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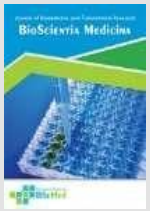

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# Ecthyma Contagiosum (Orf Virus) Masquerading as Subcorneal Pustular Dermatosis: A Diagnostic Pitfall in an Adolescent

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**A B S T R A C T**

**Background:** Ecthyma contagiosum (Orf) is a zoonotic viral infection caused by a *Parapoxvirus*, typically presenting as a self-limiting, solitary cutaneous lesion on the hands of occupationally exposed individuals. Atypical, multifocal, or pustular presentations can pose a significant diagnostic challenge, mimicking various inflammatory dermatoses. **Case presentation:** We present the case of a 17-year-old female with no direct animal contact who developed a progressive, widespread, and painful pustular eruption on her extremities over three weeks. The clinical presentation was highly suggestive of Subcorneal Pustular Dermatosis (SPD), prompting treatment with systemic corticosteroids, which led to clinical worsening. A delayed epidemiological history revealed an environmental link to a nearby goat farm and a family cluster of similar, milder lesions. A diagnostic punch biopsy was pivotal, revealing viral cytopathic effects, including extensive ballooning degeneration and epidermal necrosis, inconsistent with SPD. Subsequent bacterial culture confirmed superinfection with *Enterobacter cloacae ssp. cloacae*. The diagnosis was established by the pathognomonic histopathological findings. **Conclusion:** The patient's steroid therapy was immediately ceased, and targeted antibiotic therapy was initiated, leading to complete resolution. This case highlights the Orf virus as a critical clinical chameleon and a diagnostic pitfall for generalized pustular eruptions. It underscores the necessity of a high index of suspicion for zoonoses, even in non-occupational settings, and confirms the indispensable role of histopathology in differentiating viral cytopathy from sterile neutrophilic dermatoses to prevent iatrogenic harm from inappropriate immunosuppression.

## 1. Introduction

Ecthyma contagiosum, or Orf, is a globally distributed zoonotic disease caused by the Orf virus (ORFV), an epitheliotropic, enveloped, double-stranded DNA virus belonging to the genus *Parapoxvirus* within the *Poxviridae* family.[1] The virus is endemic in sheep and goats, in which it causes a mucocutaneous disease known as "scabby mouth" or "contagious pustular dermatitis." Human infection is considered an accidental inoculation, typically occurring after direct contact with infected animals or contaminated fomites, such as shearing equipment, fencing, or animal feed.[2] The classic presentation of human Orf is a solitary, self-resolving lesion on an exposed site, most commonly the fingers, hands, or forearms. This lesion progresses through six characteristic clinical stages over a period of 4-8 weeks: maculopapular, target, acute (nodular or pustular), regenerative, papillomatous, and regressive. Due to this classic, self-limiting course, the

diagnosis is often made clinically based on the lesion's morphology and a clear history of occupational exposure (including farmers, veterinarians, butchers, and sheep shearers).[3,4]

However, atypical presentations of human Orf are increasingly reported and pose a significant diagnostic challenge. These include multifocal or generalized lesions, large "giant" Orf (often >5 cm), and cases complicated by bullous eruptions, erythema multiforme, or significant lymphadenopathy.[5,6] These atypical manifestations are particularly common in immunocompromised individuals but can also occur in immunocompetent hosts, leading to an extensive list of differential diagnoses, including bacterial infections (such as ecthyma and atypical mycobacteria), deep fungal infections, pyoderma gangrenosum, and other viral infections like Milker's nodule or herpetic whitlow.[7]

Among the most challenging clinical mimics are the sterile neutrophilic dermatoses. Subcorneal Pustular Dermatosis (SPD), or Sneddon-Wilkinson disease, is a rare, chronic, relapsing inflammatory condition characterized by widespread, flacid pustules that often coalesce into annular or serpiginous patterns.[8] The clinical picture of numerous "sterile" pustules can be strikingly similar. A misdiagnosis in this context is perilous; the standard-of-care treatment for SPD involves potent anti-inflammatory or immunosuppressive agents, such as dapsone or systemic corticosteroids, which can be detrimental in the setting of an active viral infection, potentially leading to dissemination and severe superinfection.[9,10]

The aim of this report is to present a unique case of severe, multi-focal Ecthyma Contagiosum in an immunocompetent adolescent with no direct animal contact, which was clinically indistinguishable from Subcorneal Pustular Dermatosis. We highlight the diagnostic journey, the critical role of histopathology in differentiating viral cytopathy from sterile neutrophilic infiltration, and the potential iatrogenic harm of misdiagnosis. This case serves as a crucial reminder for clinicians to include zoonotic infections in the differential diagnosis of any atypical pustular eruption, even in ostensibly low-risk or urban settings.

