

Large pigmented bullous lesion on left little finger

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CLINICAL FINDINGS

A 35-year-old male patient, presented with a solitary asymptomatic reddish brownish bullous plaque with some areas of hemorrhage and crusting on the distal interphalangeal joint of left little finger of 5 weeks duration (Fig. 1-A&B). The main complaint of the patient was ugly look,

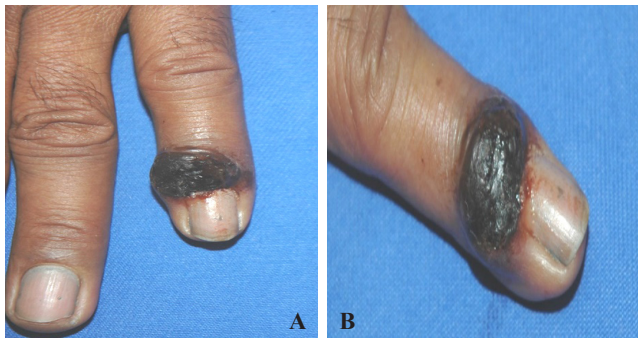


Fig. 1 A&B A solitary reddish brown to blackish bullous plaque with some hemorrhagic and crusting areas on the distal interphalangeal joint of left little finger.

which had an effect over his personal life. The disease had a sudden onset and a progressive course. This patient is a farmer and he is working in a farm containing sheep and goats. There was no history of trauma, insect bite or any drug reactions. No lymphadenopathy was detected. No family history or history of any other skin or systemic illness.

What are your clinical differential diagnoses?

Orf
 Milker nodule
 Pyoderma gangrenosum,
 Herpetic whitlow
 Pyogenic granuloma
 Melanoma

PATHOLOGICAL FINDINGS

Histopathological sections showed marked hyperplasia and necrosis of the epidermis with reticular degeneration. Epidermal vesiculation with intranuclear and intracytoplasmic inclusion bodies, in addition to vacuolization and disaggregation of keratinocytes associated with inflammatory infiltrate of lymphocytes and histiocytes (Fig. 2, 3).

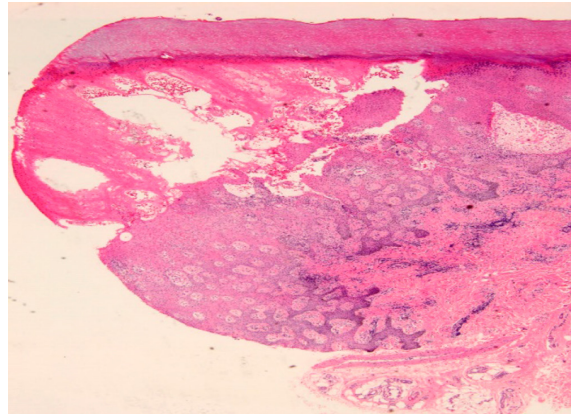


Fig. 2 Epidermal hyperplasia, necrosis, reticular degeneration and multiple vesicles. Dermis shows superficial perivascular inflammatory infiltrate of lymphohistiocytes.

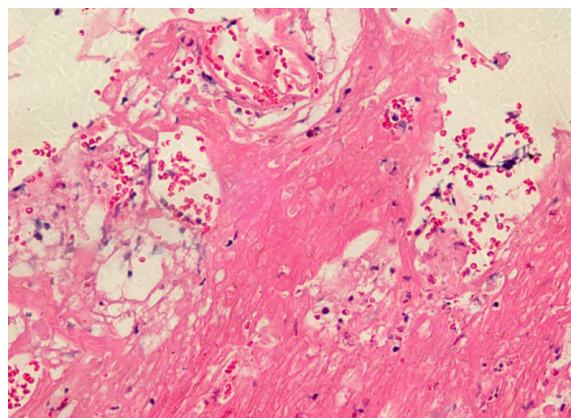


Fig. 3 Reticular degeneration and eosinophilic inclusion bodies.

