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Dermatology

Echtyma Gangrenosum Secondary to *Staphylococcus auréus* in a Child with Transient Neutropenia: A Case Report and Review of the Literature

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Abstract | **Case Report**

Introduction: Ecthyma gangrenosum (EG) is a rare necrotizing vasculitis often seen in immunocompromised patients with Pseudomonas aeruginosa bacteremia, but can also be associated with other infections such as methicillin-resistant *Staphylococcus aureus* (MRSA). ***Case Presentation***: We present the case of a previously healthy 6-month-old infant who developed EG lesions following an MRSA infection. ***Discussion***: EG requires prompt diagnosis and treatment with broad-spectrum antibiotics, as it can lead to rapid tissue damage and potentially high mortality rates. Management should include investigation of underlying hematological abnormalities, particularly transient neutropenia, which is commonly associated with EG and may be linked to bacterial or viral infections. ***Conclusion***: Recognition and treatment of EG, especially when associated with MRSA, are crucial for patient outcomes. Broad-spectrum antibiotic coverage and culturing microorganisms are essential for effective management.

Keywords: Ecthyma Gangrenosum, *Staphylococcus Aureus,* Transient Neutropenia.

INTRODUCTION

Perineal lesions in children encompass injuries to the perineum, anogenital region, and any localized skin damage occurring "under the diaper" in an infant. It is a common reason for consultation, mainly encompassing everyday occurrences like diaper dermatitis, yet also involving less common conditions that warrant recognition, such as echtyma gangrenosum (EG) [1]. EG is a necrotizing vasculitis, commonly observed in immunocompromised patients with *Pseudomonas aeruginosa* bacteremia [2]. In rare cases, it may be associated with other bacterial, fungal, and viral infections, such as the case of our previously immunocompetent patient who presents EG caused by methicillin-resistant *Staphylococcus aureus*.

CASE PRESENTATION

A previously healthy six-month-old girl presented with a hemorrhagic blister at the top of her vulva with fever of 40°C. It had started four days before as erythema, that progressively developed ulceration and edema. She was treated with oral macrolides. As there was no improvement with clinical deterioration, persistent fever, hypotonia, and a C-reactive protein (CRP) level of 450mg/l, she was hospitalized for suspected meningitis. She was put on meningitis-dose antibiotic therapy with a normal lumbar puncture, and referred to dermatology. On physical examination, the patient had two painful necrotic ulcers with an erythematous border and a fibrinous base covered by a central crust, sensitive to the touch, located in the top of the labia majora and the intergluteal fold (Figure 1), as well as multiple erythematous maculopapular lesions on both lower limbs (Figure 2). Dermoscopy was nonspecific, showing an ulceration, central crust, whitish scales, and doted vessels (Figure 3).

In the laboratory findings: normochromic normocytic anemia, neutropenia at 200/mm3, and a CRP of 450 mg/l were observed. Bacteriological pus culture and blood cultures were positive for Methicillin-Resistant *Staphylococcus aureus* (MRSA). Cytomegalovirus (CMV) serology with polymerase chain reaction (PCR) was positive. Microscopic examination of a biopsy revealed ortho- and parakeratotic hyperkeratosis, spongiosis and exocytosis with a polymorphous perivascular and interstitial dermal inflammatory infiltrate, without individualization of pathogens (patient already on antibiotics) and with no signs favoring other diagnoses (Figure 4).

We diagnosed ecthyma gangrenosum with methicillin-resistant *Staphylococcus aureus* in the

context of transient neutropenia secondary to CMV infection.

With intravenous antibiotic therapy (Ceftazidime + Metronidazole), the patient showed marked improvement and all of her lesions began to crust over and heal (Figure 5).