**2. Case Presentation**

A 17-year-old female, with no significant past medical history and no history of atopy, diabetes, or immunodeficiency, presented to our dermatology outpatient clinic with a three-week history of a painful and pruritic skin eruption. The lesions first appeared as small red bumps on her dorsal hands and rapidly progressed to form numerous pustules, subsequently spreading to her forearms, shins, and dorsal feet. She reported an initial low-grade fever and general malaise, which had subsided after the first week. She denied any lesions in her mouth, eyes, or genital area. Prior to presentation, she had been treated by a general practitioner with a topical combination of betamethasone valerate and neomycin sulfate, followed by a 5-day course of an unknown oral antibiotic, both of which provided no relief and were associated with a perceived worsening of the eruption (Table 1a).

On physical examination, the patient was well-appearing and afebrile (36.8°C). Vital signs were within normal limits, with a blood pressure of 120/76 mmHg and a heart rate of 82 beats/minute. Cutaneous examination revealed dozens of discrete and coalescing pustules, 2-5 mm in diameter, on an erythematous base. These were distributed symmetrically across the dorsal aspects of her hands and feet, as well as the extensor surfaces of her forearms and lower legs (Figure 1). Many lesions exhibited central umbilication or were covered by a dark, hemorrhagic crust. Several larger, targetoid nodules with a violaceous, edematous center and an erythematous halo were noted on the dorsal hands. Significant excoriation and healing lesions with post-inflammatory hyperpigmentation were interspersed. No lymphadenopathy was appreciated.

## Table 1a. Clinical Findings on Admission

| | |
|---|---|
| **I. Patient Demographics & History** | |
| **Patient** | 17-year-old female |
| **History of Present Illness** | • 3-week history of painful and pruritic skin eruption<br>• Progression: Started on dorsal hands, spread to forearms, shins, and dorsal feet<br>• Systemic: Initial low-grade fever and malaise (subsided)<br>• Negative: No mucosal, ocular, or genital lesions reported |
| **Prior Treatment** | • Topical betamethasone/neomycin: No relief<br>• Oral antibiotic (unknown): Perceived worsening of eruption |
| **Past Medical History** | Unremarkable. No history of atopy, diabetes, or immunodeficiency. |
| **II. Physical Examination** | |
| **Vital Signs** | • Temperature: 36.8°C (Afebrile)<br>• Blood Pressure: 120/76 mmHg<br>• Heart Rate: 82 beats/minute |
| **Cutaneous Examination** | • **Lesions:** Dozens of discrete and coalescing pustules (2-5 mm) on an erythematous base.<br>• **Distribution:** Symmetrical eruption on dorsal hands, dorsal feet, extensor forearms, and lower legs.<br>• **Specific Features:**<br>Central umbilication observed in many pustules<br>Dark, hemorrhagic crusts<br>Larger, targetoid nodules with violaceous centers and erythematous halos (noted on dorsal hands)<br>• **Other Findings:** Significant excoriation marks and post-inflammatory hyperpigmentation.<br>• **Lymph Nodes:** No cervical, axillary, or inguinal lymphadenopathy appreciated. |

