infected after contact with recently vaccinated animals or via accidental inoculation with the live

vaccine. Because orf virus can remain viable in the environment for months to years, transmission can also occur through infected fomites [2]. Human-to-human transmission is rare [3]. Orf virus infection usually spontaneously resolves in six to eight weeks and is not lethal. Nevertheless, orf virus has far-reaching health, environmental, and economic ramifications worldwide, particularly on the farming industry. Although human orf is typically diagnosed in animal handlers such as veterinarians and farm workers, physicians may also encounter the characteristic lesions in individuals following certain cultural practices, such as the traditional animal sacrifice for the Muslim holiday Eid al-Adha [4–6].

Case

A 45-year-old man in Louisiana, USA presented to the emergency department (ED) with skin lesions on his hands. Approximately two weeks before presentation, he had punctured his right hand with a knife while skinning a sheep for Eid al-Adha. He had purchased the sheep from a farm in Texas and recalled that it had pimple-like lesions on its lips. He was not wearing gloves at the time of butchering. One week later, he developed skin lesions on both hands overlying the dorsal surface of several joints. The lesions initially started as localized erythema and progressed to become painful and swollen, restricting joint movement. He had

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never developed similar lesions in the past and denied fevers, chills, night sweats, weight loss, neurologic deficits, shortness of breath, or hives.

The patient had a past medical history of benign prostatic hyperplasia treated with tamsulosin. He was an avid gardener and had planted mint trees two days before the lesions appeared, denied contact with aquariums or natural bodies of water and did not own any pets. He was born in Morocco and immigrated to Louisiana, USA 20 years before and had not traveled outside of the USA, including to Morocco, in the last 20 years. His occupation was transporting equipment and luggage at an airport.

In the ED, vital signs were normal. Examination of the right hand revealed a violaceous, targetoid plaque on the dorsal second digit and a fissured, dome-shaped dusky nodule on the dorsal fifth digit. On his left hand the patient was noted to have an edematous, periungual plaque with dull erythema at the junction of the proximal and lateral nail folds of the fourth digit (Fig. 1). Physical exam also revealed bilateral, tender axillary lymphadenopathy. There were no abnormal cardiovascular, pulmonary, or abdominal exam findings.

Laboratory studies did not reveal any significant abnormalities including erythrocyte sedimentation rate, C-reactive protein, white blood cell count and HIV testing. A 3-view x-ray of the right hand was noted to have mild soft tissue swelling overlying the dorsal aspect of the metacarpophalangeal joints with more focal soft tissue irregularity at the dorsal aspect of the fifth digit. Incision and drainage of the lesion on the left fourth digit were attempted but produced no purulent discharge. The patient was discharged from the ED with trimethoprim-sulfamethoxazole 800–160 mg two tablets twice daily and itraconazole 100 mg twice daily for empiric treatment of suspected nocardiosis or sporotrichosis. Punch-biopsies of the lesion involving the right second digit were performed the following day in dermatology clinic. Histopathology showed neutrophilic infiltrates and inclusion bodies within vacuolated keratinocytes (Fig. 2). No organisms grew on culture of tissue for bacteria, acid fast bacilli, and fungi.

Based on the presence of classic skin lesions, exposure history, and consistent histopathology, a presumed diagnosis of orf virus infection was made. Trimethoprim-sulfamethoxazole and itraconazole were discontinued, and he was prescribed antimicrobial ointment to prevent superinfection. At a follow-up appointment 15 days later, his lesions had significantly improved, with resolution of swelling and pain (Fig. 1, Panel D).

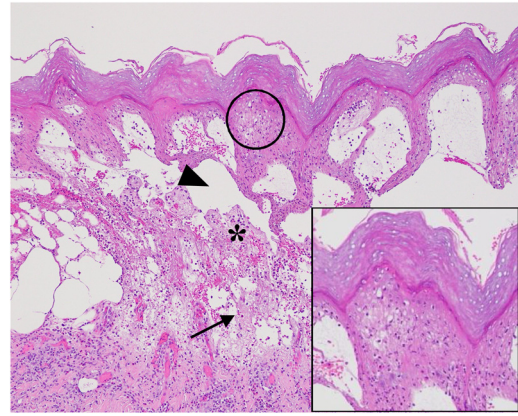


Fig. 2. Biopsy reveals prominent dermal edema with subepidermal blister formation (arrowhead), necrosis of the dermis (arrow), scattered perivascular and interstitial neutrophil infiltrate (asterisk), vascular dilation, and inclusion bodies with vacuolated keratinocytes (circle, magnified in bottom right) (Hematoxylin-eosin stain; original magnification 100 \times).

Discussion

Human orf is an uncommon although likely under-recognized entity. Orf virus infection in livestock is endemic to most geographic regions of the world, but data is lacking regarding incidence and prevalence within human populations [7]. Historically, groups with increased exposure to animals, such as veterinarians, butchers, and farmers, have been considered to be at highest risk for orf virus infection. In the United Kingdom, 30% of sheep herders in one study reported previous infection with orf virus [8]. These populations may be less likely to seek treatment due to familiarity with the disease, resulting in lack of adequate surveillance [1,9,10]. The past two decades have seen a rise in infections due to non-traditional risk factors, such as keeping livestock as pets, household meat processing, animal slaughtering for recreational or religious festivities, and children attending petting zoos [10–12]. Thus, clinicians should be familiar with recognizing human orf in individuals without traditional risk factors in order to avoid diagnostic delays and unnecessary treatments.

