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Case Reports

Urticaria Multiforme in a 16-day-old Neonate

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Abstract Urticaria multiforme (UM), a relatively new defined disease, is a morphological subtype of urticaria seen in infants and young children, characterised by acute onset of annular or polycyclic wheals with dusky centres in fleeting duration, associated with acral oedema. We report a case of UM in a neonate diagnosed clinically, emphasizing the distinctive dermatologic manifestations of the disease.

Key words Erythema multiforme; Urticaria

Case Report

A 16-day-old Chinese female term neonate presented to the emergency department with few hours duration of skin rashes, beginning in the dorsum of both feet, then to the trunk and upper limbs including hands, while head and neck were spared. She had no systemic complaint. Her history was negative for any drug use, insect bite, topical cream application or injury. She was fed well on formula milk since birth. Pregnancy history of her mother was unremarkable with no evidence of congenital infection.

On admission to the paediatric ward, the patient was non-toxic and afebrile. The skin rashes appeared as well-demarcated, blanchable, irregularly shaped macules, papules, and plaques, over the trunk and the limbs. Oedema over hands and feet was also noted (Figure 1). The mucosal membrane was intact. No facial/joint swelling, no lymphadenopathy or hepatosplenomegaly was found. We kept close observation on her without prescribing any medications: neither oral antihistamines nor topical cream.

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The patient had remained clinically well despite having rashes progressively enlarged over the next few hours, which evolved into large urticarial patches forming polycyclic wheals over limbs, some with light central clearing but without target-like lesions. Complete recovery was detected in the next morning, within 24 hours after the onset of rashes.

The nasopharyngeal swab did not isolate any common respiratory viruses including influenza viruses A and B, parainfluenza viruses 1, 2 and 3, enterovirus, echovirus, adenovirus and respiratory syncytial virus. The C-reactive protein, liver and renal function tests were normal but the

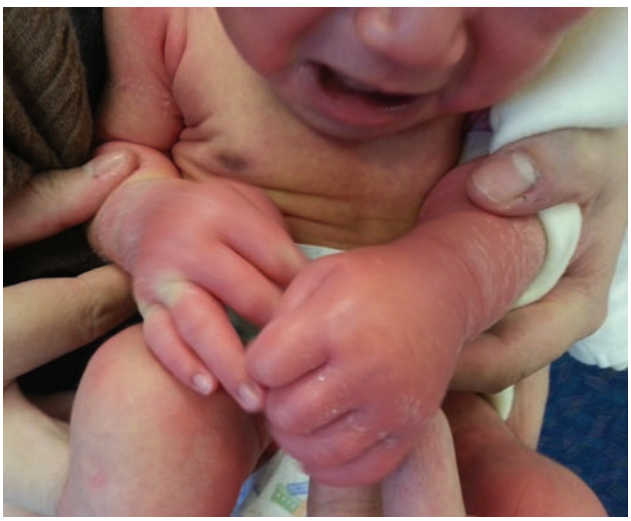

Figure 1 Urticarial rashes and acral oedema.

specimen for complete blood count was unfortunately clotted. The urine test strip analysis showed no proteinuria or haematuria.

The patient was diagnosed clinically to have UM. She had flawless resolution of all lesions and was discharged two days after admission.

Discussion

UM, a relatively new disease, was first defined by Shah et al in 2007 to replace the old term "acute annular urticaria" as a clinically distinct subtype of acute urticaria with evanescent annular or polycyclic wheals in association with angioedema of the face, hands and feet.[1] Being more common in children of four months to four years of age with neonatal involvement also reported,[2-4] UM is confirmed using the diagnostic criteria suggested by Shah et al which includes typical annular and polycyclic morphology and configuration to urticarial lesions; duration of individual lesions of less than 24 hours; dermatographism; angioedema but not arthralgia or arthritis; favourable response to antihistamines; and modest but not-significant elevations in acute-phase reactants.[4] Believed to be an immunoglobulin E dependent or independent allergic hypersensitivity reaction,[2] infections by human herpes virus 6, group A streptococcus, adenovirus, and mycoplasma, drugs like antibiotics such as amoxicillin, cephalosporins, and macrolides as well as vaccinations can be the potential triggers of UM.[3,4] Apart from rashes which usually last less than 24 hours, mild systemic symptoms like low grade fever may be present.