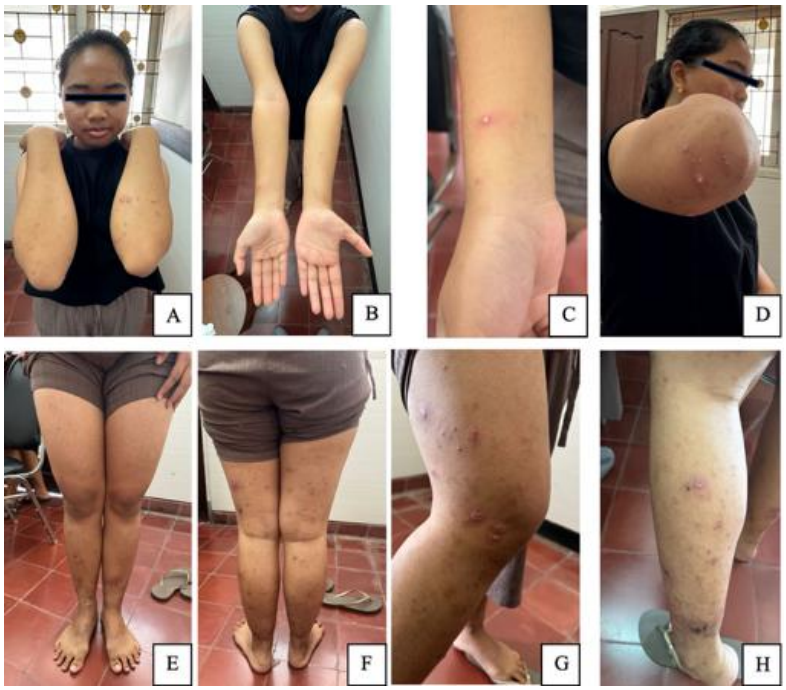


Figure 1. Clinical presentation at initial visit. (A-D) Multiple discrete and confluent pustules with surrounding erythema on the dorsal hands and extensor forearms. (E-H) Similar pustular and crusted lesions on the shins and dorsal feet, with evidence of excoriation.

Given the widespread pustular eruption, an initial infectious and inflammatory workup was performed. Laboratory investigations revealed a mild leukocytosis (11,200 cells/µL; reference range 4,100–11,000/µL) with a neutrophilic predominance (78%; reference range 40–75%). A comprehensive metabolic panel, including liver and renal function tests, was unremarkable. Inflammatory markers were elevated, with a C-reactive protein (CRP) of 45 mg/L (reference range < 5 mg/L) and an erythrocyte sedimentation rate (ESR) of 38 mm/hr (reference range < 20 mm/hr).

A Gram stain from an intact pustule was performed, which revealed numerous neutrophils (>50 per high-power field) but no visible organisms. A subsequent bacterial culture of the pustule contents showed no growth after 48 hours. To evaluate for an autoimmune or autoinflammatory etiology, further serological tests were conducted, including Antinuclear Antibody (ANA) and Antinuclear Cytoplasmic Antibody (ANCA), both of which were negative (Table 1b).

Table 1b. Clinical findings on admission (initial workup and diagnosis).

| | |
|---|---|
| **III. Initial Workup & Laboratory Findings** | |
| **Hematology (CBC)** | • Leukocytosis: 11,200 cells/µL (Ref: 4,100–11,000)<br>• Neutrophilic Predominance: 78% (Ref: 40–75%) |
| **Inflammatory Markers** | • C-Reactive Protein (CRP): 45 mg/L (Ref: < 5 mg/L)<br>• Erythrocyte Sedimentation Rate (ESR): 38 mm/hr (Ref: < 20 mm/hr) |
| **Biochemistry** | Comprehensive Metabolic Panel: Unremarkable |
| **Microbiology (Pustule)** | • **Gram Stain:** Numerous neutrophils (>50/hpf); No organisms visible.<br>• **Bacterial Culture:** No growth after 48 hours. |
| **Serology** | • Antinuclear Antibody (ANA): Negative<br>• Antinuclear Cytoplasmic Antibody (ANCA): Negative |
| **IV. Initial Diagnosis & Plan** | |
| **Initial Working Diagnosis** | Subcorneal Pustular Dermatosis (Sneddon-Wilkinson Disease) |
| **Initial Treatment Plan** | • Oral Methylprednisolone 8 mg TID (24 mg/day)<br>• Cetirizine 10 mg at night<br>• Sterile 0.9% NaCl compresses<br>• Topical Natrium Fusidate 2% cream<br>• Plan for 4-mm punch biopsy at follow-up |

Based on the clinical picture of a widespread, relapsing, sterile pustular eruption with negative initial cultures and serologies, a working diagnosis of Subcorneal Pustular Dermatosis (SPD) was made. Eosinophilic Pustular Folliculitis (Ofuji's disease) was considered a less likely differential. The patient was initiated on a treatment regimen for suspected SPD, consisting of oral methylprednisolone 8 mg three times daily (24 mg/day), cetirizine 10 mg at night for pruritus, twice-daily sterile compresses with 0.9%

sodium chloride, and topical Natrium Fusidate 2% cream applied twice daily to crusted lesions to prevent secondary infection. A 4-mm punch biopsy was scheduled for the next follow-up visit.

