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CASE REPORT

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A Case Report on Toxic Epidermal Necrolysis in an Adult Filipino Pregnant Patient*

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ABSTRACT

Toxic epidermal necrolysis (TEN) is a rare, life-threatening dermatologic emergency characterized by extensive epidermal detachment, blistering, and painful mucocutaneous erosions. It is often associated with complications such as electrolyte imbalance, infections, sepsis, and even death. TEN prevalence in the general population is estimated at 1-2/1,000,000 per year. In the pregnant population, TEN occurrence is even more uncommon, as limited studies have been reported. This case report adds to the existing literature on TEN in a pregnant patient in the local setting.

The patient is a 26-year-old Gravida 3 Para 1 (1011) who presented at 12 weeks age of gestation with progressive vesiculobullous lesions and skin detachment after intake of omeprazole, hyoscine, and metoclopramide for abdominal pain. A skin biopsy confirmed the diagnosis of TEN. Systemic corticosteroid was initiated and was gradually tapered with complete resolution of symptoms.

TEN in pregnancy may pose a potentially life-threatening risk for the mother and the fetus. In this case, the use of systemic steroids was noted to be beneficial in preventing the potential sequelae in TEN. Emphasis on pharmacovigilance in TEN, even in low-risk drugs, especially during pregnancy, is paramount.

Keywords: toxic epidermal necrolysis, pregnancy, prednisone, systemic steroids, omeprazole

INTRODUCTION

Epidermal necrolysis (EN) is a rare and life-threatening dermatologic emergency. It presents with skin detachment and necrosis of the skin and mucosa. The condition is further categorized according to the body surface area involved: Stevens-Johnson Syndrome (SJS) affects less than 10% of the body surface area (BSA), SJS-TEN Overlap affects 10-30%, and toxic epidermal necrolysis (TEN) affects more than 30% of BSA.[1]

The prevalence rate ranges from 1-2/1,000,000 per year, with a slight female predilection at 0.6 sex ratio. The risk increases with age, with a mean onset at 65 years old and above.[2] EN in pregnant patients has been rarely reported. To the extent of our knowledge, there are no published studies on TEN during pregnancy in the local setting.

This study highlights a rare case of toxic epidermal necrolysis in a 26-year-old Filipino pregnant patient with complete resolution following the initiation of systemic steroid.

CASE

A 26-year-old Gravida 3 Para 1 (1011) pregnant patient was admitted due to a two-week history of progressive vesiculobullous lesions. Two weeks prior to admission, the patient complained of hypogastric pain, graded 5/10, with associated nausea. The patient consulted a general physician and was administered intravenous (IV) metoclopramide, IV omeprazole, and oral hyoscine, which afforded relief.

One week later, several erythematous papules on the extremities were noted, with no other associated symptoms. The patient consulted another physician, though the diagnosis was not recalled. She was given cetirizine and betamethasone lotion but noted no improvement. During this time, a pregnancy test revealed a positive result.

In the interim, the lesions evolved into multiple serous-filled vesicles and bullae affecting the face, trunk, and extremities. Mucosal erosions also began to develop in the eyes, lips, and genital area. The lesions progressed despite the use of cetirizine and betamethasone lotion.

One day prior to consultation, further progression of vesiculobullous lesions with extensive erosions, skin detachment, and severe pain prompted admission and referral to the dermatology service.

The past medical history noted an allergy to amoxicillin, with no other co-morbidities. The drug history revealed the first-time use of omeprazole, metoclopramide, hyoscine, cetirizine, and betamethasone lotion. No other medications were taken or applied within 3 months prior to the onset of lesions (Table 1). The family history was unremarkable; no other family members had similar lesions.

Obstetric and gynecologic history revealed a Gravida 3 Para 1 (1011) patient. During the first pregnancy, the patient had a stillbirth at seven months age of gestation. The second pregnancy was uneventful. The patient is a heterosexual female in a monogamous sexual relationship and denies any history of sexually transmitted infection.

