# Erythema multiforme in a child with Kawasaki disease

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***Key words:*** erythema multiforme; Kawasaki; mucocutaneous lymph node syndrome; streptococcal pharyngitis; streptococcus pyogenes; vasculitis.

## INTRODUCTION

Kawasaki disease (KD; previously known as *mucocutaneous lymph node syndrome*) is an acute febrile vasculitis predominately affecting children. Diagnosis of KD is based on well-known clinical criteria; however, various cutaneous presentations can make diagnosis difficult and delay treatment. Here we report a case of KD associated with erythema multiforme (EM) as a variation from the expected cutaneous manifestations of the disease. Additionally, we discuss a potential causal relation between *Streptococcus pyogenes* infection and the development of KD and EM in our patient.

*Abbreviations used:*

EM: erythema multiforme
KD: Kawasaki disease
SJS: Steven-Johnson syndrome

## CASE REPORT

A 6-year-old previously healthy female presented with 1-week history of sore throat and 4-day history of fever and targetoid eruption. She initially presented to her primary care provider with concern her rash was spreading, and throat swab found *Streptococcus pyogenes* pharyngitis. The patient was started on ceftriaxone. One day later, pedal edema and blisters developed prompting admission to the burn unit with concern for Steven-Johnson syndrome (SJS). She had not been on any medications previously but did receive an unknown antibiotic in Sri Lanka 5 weeks prior for mild diarrhea. Reportedly, the patient had received this same antibiotic in the past with no issues. As she had skin manifestations before administration of ceftriaxone and had only received 2 doses of ceftriaxone before onset of bullae, there was very low suspicion for reaction to ceftriaxone. Thus, this medication was continued throughout her hospitalization for treatment of streptococcal pharyngitis. Her parents denied sick contacts or other recent travel. She did not have skin pain/tenderness, pruritus, or arthralgias.

On admission, the patient was febrile, but otherwise vital signs were normal. Skin examination found generalized, scattered, dusky erythematous macules and patches, many of which were targetoid, on the torso and extremities (Fig 1). There was no desquamation. She had pedal edema and tense bullae on the bilateral feet. Additional physical examination findings were pertinent for strawberry tongue mucositis (Fig 2) and bilateral nonexudative conjunctival injection.

Punch biopsy of the left foot found an intraepidermal cleft and subtle vacuolar interface suggestive of EM. Mycoplasma and herpes simplex virus serologies were negative. Polymerase chain reaction for influenza/respiratory syncytial virus, parainfluenza, metapneumovirus, and adenovirus was negative. Erythrocyte sedimentation rate was elevated at 95. Echocardiogram found no coronary artery abnormalities.

Taken together, the clinical, laboratory, and histologic findings were consistent with a diagnosis of KD with EM. Fortunately, KD was suspected early in our patient's course, leading to initiation of aspirin and intravenous immunoglobulin. Soon after receiving treatment, the patient defervesced, and her cutaneous manifestations improved.

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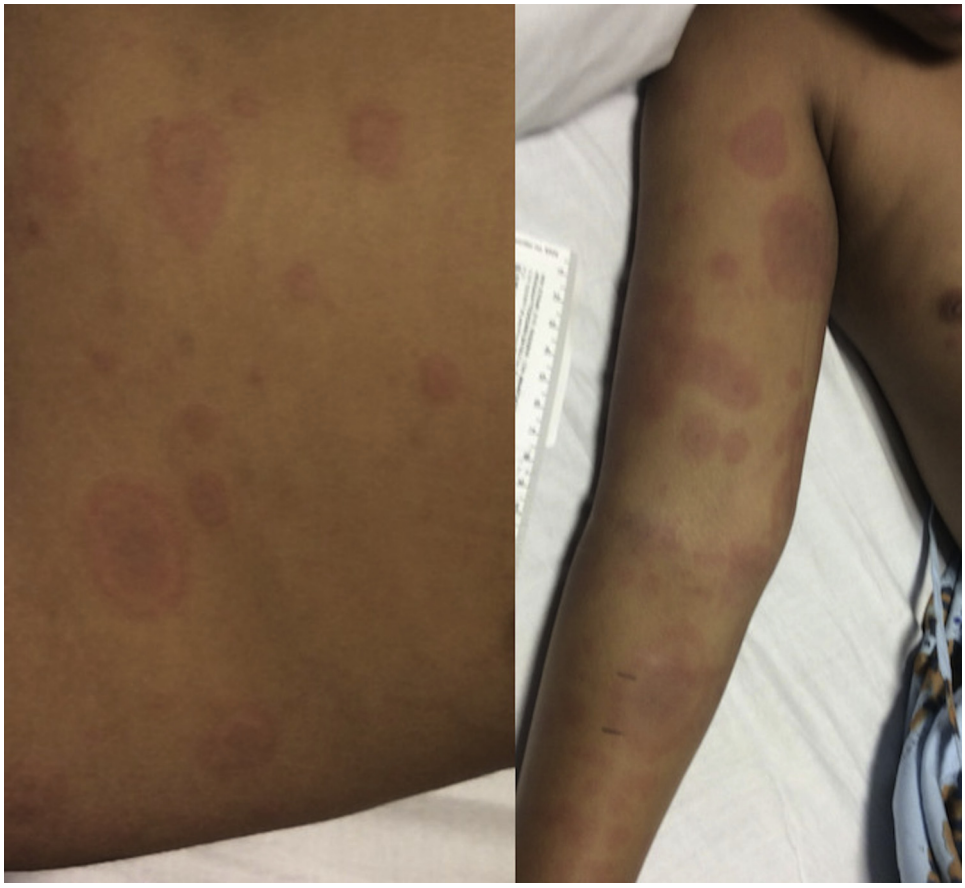