The patient returned 13 days later with significant clinical worsening. The number of pustules had nearly doubled, and the existing lesions appeared more inflamed, edematous, and purulent. The patient was distressed by the pain, pruritus, and cosmetic appearance. Crucially, upon this visit, the patient reported that her mother and younger brother had developed similar, though much milder, "red bumps" on their hands within the last five days. This new information about family clustering prompted an immediate and detailed re-interrogation of the patient's social and environmental history. The family denied owning any pets, but revealed they live approximately 1 kilometer from a large commercial goat farm. The patient confirmed she passes this farm daily on her walk to and from school. While she denied any direct contact with the animals or farm equipment, this strong epidemiological link, combined with the family cluster, shifted the diagnostic suspicion dramatically away from an inflammatory dermatosis and towards a zoonotic infection, specifically Orf.

A new 4-mm punch biopsy was immediately obtained from a new, active targetoid nodule on the patient's left forearm. A deep tissue swab from the base of a de-roofed pustule was also sent for comprehensive bacterial, fungal, and mycobacterial culture. The histopathological findings were definitive. The epidermis showed marked acanthosis and pseudoepitheliomatous hyperplasia. The superficial epidermis was characterized by extensive necrosis and ulceration, with a dense intraepidermal infiltrate of neutrophils and lymphocytes. The most critical finding was in the adjacent, intact stratum spinosum and granulosum, which displayed prominent ballooning degeneration of keratinocytes. These cells were swollen, pale, and showed marginated chromatin. Numerous large, eosinophilic intracytoplasmic inclusion bodies (Guarnieri-like bodies), characteristic of *Parapoxvirus* infection, were identified within the degenerate keratinocytes. The upper dermis exhibited marked papillary edema, a dense, mixed inflammatory infiltrate (lymphohistiocytic and neutrophilic), and significant proliferation of small blood vessels with prominent endothelial swelling. These findings were diagnostic of Ecthyma Contagiosum. The bacterial culture from Day 10, taken from a purulent lesion, subsequently grew $>10^5$ CFU/mL of *Enterobacter cloacae ssp. cloacae*. Susceptibility testing demonstrated resistance to ampicillin, amoxicillin/clavulanic acid, and cefazolin, but sensitivity to ciprofloxacin, gentamicin, and meropenem.

A final diagnosis of severe, multifocal Ecthyma Contagiosum (Orf) with *Enterobacter cloacae* superinfection was established based on the definitive clinico-histopathological findings and supportive epidemiological linkage. The systemic methylprednisolone was immediately discontinued. A targeted antimicrobial and supportive care plan was initiated. Based on culture sensitivities, the patient was prescribed oral ciprofloxacin 500 mg twice daily for 7 days. Topical therapy was adjusted to a combination of hydrocortisone 2.5% cream and chloramphenicol 2% cream, applied twice daily to the inflamed and crusted lesions to manage both inflammation and the bacterial load. She was educated on strict wound care, hygiene, and avoiding contact with the lesions of her family members.

At the 35-day (5-week) follow-up, the patient showed remarkable improvement. All pustular and nodular lesions had fully resolved. No new lesions were reported. The skin was intact, with residual, non-scaly post-inflammatory hyperpigmentation (PIH) at the sites of previous lesions. The pruritus had ceased. The patient was then prescribed desoximetasone 0.25% cream and urea 10% cream to manage the residual inflammation and hyperpigmentation. Her family members, who had milder, non-superinfected lesions, reported spontaneous resolution of their lesions over the same period.