Physical examination noted tender, multiple flaccid serous-filled vesicles, bullae, and areas of erosions on the face, neck, trunk, and extremities covering 90% BSA. Conjunctivitis with purulent discharges, lip fissures, and genital erosions were also present (Figure 1A). Nikolsky sign and Asboe-Hansen sign were elicited. The patient was hemodynamically stable. Her abdomen was globular, non-tender, and soft, with bilateral pitting edema of the lower legs and equal pulses.

The complete blood count revealed peripheral blood leukocytosis with neutrophilia. Pyuria was noted in the urinalysis. Creatinine, urea, blood sugar, and liver function tests were normal. No multinucleated giant cells were noted in Tzanck Smear. Antinuclear antibody (ANA) was requested but was not done due to financial constraints. Histopathology showed the presence of subepidermal blister with epidermal necrosis (Figure 2A). Direct immunofluorescence revealed a negative result, ruling out

Table 1. Drug Timeline

	2 weeks Prior to Admission	1 week	5 Days	4 Days	1 Days	Admission
	None	Papules	Papules	Bullae, Vesicles		
Omeprazole						
Metoclopramide						
Hyoscine						
Cetirizine						
Betamethasone Lotion						

Figure 1. **(A)** Multiple flaccid serous-filled bullae and vesicles with erosions on the face, neck, trunk, inguinal areas, upper and lower extremities (90% body surface area) associated with Asboe-Hansen Sign and lip fissures. **(B)** There is noted improvement of the lesions after 8 days of steroid therapy.

autoimmune blistering disorders (Figure 3). Dermoscopic findings noted epidermal detachment on an erythematous background. Histologic and dermoscopic findings were consistent with epidermal necrolysis[1,3] (Figure 2B).

Management involved a multidisciplinary approach. The patient was referred to the obstetric service, confirming a live, singleton pregnancy uterine at 12 weeks and 2 days by crown-rump-length via pelvic ultrasound. She was also seen by the ENT and Ophthalmology department to address the mucosal erosions. Our service started with intravenous hydrocortisone at 5 mg/kg/day for 5 days, and it was later tapered to oral prednisone at 0.5 mg/kg/day for an additional 5 days, with noted improvement of symptoms. Petrolatum-impregnated gauze and mupirocin 2% ointment were applied to the eroded areas. Given the limited resources, aseptically prepared banana leaves were used as bed linings. The patient showed significant improvement and was discharged.

On follow-up via telemedicine, complete resolution of symptoms with residual hyperpigmentation was reported after completing 14 days of systemic corticosteroids. No recurrences were observed. The patient then delivered preterm at 36 weeks age of gestation, giving birth to a live baby girl weighing 2.2 kg (appropriate for AOG) via normal spontaneous delivery. The patient and the neonate were discharged well after 3 days with no fetomaternal complications.

DISCUSSION

EN is rare in the general population and even more uncommon in the pregnant population.[4,5] Both EN and pregnancy have been associated with complex immunologic states.[6] Although the exact relationships between pregnancy and EN have not been fully defined, pregnancy has been associated with an increased risk of EN.