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FINAL DIAGNOSIS

- Orf

DISCUSSION

The Orf virus is of the Parapoxvirus genus of the family Poxviridae. It induces acute pustular skin lesions in sheep and goats, and is transmissible to humans. This double-stranded DNA poxvirus is a member of the Paravaccinia subgroup.¹ Orf is rarely diagnosed in North America, although large series from Norway and New-Zealand have been described.^{2,3} Primarily, infected young sheep or goats develop contagious ecthyma, which is also known as contagious pustular dermatitis or scabby mouth, involving the lip and mouth.⁴ In most instances, the human disease occurs among sheep handlers and is transmitted by direct contact with the papulovesicular lesions or the crusts from an infected animal, and only rarely through contact with meat or objects.^{5,6} Although, human-to-human transmission is extremely rare, some cases have been reported.⁷

The infection is usually clinically diagnosed on the basis of exposure history and the presence of a characteristic lesion.⁸ Virus isolation in tissue culture usually requires primary ovine or bovine cells and may be difficult to attain.⁹ The development of immunologic sera specific for parapoxviruses is another source for diagnostic reagents.⁹

The lesions in humans are morphologically similar to those seen in sheep and goats. They evolve through characteristic morphologic stages after an incubation of 3 to 10 days.¹⁰ The lesions begin as macules and/or papules and progress to 'boggy' umbilicated nodules 0.5 cm to 5.0 cm in diameter.¹¹ Resolution usually occurs spontaneously in 4-8 weeks with little to no scarring. Recurrent lesions are possible, as the infection does not confer immunity in humans.¹³

Differential diagnoses include pyoderma, herpetic whitlow, cowpox, pseudo cowpox (Milker's nodule), cat-scratch disease, anthrax, tularemia,

primary inoculation tuberculosis, atypical mycobacteria, syphilitic chancre, sporotrichosis, keratoacanthoma, and pyogenic granuloma.¹³

Milkers' nodules occur most frequently on the fingers or hands of people who have had contact with an infected sheep. Following an incubation period of 3-7 days, the lesions begin as an erythematous papule, possibly with associated vesicles. This progresses over a period of weeks and forms a firm nodule that is reddish blue to brown in color. In some cases, there may also be suppuration and scabbing.¹⁴ We diagnosed our case depending on pathological features and occupation history.

Both human orf and cutaneous anthrax can be acquired from sheep and goats. Thus, history alone cannot be helpful in establishing definitive diagnosis. Cutaneous anthrax lesions are fast spreading and ulcerating, and they quickly respond to an appropriate antibiotic. If diagnosis remains unclear, then electron microscopy can confirm a diagnosis of Parapoxvirus infection; only polymerase chain reaction can definitely identify a viral infection such as orf.¹⁵

Pyoderma gangrenosum is most common in patients with underlying systemic disease. It starts as a vesicle or papule on the trunk or limbs, which then enlarges and ulcerates. Herpetic whitlow manifests as a vesicular rash on fingers, often after contact with a vesicle caused by the herpes simplex virus.¹⁶

Routine histopathological examinations of an orf lesion evolves with the clinical stages and helps to secure the diagnosis. The maculopapular and target stages are characterized by vacuolated epidermal cells. In the maculopapular stage, cells have intracytoplasmic inclusions; in the target stage, they have both intracytoplasmic and intranuclear inclusions.¹⁷ The acute stage is marked by patchy areas of lost epidermis, reticular degeneration of the dermis, and a dermal infiltrate composed primarily of lymphocytes.¹⁸ The regenerative stage involves epidermal regeneration and extrusion