## Table 2. Treatment, Follow-up, and Outcome

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|---|---|
| **I. Follow-up Visit (Day 13) - The Diagnostic Turning Point** | |
| **Clinical Status** | • **Significant clinical worsening** while on oral methylprednisolone.<br>• Number of pustules nearly doubled.<br>• Existing lesions more inflamed, edematous, and purulent. |
| **New Historical Data** | • **Family Cluster:** Mother and younger brother developed similar, milder "red bumps" 5 days prior.<br>• **Epidemiological Link:** Patient lives 1 km from a large commercial goat farm. |
| **Definitive Diagnostic Findings** | • **Histopathology (4mm punch biopsy):**<br>Marked epidermal necrosis and pseudoepitheliomatous hyperplasia.<br>**Pathognomonic:** Prominent ballooning degeneration of keratinocytes.<br>**Pathognomonic:** Large, eosinophilic intracytoplasmic inclusion bodies (Guarnieri-like bodies).<br>**Inconsistent with SPD:** Findings confirm viral cytopathic effect, not a sterile neutrophilic process.<br>• **Bacterial Culture (from purulent lesion):**<br>Grew >$10^5$ CFU/mL of *Enterobacter cloacae ssp. cloacae*.<br>Sensitive to Ciprofloxacin. |
| **Revised Diagnosis** | **Severe, Multifocal Ecthyma Contagiosum (Orf) with *Enterobacter cloacae* Superinfection** |
| **Revised Treatment Plan** | • **STOP:** Oral Methylprednisolone (immediately discontinued).<br>• **START:** Oral Ciprofloxacin 500 mg twice daily for 7 days.<br>• **START:** Topical Hydrocortisone 2.5% + Chloramphenicol 2% cream, twice daily.<br>• **COUNSELING:** Strict wound care, hygiene, and avoidance of contact with family lesions. |
| **II. Follow-up Visit (Day 35 / 5 Weeks)** | |
| **Clinical Status** | • **Remarkable improvement.**<br>• All pustular and nodular lesions completely resolved.<br>• No new lesions reported.<br>• Pruritus and pain had ceased. |
| **Residual Findings** | Residual, non-scaly post-inflammatory hyperpigmentation (PIH) at former lesion sites. |
| **Treatment Plan** | • Topical Desoximetasone 0.25% cream for residual inflammation.<br>• Topical Urea 10% cream to manage PIH and skin texture. |
| **III. Final Outcome** | |
| **Patient Outcome** | **Complete resolution of all active lesions with no scarring.** Mild, fading PIH remained. |
| **Family Outcome** | Milder lesions in the mother and brother resolved spontaneously over the same period, consistent with the self-limiting nature of uncomplicated Orf. |

**3. Discussion**

We have presented a complex case of Ecthyma Contagiosum (Orf) in an adolescent, which is novel for three primary reasons: 1) the clinical presentation was a widespread pustular eruption, a potent mimic of Subcorneal Pustular Dermatosis (SPD); 2) the patient

had no direct, occupational contact with livestock, highlighting an environmental or indirect transmission vector; and 3) the initial misdiagnosis led to iatrogenic harm via systemic corticosteroids, illustrating a critical diagnostic pitfall.

The core of this case lies in the pathophysiology of the Orf virus and its ability to masquerade as a sterile inflammatory disease. The Orf virus (ORFV), a member of the *Parapoxviridae* family, is a large, complex, double-stranded DNA virus that has evolved a sophisticated and multi-faceted strategy to infect its host, replicate within the epidermis, and meticulously subvert the host's immune response. The pathophysiology of the lesion seen in this patient is not merely a passive result of viral presence but an active, virally-orchestrated process of tissue manipulation and immunological disarmament.[11]

The infection cascade begins with mechanical inoculation, requiring micro-abrasions in the skin barrier. This is a critical first step, as the virus cannot penetrate intact stratum corneum.[12] ORFV, like other poxviruses, initiates entry by binding to cell surface glycosaminoglycans (GAGs), such as heparan sulfate, which act as initial attachment receptors. This is followed by a more complex interaction with other host cell proteins, leading to cell membrane fusion and the release of the viral core directly into the cytoplasm.

Once inside the cytoplasm, the *Poxviridae* family distinguishes itself. Unlike most DNA viruses, which must hijack the host's nuclear machinery, ORFV replicates entirely within the cytoplasm. It achieves this autonomy by carrying its own viral-encoded DNA-dependent RNA polymerase and all necessary transcription factors. The viral core uncoats, and a temporally-regulated cascade of gene expression begins. This process leads to the formation of discrete, membrane-bound cytoplasmic "factories" known as viroplasm. On histopathological examination, these viroplasms, engorged with newly synthesized viral proteins and genomic DNA, become visible as the pathognomonic, large, eosinophilic intracytoplasmic inclusion bodies (Guarnieri-like bodies). These inclusions are the morphological hallmark of active viral replication and a key diagnostic feature differentiating this viral process from a sterile inflammatory disease.[13]

The true sophistication of ORFV lies in its extensive genome, a significant portion of which is dedicated to encoding immunomodulatory proteins designed to neutralize virtually every arm of the host's innate and adaptive immune response. This case is a direct reflection of this strategy's success. A hallmark of Orf lesions is their "targetoid" and highly vascular nature. This is not a simple inflammatory reaction; it is a deliberate viral construction. ORFV encodes a potent homolog of Vascular Endothelial Growth Factor, designated vVEGF-E. This viral protein binds to and activates the host's VEGFR-2 (KDR) receptor on dermal endothelial cells. This activation triggers a cascade of intracellular signaling (via the Akt/mTOR/p70S6K pathway), resulting in profound endothelial cell proliferation (angiogenesis) and increased vascular permeability. The "prominent vascular proliferation and endothelial swelling" noted in our patient's biopsy is the direct histopathological correlate of this vVEGF activity. This virally-induced angiogenesis serves two purposes: it creates the edematous, hemorrhagic, and nodular clinical lesion, and, more critically, it recruits a robust blood supply to the "viral factory," feeding the metabolically demanding process of viral replication.[14]