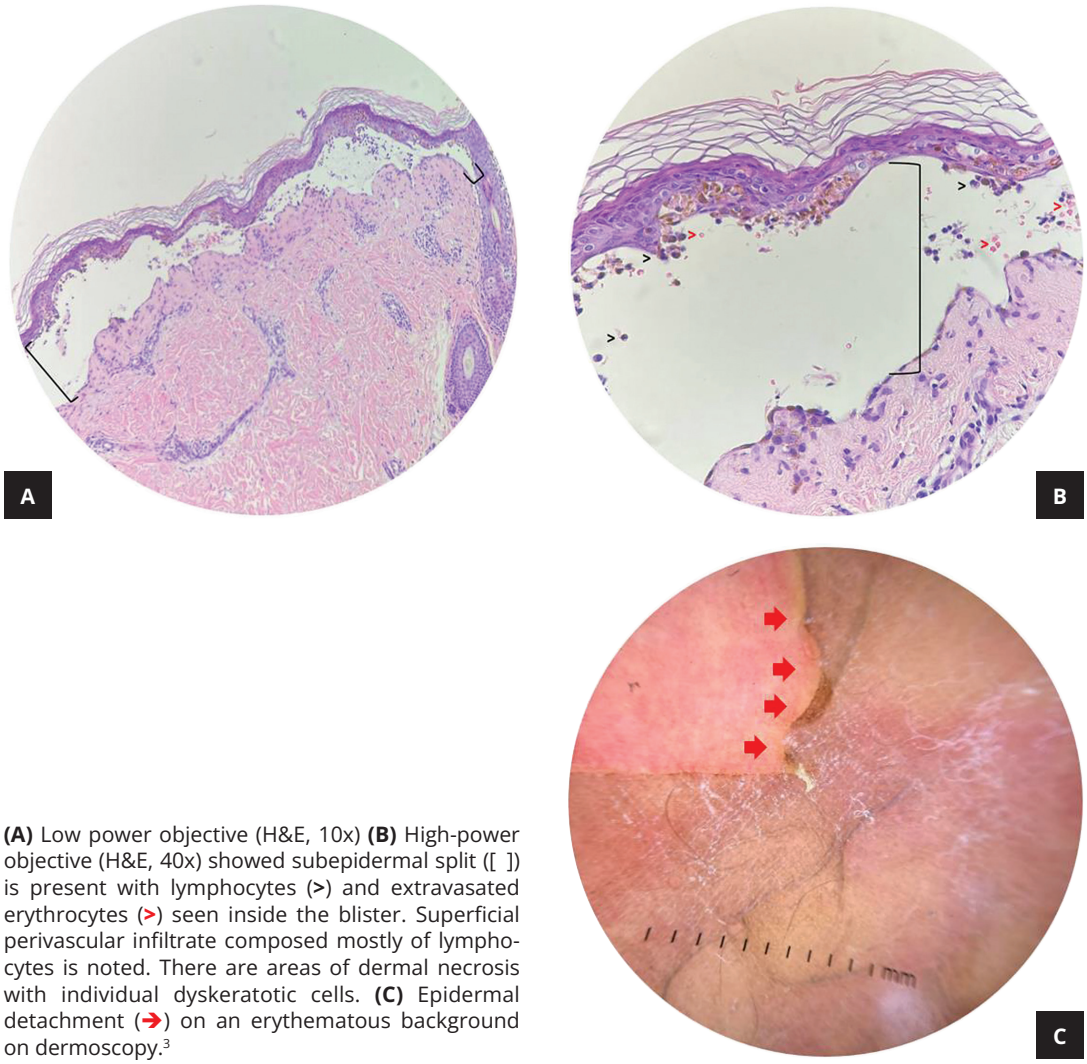

Figure 2. **(A)** Low power objective (H&E, 10x) **(B)** High-power objective (H&E, 40x) showed subepidermal split ([ ]) is present with lymphocytes (**>**) and extravasated erythrocytes (**>**) seen inside the blister. Superficial perivascular infiltrate composed mostly of lymphocytes is noted. There are areas of dermal necrosis with individual dyskeratotic cells. **(C)** Epidermal detachment (➔) on an erythematous background on dermoscopy.[3]