Treatment of UM is exclusively symptomatic. The rashes have favourable response to antihistamines, though their

Table 1 Distinguishing features of urticarial multiforme, erythema multiforme, and serum-sickness-like reaction[4]

Feature	Urticaria Multiforme	Erythema Multiforme	Serum-Sickness-Like Reaction
Appearance of individual lesions	Annular and polycyclic wheals with central clearing or ecchymotic centres	Classic target lesions with annular lesions with purpuric or dusky, violaceous center (may blister), middle ring of pallor and oedema, outer ring of erythema or blisters	Polycyclic urticarial wheals with central clearing; may appear purpuric
Location	Trunk, extremities, face	Involvement of palms, soles common	Trunk, extremities, face, lateral borders of hands and feet
Duration of individual lesions	<24 hours	Days to weeks	Days to weeks
Fixed lesions	No	Yes	Yes
Total duration of rash	2-12 days	2-3 weeks	1-6 weeks
Mucous membrane involvement	Oral oedema common, no erosions or blisters	May see oral erosions or blisters of lips, buccal mucosa, and tongue; rarely involves conjunctival, nasal, or urogenital mucosa; usually involving only a single site	Oral oedema common, no erosions or blisters
Facial or acral oedema	Common	Rare	Common
Dermatographism	Yes	No	No
Fever	Occasionally, low-grade	Occasionally, low-grade	Prominent, high-grade
Associated symptoms	Pruritis	Mild pruritis or burning	Myalgias, arthralgias, lymphadenopathy
Common triggers	Antibiotics, immunisations, viral illness	Herpes simplex virus, other vial illness	Antibiotics
Treatment	Discontinue any new or unnecessary antibiotics or medications; combinations of H1 and H2 antihistamines may be helpful; systemic steroids can be helpful in more recalcitrant cases	Supportive care; early institution of systemic steroids can sometimes be helpful	Discontinue any new antibiotics or medications; H1 and H2 antihistamines; supportive care; consider systemic corticosteroids

use in neonates or small infants is questionable,[2] justifying us of prescribing no medications to our neonatal patient. Systemic corticosteroids are rarely required except in the most severe cases refractory to combination antihistamines treatment and should be avoided if underlying infection is suspected.[4] Topical therapy by antipruritic agents can also be considered.[4] Suspected culprits of UM such as infections should be treated and triggering medications should be removed. Should UM be diagnosed by history and physical examinations in accordance to the diagnostic criteria, extensive laboratory investigations or even skin biopsy are unnecessary. UM is a self-limiting disease of duration 2 to 12 days with no residual of any skin lesions.[1]

As a result of paucity of reported cases in the literature, not to mention local Hong Kong data, probably related to similarities shared with other differential diagnoses of annular rashes, namely erythema multiforme (EM) and less often serum-sickness-like reaction,[5] UM is commonly underdiagnosed. Table 1 shows differentiating clinical features among these three clinical entities in terms of pathogenesis, prognoses and management strategies.

UM is more prevalent among young children while EM is rare in infants among which 50% of cases are under 20 years old.[2] The distinct ecchymotic or dusky centre in UM can mimic the pathognomonic targetoid papule or bull's eye in EM that often shows a central vesicle or necrotic crust.[6] Oral and conjunctival mucosal involvement in terms of erosions or blisters are common in EM while UM shows no skin necrosis or blistering.[4] UM has dermatographism and angioedema of face, hands and feet representing subcutaneous vascular leak with resultant dermal oedema, which are uncommonly found in both EM and serum-sickness-like reaction. Our patient had urticarial rashes appeared first in feet, spreading to trunk and then upper limbs, with oedema over hands and feet. The evanescent nature of the UM rash is similar to any urticarial eruption which lasts from minutes to hours or even days with normal skin after rash resolution, featured in our patient who had achieved full recovery within 24 hours of onset of rashes. Rather, the lesions of EM and serum-sickness-like reactions last for days to weeks and are fixed.[1,4-6] Affected children of UM are usually non-toxic and so was our patient. On the contrary, EM patients often complain of burning and pain in their skin lesions whereas in serum-sickness-like reaction, fever, arthralgia, myalgia and lymphadenopathy are the chief complaints.[1] Both UM and EM share similar causes or precipitating agents; yet, we could not identify any in our case.

Skin biopsies of UM are indistinct from other types of acute urticaria. UM shows dermal oedema with a perivascular lymphocyte infiltrate with few intermingled eosinophils.[2] Histology of EM, dissimilar from UM, consists of exocytosis and spongiosis in conjunction with varying degrees of epidermal necrosis, while biopsy findings of serum-sickness-like reaction are consistent with acute urticaria but without evidence of vasculitis.[2] Skin biopsy, nevertheless, is not a prerequisite to confirm UM.

Conclusion

UM, a newly defined disease, is well documented in infants and toddlers.[7] EM and serum-sickness-like reaction are the differential diagnoses. The important distinctive features of UM are the predominance in young infants, the fleeting duration of skin rashes, the presence of dermatographism and the angioedema of face, hands and feet. Paediatricians should not only be aware of its differential diagnoses but also be able to confirm the diagnosis clinically so as to avoid unnecessary investigations. Parents should be reassured about the alarming presenting symptoms in UM – benign and self-limiting.

Declaration of Interest

None

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