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Case Report

A case of urticaria multiforme with unusual presentation

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ABSTRACT

Urticaria multiforme is a condition which manifests as acute, polycyclic, annular oedematous pink plaques with an ecchymosis hue that is associated with acral edema. The condition is often misdiagnosed as erythema multiforme, serum-sickness-like reactions, or urticarial vasculitis. Author present a case of acute annular urticaria in a 3-year-old girl who presented with unusual clinical manifestations of the condition. Through this case report, Author aim to emphasize the wide range of morphologic manifestations that can be seen in urticaria multiforme. This can assist pediatric physicians to differentiate urticaria multiforme from other clinical dermatologic conditions and prevent misdiagnosis. A detailed case history and physical examination, along with relevant diagnostic tests can enable prompt and effective management of the condition.

Keywords: Acute annular urticaria, Childhood hypersensitivity reaction, Erythema multiforme, Hypersensitivity, Serum sickness reaction, Urticaria, Urticaria multiforme

INTRODUCTION

Urticaria Multiforme (UM) is a morphologic subtype of urticaria that usually affects infants and young children. It is a benign cutaneous hypersensitivity reaction that is characterized by acute, blanchable, transient, arcuate, and polycyclic urticarial plaques with a violaceous center. At times, the condition is associated with acral edema and fever.[1-3] Urticaria multiforme is also known as acute annular urticaria or acute urticarial hypersensitivity syndrome. It is commonly misdiagnosed as erythema multiforme, serum-sickness-like reactions, acute hemorrhagic edema of infancy, or urticarial vasculitis.[2,4]

Establishing the correct diagnosis of an urticarial rash in a pediatric patient is critical to minimize the unnecessary workup of a self-limiting condition and to appropriately recognize and evaluate other inflammatory conditions.[2,5,6] The presentation of urticaria multiforme is very characteristic to the condition, hence, prompt diagnosis can help us avoid extensive laboratory tests and admission to the hospital. Despite the severity and dramatic look of the skin lesions, children with urticaria multiforme have minimal systemic involvement.[3] Herein, Author report a case of urticaria multiforme with atypical presentation occurring in a 3-years-old girl, who is resistant to oral antihistamine, but responded very well to a short course of oral steroids. The report also aims to highlight the presence of distinctive morphologic manifestations observed in urticaria multiforme.

CASE REPORT

A 3-year-old girl, who was previously healthy, presented to the emergency department with a 2-days history of itchy rash on her trunk and extremities. The rash started on her palms and soles, eventually spreading to the rest of the body. Parents reported no recent illness or any drug histories. Patient was prescribed oral antihistamine and was discharged home. However, the rash persisted, progressing and worsening every day.

The parents brought the patient was brought to the dermatology clinic on the fifth day since her initial check-up. The patient's physical examination revealed generalized, 1 to 5 cm in diameter, polycyclic, annular wheals (some with violaceous centers) on the trunk and the extremities including her cheeks, chest, back, palms, and soles, which were associated with acral edema (Figure1-2). There was negative dermographism. The scalp, mucous membranes, genitals, joints, and lymph nodes were spared. Review of systems revealed low grade fever, loss of appetite, and malaise. As per the parents, the patient was up to date with her immunization schedule.

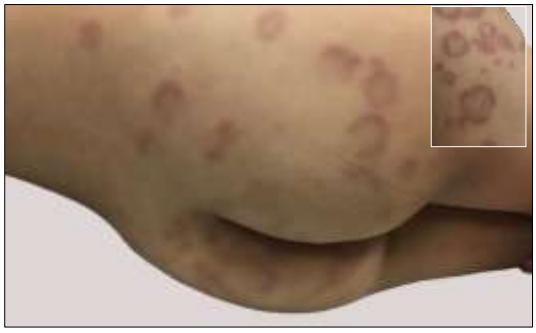

Figure 1: Multiple polycyclic, annular wheals with violaceous centers over the back extending to the buttock.

