CLINICAL VIGNETTE

Erythema Multiforme

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Case Presentation

A 61-year-old female with stage 3 lung cancer presented to the emergency room with eye pain, sore throat, and hives. Her lung cancer was diagnosed a few months ago, and she had been started on osimertinib approximately 3 weeks prior to presentation. She was doing well on the medication for about two weeks, when she developed bilateral eye redness and pain, as well as a pruritic rash over her face and upper back. Two days later, she developed sore throat and noted her rash was spreading to her trunk and upper extremities. She denied subjective fevers/chills and skin pain, blistering, or peeling.

On arrival to the emergency room, she was febrile to 38 degrees Celsius and tachycardic to 125bpm. Her blood pressure was stable at 130/90, and she was breathing at 20/min with oxygen saturation of 96% on room air. Exam noted bilateral scleral injection without discharge. She also had ulcers on her lateral tongue, as well as multiple scattered blanching erythematous papules over her face, trunk, bilateral upper extremities and bilateral thighs. No blistering was noted, and the lesions were Nikolsky negative (Figure 1).

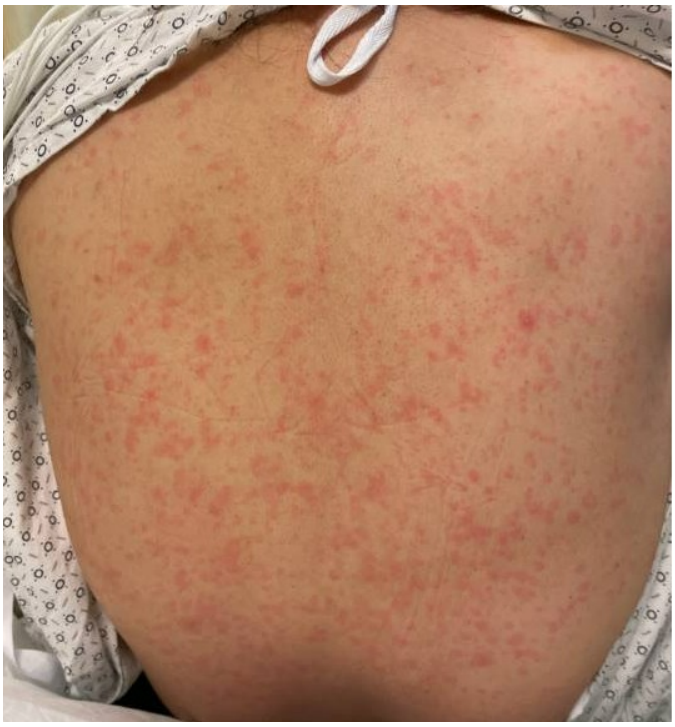

Figure 1: Rash on patient's back as seen on hospital day 2.

Dermatology and ophthalmology both consulted and tongue ulcers were swabbed for herpes simplex virus (HSV) and varicella zoster virus (VZV), and one of the skin lesions was biopsied. Given rash with mucosal involvement following recent initiation of a new medication, there was high concern for possible Stevens-Johnson syndrome/toxic epidermic necrolysis. Her osimertinib was held, she was started on systemic and topical steroids and also given one dose of etanercept. Her lesions remained Nikolsky negative without evidence of blistering or peeling (Figure 2). HSV swab returned positive for HSV-1, and it was felt her presentation was most consistent with erythema multiforme. She was started on valacyclovir for treatment of HSV as well as a steroid taper with improvement in her symptoms.

