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CLINICAL VIGNETTE

Urticaria Multiforme as a Cause of “Target Lesion” Rash

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Case Presentation

A previously healthy 2-year-old fully-vaccinated male presented with several days of target lesions. He had been seen 9 days earlier in an urgent care and diagnosed with acute otitis media while traveling in Hawaii. He was prescribed amoxicillin for the first time in his life and was tolerating it well until 2 days prior to the visit. At that point, he developed an intensely pruritic raised, erythematous, and amorphous rash consisting of 2-10 cm target lesions, which appeared and disappeared in assorted locations along with intermittent swelling of the fingers and toes. The rash appeared on his trunk and upper and lower extremities, sparing the palms and soles. He became febrile to 101.9, extremely irritable, fatigued, and refused to bear weight on his lower extremities. Two of the target lesions had dusky centers although most did not. No mucosal lesions were identified. He was diagnosed originally with erythema multiforme or serum sickness and was treated with oral diphenhydramine, as well as 2 mg/kg/day of prednisone.

The rash continued to spread and migrate over the next 2 days and was minimally responsive to the initial treatment. He was subsequently referred to dermatology and admitted briefly to the hospital for poor PO intake and to expedite the workup. Diagnostic tests including CBC, CMP, mycoplasma, parvovirus, and coccidiomycosis titers were normal, as was PCR analysis for 16 common respiratory viruses. CRP was markedly elevated at 12.4, which was 15 times greater than the upper limit of normal. A skin biopsy was ultimately performed and showed a mild perivascular inflammatory response with mast cells and rare eosinophils consistent with an urticarial reaction. There was no evidence of vasculitis and no findings suggestive of erythema multiforme on biopsy. He was discharged on diphenhydramine and slowly improved over the next 10 days.

Discussion

Urticaria multiforme, originally described as acute annular urticaria by Tamayo-Sanchez in 1997, can be a challenging diagnosis at initial presentation and can closely mimic the findings of erythema multiforme, vasculitis, and Lyme disease.¹⁻³ This can lead to a more extensive and costly workup and greater parental concern than is warranted for this benign self-limited condition. It occurs largely in infants and children under age 4, although it has been described in adolescents as old as 17 as well.⁴ It classically presents with large raised amorphous urticarial with central clearings, as well as

angioedema which self resolves after 2 weeks.^{1,4} Most affected patients experience swelling in the fingers and toes as well as intense pruritis.⁴ Fever was common, and usually short lived, lasting up to 3 days with no other systemic symptoms.¹ The rash in no cases was found to be blistering or scarring, nor are the mucosa involved.⁴ Dermatographism, although described in some case reports, was present in less than half of cases and not found in this patient.⁴ Although the original case report described the anti-diarrheal drug furazolidone associated with most cases, it is now typically seen after antibiotic therapy such as penicillins or sulfonamides, use of antipyretics, vaccine administration, or an antecedent illness such as a viral upper respiratory infection or pharyngitis.^{1,4-6} In this case, it is difficult to say if the reaction was due to the penicillin antibiotic or the antecedent otitis media, which prompted its use, although subsequent penicillin allergy skin testing was negative. Biopsies show typical findings of urticaria such as perivascular lymphocytic infiltrates and scattered eosinophils.²

Unlike with erythema multiforme, the lesions of urticarial multiforme are not fixed, do not blister, and are intensely pruritic.^{2,5,7} Whereas serum sickness may cause similar distal extremity swelling, it is typically painful, also causes fixed lesions, and typically lacks the angioedema and dermatographism which can help distinguish urticarial multiforme.^{2,7,8} Vasculitis, which is also typically in the differential due to the dusky appearance of both lesions is also less migratory, often blisters, and not itchy.^{2,7} The erythema migrans of classic Lyme disease will also not be pruritic, expand outward from a fixed initial area, not have the characteristic edema associated with urticarial multiforme, and the patient would be expected to have travel to a Lyme endemic area.⁹

Conclusion

Urticaria multiforme is a condition likely to be encountered by primary care physicians at first presentation, yet remains largely unrecognized. Although not a particularly common condition, with careful attention to history and physical exam findings, it can be rather easily distinguished from erythema multiforme, vasculitis, or serum sickness, which are its most common mimickers. Luckily by further educating our primary care physicians about this variation of urticaria and its unique clinical features, needless office visits, hospitalizations, skin biopsies, and parental worry can be easily avoided.

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