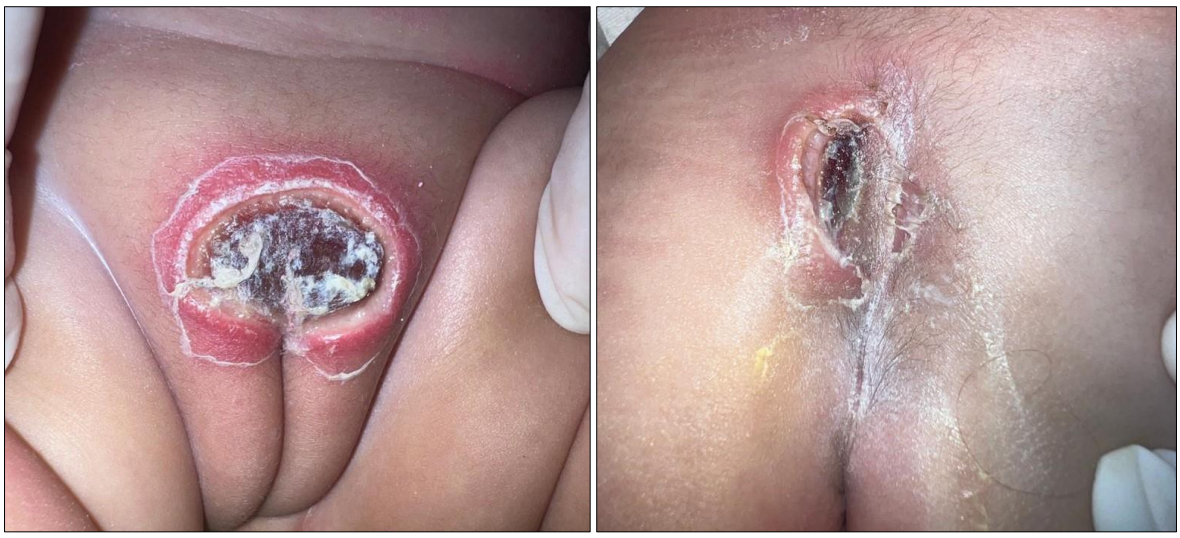

Figure 1: Ecthyma gangrenosum in labia majora and perianal area of the patient

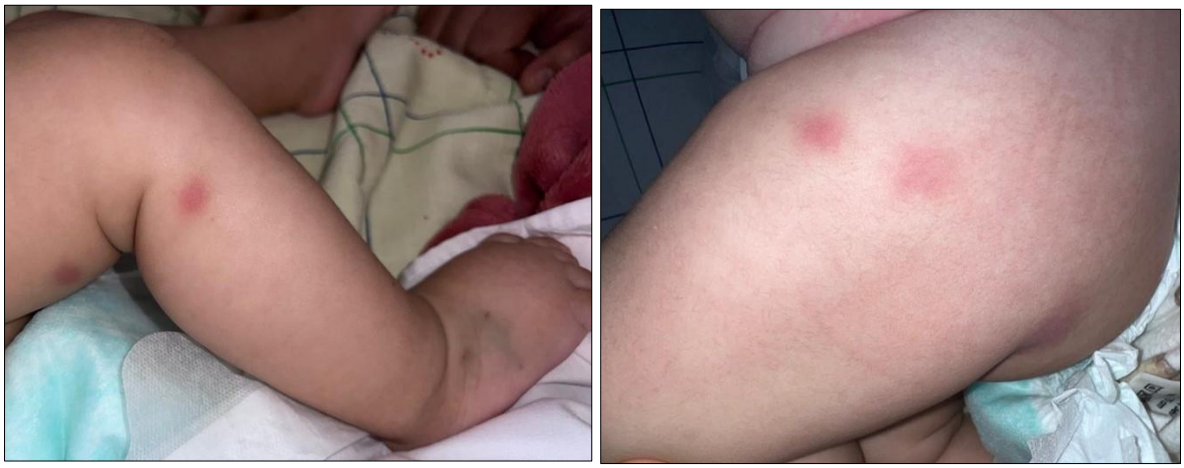

Figure 2 : Numerous erythematous maculopapular lesions scattered over both lower extremities