Human orf may pose a difficult diagnosis without accurate history taking. However, the predictable clinical progression of human ecthyma contagiosum, in combination with exposure to an

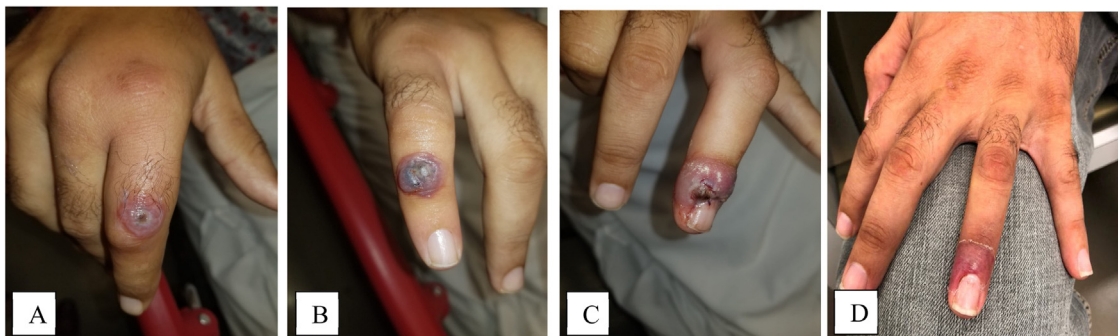


Fig. 1. A) Violaceous, targetoid plaque with central necrosis and peripheral rim of erythema on the dorsal second digit of the right hand just proximal to the proximal interphalangeal joint. B) Violaceous, smooth, dome-shaped nodule with central dusky blue hue and fissure as well as peripheral rim of erythema on the dorsal fifth digit of the right hand overlying the distal interphalangeal joint. C) Edematous periungual plaque with dull erythema at the junction of the proximal and lateral nail folds of fourth digit of the left hand. D) Thin erythematous periungual plaque with fine collarette of scale on the proximal and lateral nail folds and skin overlying the distal interphalangeal joint of the fourth digit of the left hand. This image was taken fifteen days later, when the lesions were healing in the regression stage. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article).

infected animal, can delineate orf from other infections. Orf lesions typically appear three to seven days after inoculation and progress through six clinical stages, each lasting approximately one week and ending in resolution. The first maculopapular stage is characterized by a solitary erythematous or violaceous macule that develops a central papule. The targetoid stage is a papule or nodule with a gray-white, necrotic center and red outer halo, which progresses to the acute-nodular weepy stage. The regenerative-nodular dry stage appears as a firm, crusted papule or nodule and progresses to the fifth, dry papillomatous stage. In the last stage, the regression stage, the lesion progressively shrinks in size and resolves, usually without a residual scar. Orf can be further complicated by secondary bacterial infections, giant recurring lesions, erysipelas, lymphangitis, and lymphadenopathy. A frequent complication of orf infection is erythema multiforme, a hypersensitivity reaction that develops 2–4 weeks after primary onset of orf lesions and resolves in 1–4 weeks [1]. Lymphangitic spread along the arm in a sporotrichoid fashion has also been reported [6]. Once infected, individuals have the potential to become re-infected. However, lesions in reinfection tend to be smaller and resolve faster than in primary infection [1].

Orf virus infection is typically diagnosed based on patient history and physical examination alone. However, biopsy, serologic testing, and molecular testing can aid in confirmation of the diagnosis in difficult cases. When biopsy is conducted, histological characteristics include necrosis, nuclear and cytoplasmic vacuolation, and a dense mixed inflammatory infiltrate comprised of eosinophils, lymphocytes, neutrophils, and histiocytes. Real-time polymerase chain reaction (PCR) and standard PCR have a high sensitivity for detection of poxvirus, and other viral detection methods available for diagnostics include western blot, cell culture isolation, and enzyme-linked immunosorbent assay [1,13].

As the lesions caused by orf virus can resemble those of other infections, the differential diagnosis is broad and includes: milker's nodule, fish tank granuloma (*Mycobacterium marinum*), pyogenic granuloma, keratoacanthoma, fungal infections, cutaneous anthrax, giant molluscum, herpetic whitlow, tularemia, sporotrichosis, and cutaneous leishmaniasis. The lesion of milker's nodule secondary to paravaccinia virus may be particularly difficult to differentiate from orf virus from clinical examination alone. Though paravaccinia virus and orf virus are members of the same family and genus, they are acquired through interaction with different animals. Milker's nodule, acquired from bovine cattle, also progresses through six stages but presents as one or more erythematous maculopapular lesions that develop into exudative nodules rather than ulcers [14]. Similar to orf, these lesions are self-limiting. Cutaneous anthrax can be acquired from many animals, including sheep and goats. However, cutaneous anthrax presents with rapid development of a painless ulcer with surrounding edema, followed by a classic black eschar [15]. To confirm the diagnosis of cutaneous anthrax, culture, gram stain, and PCR may be used. Additionally, sporotrichosis and orf may both present with lymphangitic spread. A history of gardening and growth of the organism on culture may help point to sporotrichosis. Because clinicians must consider a broad differential diagnosis when evaluating a patient with skin lesions suspicious for orf virus infection, it is crucial to obtain a complete and accurate epidemiological and social history in addition to a careful physical exam.