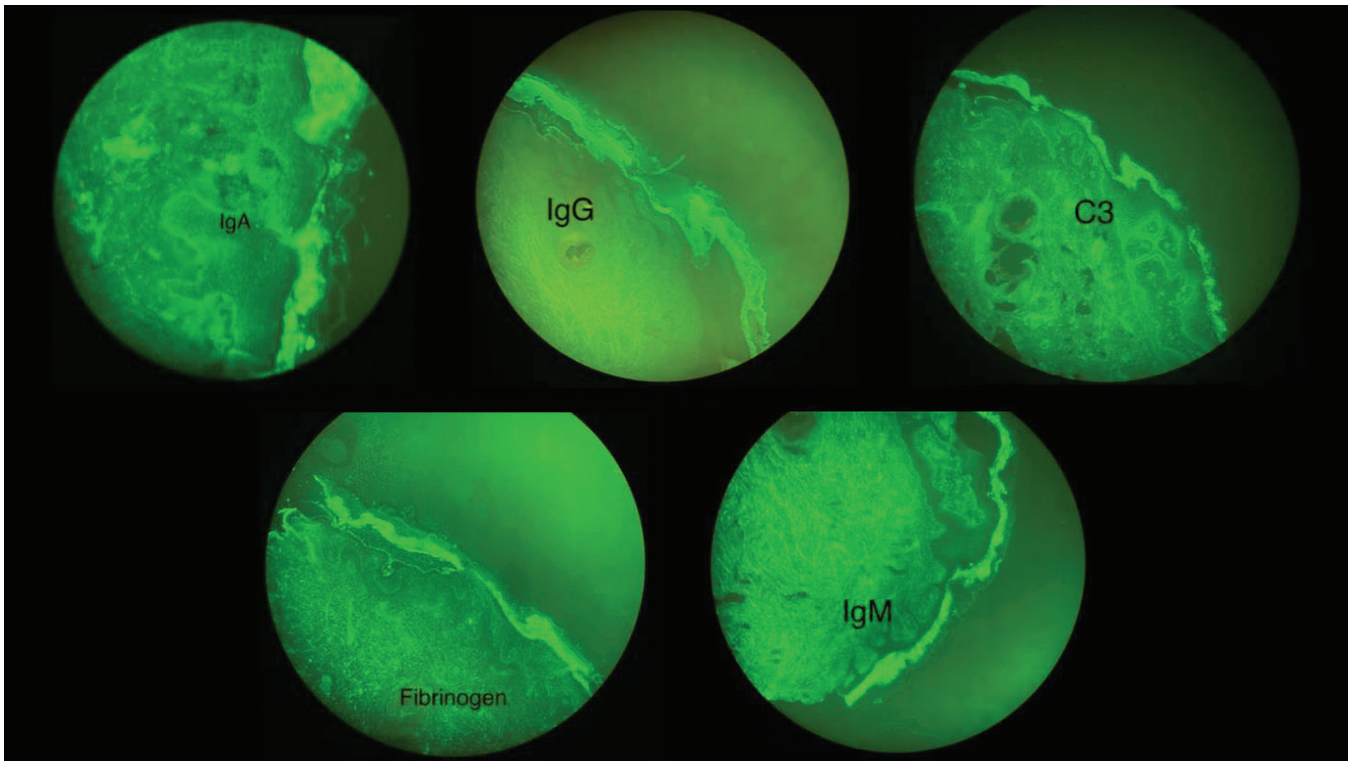

Figure 3. Direct Immunofluorescence Findings. Epidermis is negative for intercellular deposits of IgG, IgA, IgM, C3, and fibrinogen. Basement Membrane Zone is negative for deposits of IgG, IgA, IgM, C3, and fibrinogen. Vascular components are negative for deposits of IgG, IgA, IgM, C3, and fibrinogen.

Cases of EN in pregnant patients typically occur around the age of 30, beginning at 25 weeks of gestation, with a predilection during the third trimester. The average onset is about 28 days following the initiation of a causative drug.[4,5]

Similar to the general population, EN in pregnant individuals is predominantly drug-induced. However, other risk factors—such as genitourinary tract infections, systemic lupus erythematosus, herpes simplex virus, and malignant neoplasms—have also been associated with the condition.[4,5]