The primary antiviral defense of the host is the T-helper 1 (Th1) cellular immune response, characterized by the production of Interferon-gamma (IFN-γ) and Tumor Necrosis Factor-alpha (TNF-α). ORFV actively decapitates this response by encoding a functional homolog of Interleukin-10 (vIL-10). Host IL-10 is a powerful anti-inflammatory cytokine that shifts the immune system towards a Th2 (humoral/tolerant) profile. The ORFV vIL-10 mimics this perfectly. It binds to the host IL-10 receptor, suppressing the maturation of dendritic cells, inhibiting their ability to present antigens, and directly preventing T-cells and natural killer (NK) cells from producing IFN-γ. This action creates a locally immunosuppressed microenvironment, effectively

blinding the host's most potent antiviral fighters to the ongoing infection.

Even if a host cell detects the virus, its primary defense is to secrete Type I interferons (IFN-α/β) to warn neighboring cells. These interferons bind to receptors on adjacent cells, activating the JAK/STAT signaling pathway, which in turn upregulates hundreds of "Interferon-Stimulated Genes" (ISGs) that establish a potent "antiviral state." ORFV has evolved multiple mechanisms to sever this communication line. It encodes proteins (such as OVIFZ) that specifically bind to and inhibit key components of this pathway, such as STAT1 and STAT2. By blocking JAK/STAT signaling, ORFV renders the host cells "deaf" to the interferon alarm, allowing the virus to spread from cell to cell without encountering this pre-established defense. To ensure the host "factory" cell does not die prematurely, ORFV encodes proteins that inhibit apoptosis (programmed cell death), including homologs of the B-cell lymphoma 2 (Bcl-2) family. It also encodes chemokine-binding proteins that act as "sinks," soaking up host chemokines (like IL-8 and MCP-1) to prevent the early recruitment of neutrophils and macrophages.[15]

In summary, the pathophysiology of Orf is a masterpiece of viral subversion. The virus enters the skin, builds its own blood supply (vVEGF), disables the host's targeted antiviral response (vIL-10), and silences the local alarm system (JAK/STAT blockade), all while keeping the host cell alive.[16] This multi-pronged strategy allows for unchecked replication, leading to the profound viral cytopathic effects—ballooning degeneration and necrosis—seen on this patient's biopsy. The initial misdiagnosis of Subcorneal Pustular Dermatosis (SPD) was not a result of clinical negligence but rather a testament to the virus's ability to act as a "great mimic." The diagnostic pathway was confounded by a series of red herrings that perfectly aligned with the criteria for a sterile neutrophilic dermatosis.

The clinical similarity between our patient's presentation and classic SPD was profound. SPD, first described by Sneddon and Wilkinson, is an autoinflammatory disease defined by waves of sterile, flaccid pustules, often coalescing into annular and serpiginous patterns. Our patient presented with widespread, relapsing pustules and systemic inflammation (fever, elevated CRP, neutrophilic leukocytosis). This clinical picture is a textbook presentation for an acute flare of SPD. The pustules in Orf, especially in a severe, multifocal case, are not the primary lesion but a secondary event. The virus-induced necrosis of keratinocytes releases a flood of Damage-Associated Molecular Patterns (DAMPs), such as ATP, uric acid, and high-mobility group box 1 (HMGB1) protein. These DAMPs are intensely pro-inflammatory and act as a powerful chemoattractant for neutrophils. The result is a "pustule" filled with neutrophils, but the reason for their presence is fundamentally different. In SPD, the neutrophils are the primary effector, driven by a presumed cytokine dysregulation (perhaps involving the IL-36 pathway). In Orf, the neutrophils are the secondary responders, arriving to clean up the necrotic debris caused by the virus.[17]