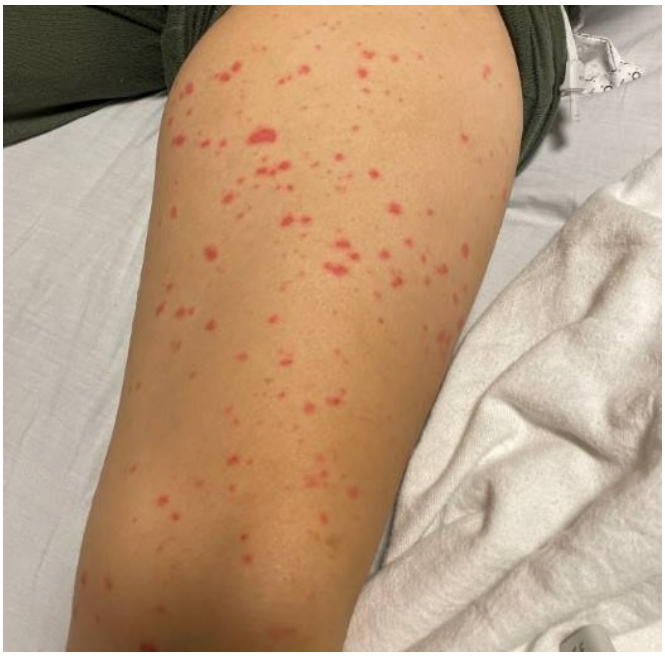

Figure 2: Rash on patient's leg as seen on hospital day 2

Discussion

Erythema multiforme (EM) is an immune-mediated reactive mucocutaneous condition. Infection is a major trigger of EM and is responsible for approximately 90% of cases. HSV is the most commonly associated infection and *Mycoplasma pneumonia* is also frequently found. Development of EM has also been linked to medications, malignancy, autoimmune diseases,

contact dermatitis, and other etiologies. EM is relatively rare, with an annual incidence less than one percent. Most patients with EM have been between 20 to 40 years old, though it has been reported in patients of all ages.[1]

Clinically, EM can present in many different ways. Classically patients present with target lesions, less than 3cm diameter in a symmetrical distribution. The lesions are frequently found on extensor surfaces but can involve almost any part of the body including face, neck, flexor surfaces, trunk, palms or soles. EM is often further classified into EM minor and EM major. In EM minor, cutaneous lesions usually involve less than 10% of the total body surface area, with minimal to no mucosal involvement. EM minor usually does not present with systemic symptoms such as fever or arthralgias. EM major, is characterized by more extensive skin involvement as well as involvement of one or more mucosal membranes. It also may be associated with other systemic symptoms.[2]

Stevens-Johnson syndrome and toxic epidermal necrolysis (SJS/TEN) also present with cutaneous lesions and mucosal involvement. Because of these similarities, it can often be difficult to distinguish between EM and SJS/TEN. Historically, it was thought that these conditions represented the spectrum of the same disorder. Now increasing evidence suggests EM and SJS/TEN are two distinct diseases. Many more cases of EM have been associated with infection, while medications are a much more common cause of SJS/TEN. EM also more commonly presents with typical target or raised atypical lesions on the peripheral extremities, while SJS/TEN more commonly presents with flat atypical targets or purpuric maculae with blisters on the trunk. Similar mucosal involvement has been observed to be similar in both.[3]

Distinguishing between these conditions is crucial because they have different clinical courses and prognoses. EM is usually self-limited without significant long-term sequelae. Rarely, patients may experience recurrent or persistent EM, or severe EM that can lead to fluid or electrolyte losses, or ocular disorders such as conjunctival scarring or visual impairment.[1] By contrast, SJS/TEN causes skin detachment that often leads to sepsis and multiorgan failure, and is associated with significant morbidity and mortality. Mortality rates of 13%, 21%, and 39% have been reported for SJS, SJS/TEN, and TEN.[4] Therefore, early identification of SJS/TEN and withdrawal of the offending drug is extremely important.

Our patient presented with widespread cutaneous involvement without typical target lesions or raised lesions. Her rash was more concentrated on her face, neck, and trunk rather than her acral extensor surfaces. She also had involvement of at least two mucosal surfaces (eyes, tongue), and associated systemic symptoms (fever, malaise). Her history was notable for starting a new medication in the last couple weeks. Because her presentation was not completely clear and the morbidity/mortality of SJS/TEN is high, she was treated for possible SJS/TEN for a few days until her rash did not show any blistering, peeling, or desquamation, and her tongue ulcer returned positive for HSV. At that time her presentation was more consistent with EM. She was discharged from the hospital and restarted on her osimertinib a couple weeks later without incident.

REFERENCES

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