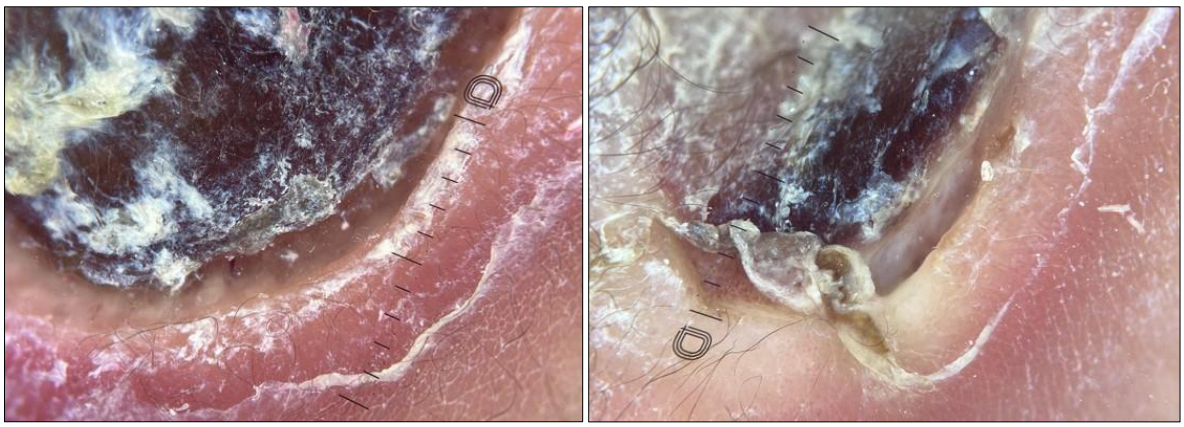

Figure 3 : Dermoscopic examination demonstrated central ulceration with crust formation, accompanied by whitish scales and dotted vessels

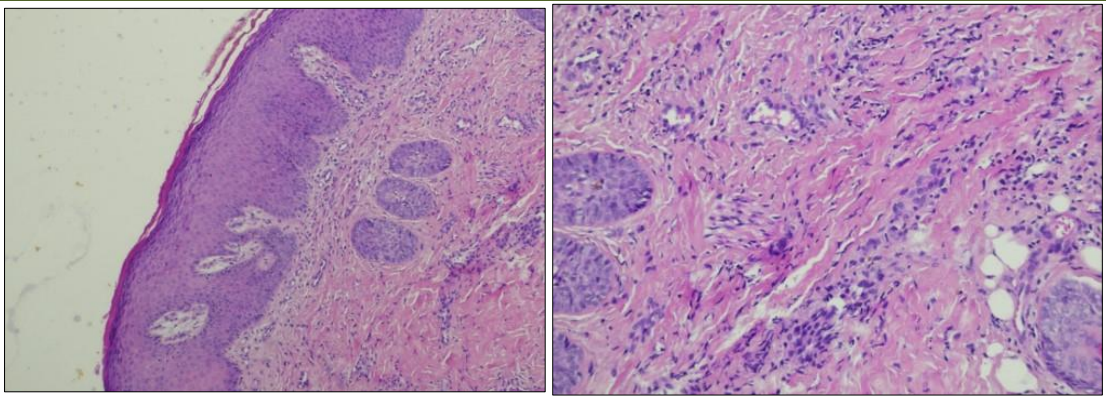

Figure 4: Magnification Gx4 and Gx40. Microscopic analysis showed hyperkeratosis with both ortho- and parakeratosis, epidermal spongiosis and exocytosis, and a mixed perivascular and interstitial dermal infiltrate