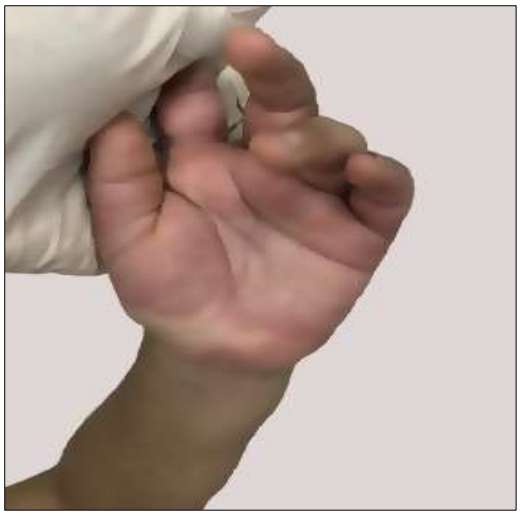

Figure 2: Acral swelling and erythema.

A preliminary diagnosis of erythema multiforme minor was proposed and a skin biopsy was taken. The patient was started on oral prednisolone 0.5 mg/kg/day for 5 days, oral antihistamine, in addition to topical mometasone furoate twice daily.

Laboratory workups, including a serum Complete Blood Count (CBC) with differential, Erythrocyte Sedimentation Rate (ESR), Liver Function Test (LFT), Renal Function Tests (RFT), and antinuclear antibody test (ANA), all were within the normal limit. Skin biopsy showed unremarkable epidermis with underlying dermal edema with few perivascular lymphocytes and scanty eosinophils suggestive of urticaria. The patient was seen after 5 days. In the follow-up visit, most of her lesions had resolved.

DISCUSSION

Urticaria Multiforme (UM) was first described by Tampayo-Sanchez et al, in 1997 as "acute annular urticaria".[3] In 2007, Shah et al, introduced the term "urticaria multiforme", as a benign cutaneous hypersensitivity reaction that is commonly confused with erythema multiforme.[2] It is a clinical variant of urticaria and presents as an acute onset of arcuate, annular, polycyclic, and erythematous plaques with central areas that are dusky, violaceous to brown colored in association with acral edema.[2,5] Although UM was reported in neonates and adults, it mostly affects children between 4 months and 4 years of age.[2,7-9] Suggested possible triggers include infections (e.g. pharyngitis, otitis media and upper respiratory infections), drugs (e.g., furazolidone, amoxicillin, nitrofurantoin), and immunizations.[2,3,9] Other associated findings include pruritus as the most prominent symptom, facial or acral angioedema, or both, dermographism, and fever.[2]

UM can be conveniently diagnosed using clinical evaluation alone, without need of any skin biopsy or extensive laboratory investigations.[1,2] Histologically, it is similar to urticaria demonstrating dermal edema with perivascular lymphocytic infiltrate and few eosinophils, as in this case.[4] Treatment includes discontinuation of any triggering and unnecessary drugs; use of a combination of systemic antihistamine is recommended over oral antihistamine alone, as the patient seems to benefit more from both systemic H1 antihistamine (e.g., cetirizine, diphenhydramine, or hydroxyzine) and an H2 antihistamine (e.g., ranitidine). Oral corticosteroids can be given in refractory cases.[2,5,9]

UM is underrecognized as a result of the paucity of reported cases in the literature mainly due to similarities between distinct clinical entities.[10] The differential diagnosis of such lesions include erythema multiforme (EM), Serum-Sickness-Like Reactions (SSLR), urticarial vasculitis, and acute hemorrhagic edema of infancy which have different pathogenesis, prognosis, and management.[1,2,6,9]

An overview and update of the clinical findings, etiologies, histopathology, management, and complications of urticaria multiforme mimickers is listed in (Tables 1).[4-6,10]

Erythema multiforme is the most common misdiagnosis. It is caused by virally induced cell-mediated immune reaction in genetically susceptible individuals; Herpes Simplex Virus (HSV) being the most frequent precipitant. EM presents and progresses in a similar manner as UM

and has relatively similar morphology, as in polycyclic lesions with ecchymosis centers. However, EM lesions present as fixed, painful, and burning lesions, and histologically show spongiotic pattern with skin necrosis and blistering. On the other hand, UM lesions are transient and pruritic, with positive dermographism and histologically show classical findings of a typical urticaria, revealing dermal edema and perivascular lymphocytic infiltrate with few eosinophils, as in this case.[1-3,9,10]

Table 1: Summary of urticaria multiforme mimickers.