Table 1: The clinicopathological challenge of Orf

Diagnosis	Clinical	Pathological
Milker nodule	<ul style="list-style-type: none"> Clinical features resemble orf, but history of cow handling can be helpful to differentiate it from Orf 	<ul style="list-style-type: none"> As in orf with full thickness epidermal necrosis
Nodular melanoma	<ul style="list-style-type: none"> Smooth nodule covered by normal epidermis, elevated bluish black plaque or ulcerated polypoid mass Usually no lateral flat component 	<ul style="list-style-type: none"> No radial growth phase Epidermis is thin and may be ulcerated No in situ melanoma Dermal component consists of a cohesive nodule of tumor cells with pushing border and without maturation Cells are most commonly epithelioid, may be spindled or small with occasional monster cells
Whitlow	<ul style="list-style-type: none"> Viral infection of fingertips caused by the herpes simplex virus Deep seated vesicles in fingertips 	<ul style="list-style-type: none"> Keratinocyte showed cytopathic effects include the "3 Ms:" molding of nuclei, multinucleation, and margination of chromatin to the periphery of the nucleus
Pyogenic granuloma	<ul style="list-style-type: none"> Very common; rapidly growing polypoid red mass surrounded by thickened epidermis, often in finger or lips 	<ul style="list-style-type: none"> Lobular pattern of vascular proliferation with inflammation and edema resembling granulation tissue Thin epidermis at top with variable ulceration Acanthosis and hyperkeratosis at sides Central branching vessel is called capillary or vascular lobule, with no / rare red blood cells, surrounded by endothelial cells Deep lesions often lack edema and inflammation
Pyoderma gangrenosum	<ul style="list-style-type: none"> Large necrotic ulcer with violaceous border and surrounding erythema 50% of cases are associated with inflammatory bowel disease, myeloma, leukemia and hepatitis Usually seen on extremities Also new ulcers in areas of trauma (pathergy) 	<ul style="list-style-type: none"> Nonspecific ulceration with abscess formation; involves deep dermis and subcutis Adjacent dermis shows acute and chronic inflammation Early lesion may present with subcorneal pustulation Leukocytoclastic and lymphocyte mediated vasculitis; vasculitis is probably secondary to inflammation Giant cells are common; associated with inflammatory bowel disease Focal and sterile abscesses are surrounded by granulomatous inflammation, bordered by rim of lymphocytes and plasma cells Hemorrhage is common; often acanthosis and pseudoepitheliomatous hyperplasia; eosinophils are variable

of pyknotic hair-follicle cells that form the small black dots on the surface of the lesion. In the papillomatous and regressive stages, finger-like downward projections of epidermis are evident.¹⁹ Definitive diagnosis is possible through electron microscopy by demonstrating typical oval viral particles of Parapoxvirus. Polymerase chain reaction is more specific for identifying DNA of the virus in the specimen, regardless of the stage of the disease.²⁰ However, identification of the poxvirus by viral culture, a progressive increase in the serologic titer of orf virus antibodies, immunofluorescent detection of viral antigens, and complement fixation are other methods of diagnosis.²⁰ Complications of orf are generally rare but may include fever, chills, rigor, drenching sweat, malaise, lymphadenopathy, and lymphangitis.²¹ Secondary bacterial infection is the most common complication. Cases of erythema multiforme and bullous-pemphigoid like eruptions also have been described.²²

Orf is self-limited disease, requires no specific treatment. Antibiotics should be administered in cases of secondary bacterial infection, but are otherwise unnecessary. Regression of the lesion may be accelerated by application of idoxuridine. Surgical excision also can bring about rapid resolution, but is generally contraindicated because the lesion spontaneously regresses without leaving a scar.²³ Corticosteroids and other immunosuppressive drugs should be avoided, because they can exacerbate the lesion in its papillomatous stage. Cidofovir cream and cryotherapy have recently been used successfully to treat very large lesions.²⁴ Use of topical imiquimod has been beneficial in treating patients who are immunocompromised.^{25,26}

Our patient was managed with several sessions of cryotherapy accompanied by a course of ciprofloxacin 500 mg capsules twice daily and topical mupirocin ointment. Cryotherapy was repeated every two weeks for 2 consecutive months. The lesion showed significant improvement.

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