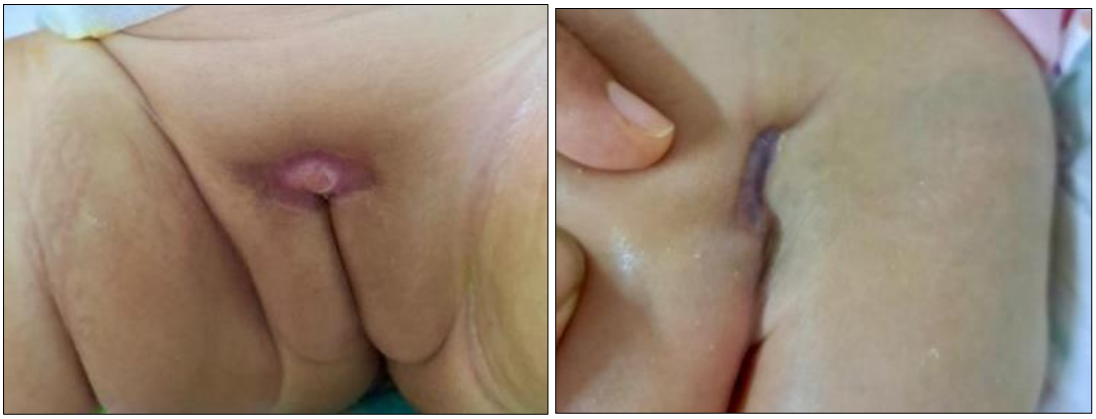

Figure 5: Follow-up photograph eight weeks post-treatment, showing a residual atrophic scarring

DISCUSSION

EG is a rare and potentially life-threatening disease, typically associated with Pseudomonas aeruginosa. However, it can also be caused by *Staphylococcus aureus*, including methicillin-resistant strains (MRSA). It is often indicative of an immune deficiency but has occasionally been reported in healthy individuals [3].

We presented the case of a previously healthy 6-month-old infant with transient neutropenia who developed characteristic skin lesions of EG following an infection with MRSA. In the literature, there are only 4 reported pediatric cases of EG associated with *Staphylococcus aureus* infection (Table 1) [4-7]. The age of the patients ranged between 8 and 16 months, among them are three cases with EG secondary to methicillin-sensitive *staphylococcus aureus* (MSSA) and one to MRSA infection, three of which were associated with neutropenia.

Table 1 : Case reports of patients with *Staphylococcus aureus* ecthyma gangrenosum in child

Author (Date)	Age (mo)	Gender (Female / Male)	Underlying pathology	Location	Pathogen	Blood culture	Tissue culture	Bacteria in pathology	Antibiotics	Outcome
Pechter *et al*., (2012) [4]	8	Female	transient neutropenia	Neck, genitals	MRSA	-	+	Gram positive cocci at epidermal area	Vancomycin: 21 d	Discharged

Our reported case	6	Female	Transient neutropenia	Genitals, perianal area	MRSA	+	-	Not observed	Ceftazidime + Metronidazole	Discharged
Zhang *et al*., (2022) [7]	16	Female	Severe persistent neutropenia	Face, perianal area	MSSA → Acinetobacter baumannii	-	+	Not assessed	meropenem + vancomycin → tigecycline + daptomycin + voriconazole	Died -septic shock
Fang *et al*., (2022) [6]	12	Male	Atopic dermatitis and transient neutropenia	Trunk, thighs	MSSA	-	+	Gram positive cocci at subepidermal area	cefepime+ amikacin + teicoplanin → cefepime	Discharged
Song *et al*., (2015) [5]	15	Female	Healthy	Trunk	MSSA	-	+	Not observed	Ceftriaxone → cefepime and clindamycin: 14 d	Discharged

