Case Report

A case of urticaria multiforme with unusual presentation

Mohammad S. Alkhowailed*

Department of Dermatology, College of Medicine, Qassim University Buraydah, Qassim, Saudi Arabia

Received: 24 August 2019
Revised: 01 September 2019
Accepted: 27 September 2019

*Correspondence:
Dr. Mohammad S. Alkhowailed,
E-mail: m.alkhowailed@gmail.com

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 (Figure 1-2). 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.

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

UM can be conveniently diagnosed using clinical evaluation alone, without need of any skin biopsy or extensive laboratory investigations. Histologically, it is similar to urticaria demonstrating dermal edema with perivascular lymphocytic infiltrate and few eosinophils, as in this case. 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.

UM is underrecognized as a result of the paucity of reported cases in the literature mainly due to similarities between distinct clinical entities. 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.

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

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.

<table>
<thead>
<tr>
<th></th>
<th>Urticaria multiforme</th>
<th>Erythema multiforme</th>
<th>Serum sickness-like reaction</th>
<th>Urticarial vasculitis</th>
<th>Acute hemorrhagic edema of Infancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Typical age of onset</td>
<td>4 months to 4 year</td>
<td>All ages: 50% under 20 years</td>
<td>18 months to 16 year</td>
<td>Adults</td>
<td>6 months to 2 year</td>
</tr>
<tr>
<td>Appearance of lesions</td>
<td>Polycyclic and annular oedematous pink plaques, with violaceous centers</td>
<td>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</td>
<td>Erythematous, annular, oedematous, urticaria-like plaques evolving to ecchymosis patches</td>
<td>Hives with dusky, purpuric centers</td>
<td>Annular and targetoid, erythematous and purpuric plaques</td>
</tr>
<tr>
<td>Typical location</td>
<td>Trunk, face, extremities</td>
<td>Dorsum of the hands, palms and soles, forearms, feet, face, elbows and knees, penis and vulva</td>
<td>Trunk, face, extremities</td>
<td>Trunk, extremities, face, lateral borders of hands and feet</td>
<td>Face, ears, distal extremities</td>
</tr>
<tr>
<td>Individual lesions</td>
<td>Transients (&lt;24 h)</td>
<td>Fixed</td>
<td>Fixed (2-3wk)</td>
<td>Fixed</td>
<td>Fixed (1-3 week)</td>
</tr>
<tr>
<td>Duration of rash</td>
<td>Days to weeks</td>
<td>Days to weeks</td>
<td>Days to weeks</td>
<td>Days to weeks</td>
<td>1-3 week</td>
</tr>
<tr>
<td>Mucous membranes</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>involvement</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Facial or acral edema</td>
<td>Common</td>
<td>Rare</td>
<td>Less common</td>
<td>Common</td>
<td>Yes</td>
</tr>
<tr>
<td>Fever</td>
<td>Variable</td>
<td>Variable</td>
<td>High grade</td>
<td>Variable</td>
<td>Variable</td>
</tr>
<tr>
<td>Associated signs/symptoms</td>
<td>Pruritus, dermographism</td>
<td>Mild pruritus or burning</td>
<td>Malaise, irritability lymphadenopathy, arthralgias, splenomegaly, refusal to walk</td>
<td>Variable</td>
<td>Malaise, Irritability</td>
</tr>
<tr>
<td>Inciting factors</td>
<td>Infection, medications, immunizations</td>
<td>Herpes simplex virus, other viral illness</td>
<td>Infection, medications, immunizations</td>
<td>Infections, autoimmune, neoplasms, drugs</td>
<td>Infection, medications, immunizations</td>
</tr>
<tr>
<td>Pathology</td>
<td>Dermal edema with variable inflammatory infiltrate</td>
<td>Exocytosis, spongiosis with epidermal necrosis. Necrotic keratinocytes are present at epidermal levels with an oedematous, papillary dermis with dilated capillaries</td>
<td>Dermal edema with mixed inflammatory infiltrate without vasculitis</td>
<td>Nuclear debris or fibrinoid alteration of the microvasculature with or without extravasation of erythrocytes</td>
<td>Leukocytoclastic vasculitis; direct immunofluorescence typically, negative</td>
</tr>
<tr>
<td>Type of hypersensitivity reaction</td>
<td>Unknown</td>
<td>Type IV</td>
<td>Type III</td>
<td>NSAIDs and antihistamines; systemic corticosteroids if severe</td>
<td>First-line therapy consists of H1 and H2 blockers plus NSAIDs</td>
</tr>
<tr>
<td>Treatment</td>
<td>Antihistamines; systemic corticosteroids if severe</td>
<td>Systemic glucocorticoids, control of herpes simplex may be considered</td>
<td>NSAIDs and antihistamines; systemic corticosteroids if severe</td>
<td>First-line therapy consists of H1 and H2 blockers plus NSAIDs</td>
<td>Supportive care</td>
</tr>
</tbody>
</table>
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.\textsuperscript{2,11} It is an immune complex-mediated (Type III) hypersensitivity reaction originally described in the setting of exposure to the cephalosporin cefaclor.\textsuperscript{12-14} Histologically, it appears to be in the spectrum of urticaria.\textsuperscript{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.\textsuperscript{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.\textsuperscript{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.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by Review Board of Qassim University, Saudi Arabia

REFERENCES