A pivotal moment in the initial workup was the "sterile" Gram stain and subsequent 48-hour bacterial culture. This negative finding was the key piece of evidence that falsely corroborated the diagnosis of a sterile neutrophilic dermatosis. This represents a critical methodological pitfall. A "sterile culture" only rules out common, fast-growing aerobic and anaerobic bacteria. It provides no information about atypical bacteria (mycobacteria), fungi, or, most importantly, viruses. The initial pustules in an acute Orf infection are sterile from a bacterial standpoint. The neutrophils are reacting to viral necrosis, not a pyogenic bacterium. This "sterility" is a known feature of the acute phase and, in this case, served as a potent diagnostic confounder, diverting the clinical team's suspicion away from an infectious etiology.[18]

This case powerfully underscores the indispensable role of histopathology as the "ground truth" when clinical and laboratory data are ambiguous. A biopsy of SPD has a distinct and characteristic appearance: a discrete, clean,

subcorneal pustule (a split just below the stratum corneum) filled almost exclusively with neutrophils.[19] The critical feature is that the underlying epidermis (stratum spinosum, granulosum) and the dermis are largely unremarkable, showing only a mild, non-specific perivascular infiltrate.

In stark contrast, our patient's biopsy revealed a scene of epidermal devastation. It was not a "quiet" epidermis. The findings included: (1) Pseudoepitheliomatous Hyperplasia: A reactive, dramatic thickening of the epidermis, representing the skin's panicked attempt to regenerate in response to viral damage; (2) Extensive Necrosis and Ulceration: Widespread keratinocyte death; (3) Ballooning Degeneration: The pathognomonic sign of viral cytopathy, where keratinocytes become swollen, pale, and lose their intercellular connections due to viral replication; (4) Intracytoplasmic Inclusion Bodies: The "smoking gun" of the virus itself—the eosinophilic viroplasms; (5) Mixed Dermal Infiltrate: The inflammatory response was not a pure neutrophilic infiltrate, as expected in SPD, but a dense, mixed infiltrate of lymphocytes, histiocytes, neutrophils, and eosinophils, reflecting a complex antiviral and wound-repair response. The diagnosis was not in the pustule itself, but in the epidermis adjacent to it. This case teaches a vital lesson: in any atypical pustular eruption, even one that appears clinically "classic" for a neutrophilic dermatosis, a biopsy is non-negotiable.[20]

The initial, logical treatment for suspected SPD—systemic methylprednisolone—was precisely the worst possible intervention for an active *Parapoxvirus* infection. This iatrogenic decision created a synergistic immunosuppression that directly explains the patient's precipitous clinical decline. The patient's clinical worsening at the 13-day follow-up was a direct and predictable consequence of this therapeutic error. The "perfect storm" of immunosuppression was created by two forces acting in concert: (1) Viral Immunosuppression: As detailed, the Orf virus was already actively suppressing the host's antiviral Th1 response via its vIL-10 and blocking interferon signaling via JAK/STAT inhibition; (2) Iatrogenic Immunosuppression: The systemic methylprednisolone (a glucocorticoid) then delivered a second, powerful blow. Glucocorticoids function by binding the glucocorticoid receptor, which then translocates to the nucleus to suppress the transcription of nearly all pro-inflammatory cytokines, including IL-1, IL-6, TNF-α, and, most critically, IFN-γ. It also broadly inhibits T-cell activation and T-cell-mediated cytotoxicity. The virus had already disabled the "targeted missile" system (the Th1 response). The clinician, by adding corticosteroids, inadvertently disabled the "general infantry" (macrophages, neutrophils, and general T-cell activation). This dual-pronged assault on the host's immunity allowed the Orf virus to replicate completely uncontrolled. The rapid proliferation of new, purulent, and more inflamed lesions was likely a direct result of exponential viral replication, leading to deeper and more extensive epidermal necrosis.

The combination of iatrogenic immunosuppression and widespread, necrotic, and ulcerated skin created an ideal nidus for opportunistic bacterial colonization. The physical barrier of the stratum corneum was gone, and the local immune surveillance was crippled. The ulcerated lesions provided a protein-rich, avascular, moist, and nutrient-dense substrate—a perfect bacterial culture medium. The isolation of *Enterobacter cloacae ssp. cloacae* is a highly sophisticated and alarming finding. This is not a typical skin commensal like *Staphylococcus epidermidis* or a primary pathogen like *Staphylococcus aureus*. *E. cloacae* is a Gram-negative rod, part of the notorious ESKAPE pathogen group (*Enterococcus, Staphylococcus, Klebsiella, Acinetobacter, Pseudomonas, Enterobacter*), which are known for their high rates of intrinsic and acquired antibiotic resistance. *E. cloacae* possesses an intrinsic AmpC β-lactamase, rendering it resistant to penicillins and early-generation cephalosporins (like the ampicillin/clavulanic acid and cefazolin noted in the sensitivity report).[17,18]