EG is characterized by direct involvement of the skin and mucous membranes [3]. It first manifests as painless red macules that gradually spread, then they transform into papules, then hemorrhagic blisters, and eventually rupture to form a grey-black eschar lesion surrounded by an erythematous halo, or ulceration with a necrotic center [6-8]. It's can also begin with a non-specific skin rash. The evolution is rapid, occurring within approximately 12-24 hours [9]. Lesions have the potential to emerge across the body, yet predominantly surface in the anogenital and axillary regions, and the most prevalent sites include the buttocks and perineal region (57%), followed by the extremities (30%), trunk (6%), and face (6%) [7-10]. Children with chronic diseases and immunodeficiency are typically at risk of developing EG. Therefore, doctors should systematically look for predisposing factors such as secondary aplasia due to chemotherapy, HIV infection, neutropenia (chronic, cyclic, or transient), functional deficit of neutrophil polymorphonuclear cells, agammaglobulinemia, hematologic disorders, malnutrition and tuberculosis [5-12].

It is important to identify any underlying hematologic abnormality, including variants of neutropenia such as chronic, cyclic, and transient neutropenia, with the latter being most commonly reported in association with EG [6]. As is the case with our patient and the three other cases in the literature. For our case, we suppose that transient neutropenia is the result of bacterial infection, which led to a failure in neutrophil production in the bone marrow or their peripheral destruction, or it could be secondary to CMV viral infection.

Diagnosis is generally based on the clinical appearance of the lesions, but the responsible pathogens should be confirmed by bacterial cultures or blood cultures [13]. Skin biopsy is not always necessary. Otherwise, we will find vasculitis following colonization of the middle and outer layers of the vascular walls, foci of dermal necrosis with overlying epidermal necrosis, and aggregates of gram-positive cocci [3-5].

Pseudomonas aeruginosa is the most commonly documented etiology in EG, but other bacterial pathogens, including *Staphylococcus aureus* and *pyogenes,* gram-negative bacilli (*E. coli, A. hydrophila, B. cepacia, C. violaceum, C. freundii, C. diphtheriae, K. pneumoniae, M. morganii, N. gonorrhea, P. stutzeri, S. marcescens, V. vulnificus, Y. pestis, X. maltophilia*), and fungal (*A. fumigatus, C. albicans, C. species, E. species, F. solani, M. species, R. species, P. boydii, S. dimidiatum*) or viral (*Herpes simplex virus*) agents, have also been reported [3].

From a clinical perspective, it's crucial to maintain a broad scope when considering EG lesions and to conduct blood cultures prior to initiating treatment. If a blood culture yields positive results, treatment can be tailored based on microbial susceptibility. However, a negative culture should not rule out the possibility of EG [4]. Wide local excision + broad-spectrum antibiotics are recommended once the diagnosis is established. Clindamycin is generally recommended for the treatment of toxin-mediated infections, given its ability to arrest protein synthesis, theoretically decreasing toxin production [5]. The authors recommend that, although

occurrences of gram-positive instances of this disease are rare, clinicians should consider administering vancomycin alongside antipseudomonal penicillin and aminoglycoside to reduce mortality risk. If there is suspicion of a fungal infection, additional antifungal medication should be prescribed to address the widest array of potential infectious causes [4].

Management of underlying factors is also essential. Prognosis depends on the promptness of diagnosis and initiation of treatment. With appropriate treatment, most patients can recover, although healing may leave significant scars. EG is an uncommon, cutaneous condition most often seen in immunocompromised patients, with mortality rates ranging from 15 to 77% [9]. Studies revealed that neutropenia at the time of EG diagnosis is the most important prognostic factor for death, other signs of a poor prognosis in addition of persistent neutropenia were found, such as multiple lesions, delay in diagnosis and treatment, high bacteremic burden, repeated catheterization and instrumentation [14, 15].

CONCLUSION

Ecthyma gangrenosum is a rare condition diagnosed clinically and bacteriologically. The majority of pediatric patients have either transient or persistent immunodeficiency that must be managed alongside appropriate antibiotic treatment. It is important to note that ecthyma gangrenosum with *Staphylococcus aureus* is a serious condition requiring immediate medical attention. Hence, the importance of broad-spectrum empirical antibiotic coverage and culturing microorganisms in any patient presenting with ecthyma gangrenosum.

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