High-risk medications that trigger epidermal necrolysis in the general population include allopurinol, carbamazepine, sulfamethoxazole, nevirapine, phenobarbital, phenytoin, lamotrigine, acetic acid/ oxicam non-steroidal anti-inflammatory drugs (NSAIDs), and quinolones.[5,7] In the majority of EN cases in pregnancy, anti-retroviral therapies (90%), antibiotics (3%), and gestational medications (2%) were identified as causative drugs.[5] In this case report, the specific drug causing the cutaneous reaction was unclear, as the patient had recently started three new medications: omeprazole, metoclopramide, and hyoscine. Omeprazole is generally considered low-risk, with an incidence rate of 1 in 1,000,000 for triggering EN.[8] Metoclopramide has been rarely implicated in TEN, with only two documented case reports. One case involved a 52-year-old male who developed TEN after intramuscular administration of metoclopramide.[9] Another case involved a 42-year-old female with suspected TEN due to metoclopramide, though another drug culprit like paracetamol for this case could not be completely ruled out.[10] Meanwhile, there are currently no reports of EN associated with hyoscine use. This further emphasizes the importance of pharmacovigilance, as even low-risk drugs may still lead to EN, especially in vulnerable populations such as pregnant women.

Currently, there is no gold standard diagnostic test for EN. However, histological analysis shows a full-thickness necrosis. A negative direct immunofluorescence rules out the possibility of other autoimmune blistering diseases that can also present similarly. Additional laboratory tests such as serum urea, serum bicarbonate, and serum glucose are often requested for prognostication using the Severity-of-illness score for Toxic Epidermal Necrolysis (SCORTEN)[1].

Differential diagnoses include but are not limited to drug eruptions. Pemphigoid gestationis, a rare autoimmune bullous disease seen during pregnancy, may be ruled out with direct immunofluorescence, which shows a sub-epidermal cleft with linear deposition of C3 and IgG.[1]

Secondary infections, sepsis, electrolyte imbalance, ocular, pulmonary, digestive, and genitourinary involvements, and even death are possible complications of EN.[1] In pregnant women, pre-term labor, vaginal stenosis, and vaginal adhesions were previously reported.[5] Mortality rate reported for cases of EN in pregnant patients is at 2.1%.[5,11]

There is still limited data on the treatment outcomes of SJS/TEN in pregnancy. Although still controversial, a few cases reported good feto-maternal outcomes after systemic steroid therapy. In a study by Shiba et al. and Pacheco et al., observations noted a 3–5-week length of disease with good outcomes for both patients and fetuses.[12,13] As in this case, steroid therapy has proven to be beneficial to both the mother and the baby.

Intensive supportive measures are individualized per patient to address the patient's mucocutaneous involvement, nutritional support, and analgesia.[14] Epidermal detachment can be managed by applying paraffin wax or petrolatum gauze with antibiotic impregnation.[14] While paraffin wax is commonly used to cover denuded skin, in areas with limited resources, such as in this case, placing the patient over autoclaved banana leaves has shown anecdotal benefits in improving comfort and reducing pain. However, these benefits remain debatable.[15]

CONCLUSION

TEN in pregnancy is a rare occurrence. This may pose a potentially life-threatening risk for the mother and the fetus. In this case, the use of systemic steroids proved to be beneficial in preventing further potential feto-maternal sequelae in TEN. Emphasis on pharmacovigilance in TEN, even in low-risk drugs, especially during pregnancy, is paramount.

Patient Perspective

"*Di nila ako pinabayaan, laging pinapaalala kung ano yung mga dapat gawin... Nagpapasalamat po ako sa panginoon at sa inyong mga naging doctor ko dahil napagaling nyo po ako at ligtas po ang baby ko.*" ("They did not neglect me, they always remind me of what should be done... I am thankful to the Lord and to all my doctors because you cured me and my baby is safe.")

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Ethical Consideration

Patient's consent was obtained before submission of the manuscript.

Statement of Authorship

All authors certified fulfillment of ICMJE authorship criteria.

Author Disclosure

The authors declared no conflict of interest.

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