**Fig 1.** Targetoid erythematous macules and patches.

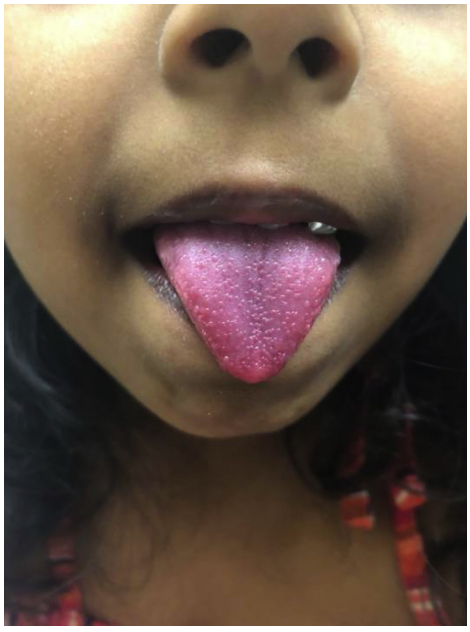

**Fig 2.** Strawberry tongue mucositis.

## DISCUSSION

KD is an acute vasculitis classically affecting Asian children less than 5 years old. Diagnosis is based on clinical criteria including fever for at least 5 days, plus 4 of 5 of the following criteria: rash, mucositis, conjunctivitis, peripheral extremity changes, and cervical lymphadenopathy.[1] Although laboratory studies are not considered in the diagnostic criteria, they may support KD diagnosis and include leukocytosis, anemia, thrombocytosis, elevated transaminases and acute-phase reactants, and pyuria. Cardiac sequelae are the leading cause of morbidity and mortality in children with KD, with thrombosis or aneurysms in the coronary arteries being the most common finding.[1] Thus, early diagnosis and initiation of treatment with aspirin and intravenous immunoglobulin is essential to prevent cardiac sequalea.[1]

Our patient fulfilled clinical criteria for KD with fever for 5 days, bilateral bulbar conjunctival injection without exudate, injection of oral and

**Table I.** Cases of erythema multiforme as a manifestation of Kawasaki disease

| Study | Year | Incomplete or classic KD | Patient age | Sex | Association |
|---|---|---|---|---|---|
| Demir et al[2] | 2016 | Classic | 5 y; 21 mo | Male; Female | None |
| Vierucci et al[3] | 2013 | Incomplete | 4 y | Male | *S pyogenes* |
| Eun et al[4] | 2010 | Classic | 16 mo | Male | None |
| Bitter et al[5] | 1979 | Classic | 22 mo | Female | None |

pharyngeal mucosa, edema of feet, and polymorphous exanthem. Although skin eruptions in KD are variable, a diffuse maculopapular rash involving the trunk and extremities is most common.[1] Our patient had targetoid lesions with interface changes on biopsy, consistent with a diagnosis of EM. To date, 4 cases of 5 patients have reported EM as a cutaneous manifestation of KD (Table I).[2-5] Additionally, there is a report of 3 patients with annular lesions as a cutaneous finding in KD.[6] Various morphologies have been implicated as the exanthem in KD, and awareness of the spectrum of cutaneous presentations is important in diagnosis.

In one case of incomplete KD, *S pyogenes* was implicated and postulated to trigger both KD and EM.[3] *Streptococcus* has been considered as an infectious etiology in EM and KD previously.[6,7] Our patient had a positive throat swab for *S pyogenes* at initial presentation, suggesting that her streptococcal infection may have played a role in the development of KD and the cutaneous findings.

Distinguishing EM clinically from drug eruptions (mainly Stevens-Johnson syndrome), vasculitis, or viral exanthems can be challenging. In this case, SJS was initially considered because the patient was exposed to an antibiotic 1 month before this episode and bullae developed. However, she reportedly tolerated prior administration of the same antibiotic, and the timeline was delayed for typical SJS. She did not have oral or genital involvement other than erythema and edema of the tongue. Furthermore, she had no desquamation or skin pain/tenderness, and, ultimately, the tense bullae on her feet were attributed to pedal edema.

Because KD is a clinical diagnosis, it is important to recognize the variable cutaneous presentations that include EM. In children, KD should be considered in the differential diagnosis of a patient with targetoid lesions, as delay in diagnosis and treatment of KD could lead to cardiac complications. Although it may be difficult to identify the inciting factor for EM, and there may be multiple triggers for EM, including infections and medications, a full skin examination and thorough review of systems should be performed in all patients. Additionally, a throat examination and culture, if warranted, should be considered in the workup of certain patients. Our case, in accordance with the case by Vierucci et al,[3] highlights the potential role of streptococci in mediating this disease. Thus, we recommend evaluating patients with findings of EM or KD for *S pyogenes* and initiating treatment when screening is positive.

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