Its presence in this adolescent patient signifies a severe opportunistic infection, likely colonized from an environmental source (soil, water) or transiently from the patient's own gastrointestinal flora. The fact that this specific, multidrug-resistant organism was isolated is a direct testament to the severity of the barrier breach and the profundity of the local immunosuppression. The immediate cessation of the steroid (allowing host immunity to rebound) and the initiation of targeted ciprofloxacin (guided by sensitivities) were both critical to resolving this dangerous superinfection, which was likely the primary driver of the patient's pain, purulence, and systemic inflammatory signs.

Finally, this case provides crucial epidemiological insights, expanding the traditional profile of human Orf and highlighting the modern relevance of the "One Health" paradigm. The classic profile of an Orf patient is a middle-aged male farmer, veterinarian, or butcher with a single, self-resolving lesion on a finger. Our patient deviates from this profile in every respect: she is an adolescent female, she has no "classic" occupational risk, and she presented with a severe, multifocal eruption. This very "atypical" host profile is what blinded the clinicians to the diagnosis. The transmission vector was not direct contact but *environmental*. This case highlights the remarkable hardiness of the *Parapoxvirus*. The virus is not delicate; it is highly resistant to desiccation and can remain viable in dried crusts, wool, soil, and on fomites (like fence posts or farm equipment) for months, and even years in some conditions. The patient's home being 1 kilometer from a goat farm is the critical epidemiological link. It is highly plausible that viral particles, protected in dust or organic matter, were transported by wind or on fomites (vehicles, clothing, insects) from the farm into the patient's surrounding environment, leading to an indirect inoculation. This case is a textbook example of the "One Health" concept, which posits that the health of humans, animals, and the environment are inextricably linked. The health status of the goats (Animal Health) led to contamination of the environment (Environmental Health), which subsequently caused a severe, misdiagnosed disease in the adolescent (Human Health). The family cluster (mother and brother) confirms a non-sporadic, point-source outbreak. This cluster could be explained by two scenarios: 1) A common-source exposure, where all three family members were exposed to the same environmental fomite (contaminated dust brought into the home), or 2) Human-to-human transmission, where the patient, with her severe, ulcerated, and high-viral-load lesions, transmitted the virus to her family members via direct contact or shared household items (towels, linens). While Orf is less efficient at human-to-human spread than other poxviruses, it is well-documented, especially in intimate household settings.[19,20]

The ultimate public health lesson from this case is that Ecthyma Contagiosum is not merely an "occupational disease" but an "environmental zoonosis." Clinicians in all settings, including urban and suburban, must maintain a high index of suspicion. Any patient presenting with an atypical, treatment-resistant pustular or nodular eruption (especially if targetoid, umbilicated, or hemorrhagic) must be questioned not just about direct animal contact, but also about indirect and environmental exposure—including proximity to farms, visiting petting zoos, or recent hiking. This case fundamentally shifts the diagnostic paradigm from "Who did you touch?" to "Where have you been?"

Finally, this case expands the epidemiological profile of human Orf. The patient, an adolescent student, had no "classic" occupational risk. The transmission vector was almost certainly environmental, originating from the nearby goat farm. This highlights the resilience of the *Parapoxvirus*, which can remain viable in the environment (on dry crusts, soil, or fomites) for months. The subsequent family cluster further suggests either a common environmental exposure or, less commonly, human-to-human transmission. This case serves as a public health reminder that Orf should be in the differential

diagnosis for any atypical pustular or nodular eruption, regardless of the patient's occupation or direct animal contact.

**4. Conclusion**

We have presented a severe, pustular case of Ecthyma Contagiosum (Orf) in an immunocompetent adolescent, which clinically and initially masqueraded as Subcorneal Pustular Dermatosis. This case serves as a critical diagnostic lesson: viral zoonoses can be potent clinical mimics of sterile inflammatory dermatoses. The misdiagnosis led to inappropriate treatment with systemic corticosteroids, resulting in iatrogenic worsening and bacterial superinfection. We underscore the indispensable role of a high index of suspicion, a thorough epidemiological history (including environmental and familial contacts), and definitive histopathological analysis in all atypical pustular eruptions. Early and accurate diagnosis is paramount to prevent iatrogenic harm and to ensure correct antimicrobial stewardship.

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