To date, there is no established treatment for orf in immunocompetent patients, as the lesions are usually self-limiting. Clinicians should provide counseling regarding preventative measures, including proper use of gloves and inspection of animals for lesions prior to butchering. Due to lack of clinician familiarity with orf virus, patients may receive unnecessary, invasive treatments or procedures that can worsen outcomes [1]. Some clinicians may opt for local resection, particularly if the patient

is immunocompromised, which is associated with recurrence at skin resection margins [16]. Furthermore, the unnecessary use of antimicrobials in the absence of superinfection may cause side effects and contribute to the ever-growing issue of antimicrobial resistance.

Immunocompromised patients are at increased risk for primary infection, superinfection, generalized cutaneous infection, prolonged illness, and other complications such as painful, atypical, giant orf lesions that can measure up to several centimeters in size [9,17,18]. For example, in 2012, a Turkish burn unit reported nosocomial spread of generalized cutaneous orf from an index patient who had butchered an animal on Eid al-Adha to 12 additional patients [19]. Patients on immunosuppressing agents such as methotrexate are also at increased risk for complications [20]. Treatments with cryotherapy, corticosteroids, curettage, electrocautery, imiquimod, and cidofovir have had varying success in immunocompromised individuals [1,17].

When evaluating patients with skin lesions suspicious for ecthyma contagiosum, clinicians should inquire about occupational, cultural, and recreational practices that may place the patient at risk for infection. Celebration of the Muslim holiday Eid al-Adha traditionally includes the practice of animal sacrifice, usually of sheep, goat, buffalo, cow, or camel. Eid al-Adha occurs on a different date each year based on a lunar calendar and takes place on or around July 30, 2020 this year. Individuals may celebrate Eid al-Adha on different days depending on their country of origin. Outbreaks of human orf following Eid al-Adha have been reported in countries with large Muslim populations, including Jordan, Saudi Arabia, Turkey, Iran, France, Italy, Belgium, and the United States [4–6]. Although the practice of animal sacrifice on Eid al-Adha occurs across the globe, many practitioners are unaware of the association between human orf and this religious custom. Cases of human orf have also occurred after lamb sacrifice for the Christian Orthodox Easter, attending petting zoos, and preparing meat at home for non-religious purposes [11,12].

We present a case of a Moroccan-born man who developed skin lesions consistent with orf virus infection after butchering a sheep for Eid al-Adha. To our knowledge, this is the first reported case of human orf in Louisiana, USA. The diagnosis in our patient did not require confirmatory molecular testing, since the clinical exam findings, history, histology, and self-resolving nature were very typical of human orf virus disease. The presence of characteristic lesions on the lips of the sheep further support the diagnosis of orf. Sporotrichosis was on the differential diagnosis due to presence of lymphadenopathy and a history of gardening, but culture of tissue was negative for fungal organisms. His occupation as a baggage handler at the airport was a risk factor for anthrax exposure but would have caused inhalational rather than cutaneous disease. Due to the self-limiting nature of human orf and the lack of immunocompromise, he was not given additional treatment aside from prophylactic topical antimicrobials.

In conclusion, clinicians should be familiar with the risk factors, clinical manifestations and management of human orf. While the appearance of orf can be quite striking with its characteristic skin lesions and potential for lymphangitic spread, knowledge of its self-resolving nature can help avoid unnecessary hospital admissions, procedures, and antimicrobial treatments. When encountering suspicious skin lesions, a thorough exposure history including both traditional occupational risk factors and additional cultural or recreational risk factors should be elicited. Many countries worldwide have reported cases of human orf after the custom of animal sacrifice on the Muslim holiday Eid al-Adha. With global migration and increasing animal contact in urban centers, clinicians historically unfamiliar with orf virus or with specific cultural traditions may soon encounter this disease entity in their practice.

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Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Individual contributions

AV, MM, SJ, JD, GV, AW contributed to data collection.
AV, MM, CZ contributed to manuscript writing.
JD, ES, CZ, GV, AW contributed to manuscript revision.

CRedit authorship contribution statement

Ashley Vellucci: Conceptualization, Writing - original draft, Project administration. **Melina Manolas:** Writing - review & editing, Visualization. **Sarah Jin:** Writing - review & editing. **John Dwyer:** Writing - review & editing. **Garrett Vick:** Writing - review & editing. **Alun Wang:** Writing - review & editing. **Edwin Swiatlo:** Conceptualization, Supervision. **Crystal Zheng:** Conceptualization, Writing - original draft, Supervision, Project administration.

Conflict of Interest

The authors have no conflicts of interest to disclose.

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