	Urticaria multiforme	Erythema multiforme	Serum sickness-like reaction	Urticarial vasculitis	Acute hemorrhagic edema of infancy
Typical age of onset	4 months to 4 year	All ages: 50% under 20 years	18 months to 16 year	Adults	6 months to 2 year
Appearance of lesions	Polycyclic and annular oedematous pink plaques, with violaceous centers	Classic “target” lesion with purpuric or dusky, violaceous center that may blister. Middle ring of pallor and edema with an outer ring of erythema or blisters	Erythematous, annular, oedematous, urticaria-like plaques evolving to ecchymosis patches	Hives with dusky, purpuric centers	Annular and targetoid, erythematous and purpuric plaques
Typical location	Trunk, face, extremities	Dorsum of the hands, palms and soles, forearms, feet, face, elbows and knees, penis and vulva	Trunk, face, extremities	Trunk, extremities, face, lateral borders of hands and feet	Face, ears, distal extremities
Individual lesions	Transients (<24 h)	Fixed	Fixed (2-3wk)	Fixed	Fixed (1-3 week)
Duration of rash	Days to weeks	Days to weeks	Days to weeks	Days to weeks	1-3 week
Mucous membranes involvement	No	Yes	No	Yes	No
Facial or acral edema	Common	Rare	Less common	Common	Yes
Fever	Variable	Variable	High grade	Variable	Variable
Associated signs/ symptoms	Pruritus, dermographism	Mild pruritus or burning	Malaise, irritability lymphadenopathy, arthralgias, splenomegaly, refusal to walk	Variable	Malaise, Irritability
Inciting factors	Infection, medications, immunizations	Herpes simplex virus, other viral illness	Infection, medications, immunizations	Infections, autoimmune, neoplasms, drugs	Infection, medications, immunizations
Pathology	Dermal edema with variable inflammatory infiltrate	Exocytosis, spongiosis with epidermal necrosis. Necrotic keratinocytes are present at epidermal levels with an oedematous, papillary dermis with dilated capillaries	Dermal edema with mixed inflammatory infiltrate without vasculitis	Nuclear debris or fibrinoid alteration of the microvasculature with or without extravasation of erythrocytes	Leukocytoclastic vasculitis; direct immunofluorescence typically, negative
Type of hypersensitivity reaction	Unknown	Type IV	Type III		Type III
Treatment	Antihistamines; systemic corticosteroids if severe	Systemic glucocorticoids, control of herpes simplex may be considered	NSAIDs and antihistamines; systemic corticosteroids if severe	First-line therapy consists of H1 and H2 blockers plus NSAIDs	Supportive care

Also, serum-sickness-like eruptions can manifest as polycyclic wheals with angioedema like UM lesions. This disease is distinguished by its fixed skin lesions that can last days to weeks, with high fever, myalgia, arthralgia, and lymphadenopathy.[1,2,11] It is an immune complex-mediated (Type III) hypersensitivity reaction originally described in the setting of exposure to the cephalosporin cefaclor.[12-14] Histologically, it appears to be in the spectrum of urticaria.[11]

Urticarial vasculitis is a leukocytoclastic vasculitis, a condition that is rarely seen in children. Typically, the lesions observed in this condition last longer than 24 hours and associated with more pain than pruritus. These patients can also show other signs and symptoms such as fever, nephritis, arthralgia, and uveitis.[6,9]

Finally, acute hemorrhagic edema of infancy is a variant of cutaneous small vessels leukocytoclastic vasculitis, that is thought to be caused by an immune complex-mediated (Type III) hypersensitivity reaction in response to infection, vaccination, or medication intake characterized with acral edema, fever, and purpuric lesions in children younger than two years old. The lesions can assume an urticarial aspect but are purpuric and last longer than the ones seen in UM, leaving a residual hyperpigmentation.[6,9,15]

CONCLUSION

Urticaria multiforme may have an alarming appearance, but it is a benign, completely treatable condition. It is vital that pediatric physicians identify UM accurately and promptly, so as to reassure the patient and their family of the curable nature of the disease. Moreover, accurate diagnosis can also help in avoiding unnecessary hospital admissions and extensive diagnostic investigations.

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