Cutaneous eruption in neonate with congenital heart defect

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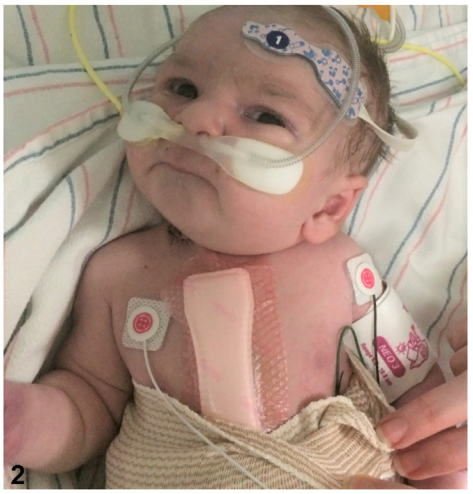

A 10-day-old infant born with hypoplastic left heart syndrome developed an urticarial eruption. He was started on prostaglandin E1 (PGE1) at birth and failed attempts to wean treatment secondary to cardiogenic shock. He also required extracorporeal membrane oxygenation (ECMO) and a dose increase of PGE1 via a peripheral intravenous line infusion. The eruption developed shortly after the PGE1 dose increase. Physical examination revealed ill-defined, bright pink, blanchable patches on the left forehead and periocular skin and polycyclic, bright red, edematous plaques without overlying scale on the left chest and upper arm (Fig 1). This eruption was transient, migratory, and asymptomatic.

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Question 1: What is the most appropriate management of this condition?

A. Diphenhydramine

B. Discontinuing PGE1 immediately

C. Hydrocortisone cream

D. Methylprednisolone

E. No acute intervention is necessary

Answer:

A. Diphenhydramine — Incorrect. PGE1-associated migratory polycyclic eruptions may appear similar to acute urticaria. In all reported cases of PGE1-associated migratory polycyclic eruptions (including our case), however, the eruption did not respond to antihistamines. Additionally, the PGE1 eruption was dose dependent and without notable pruritis, further differentiating it from acute urticaria.

B. Discontinuing PGE1 immediately — Incorrect. Discontinuing PGE1 immediately is not appropriate as it is a medically necessary drug. Its benefits of preventing cardiovascular compromise until corrective surgery significantly outweigh the risk of the PGE1-associated migratory polycyclic eruption, which has no systemic complications.[1]

C. Hydrocortisone cream — Incorrect. One previously reported case of a PGE1-associated migratory polycyclic eruption was not responsive to the use of topical hydrocortisone.[2]

D. Methylprednisolone — Incorrect. In all reports of PGE1-associated migratory polycyclic eruptions, including our case, the eruption did not respond to systemic steroid treatment.

E. No acute intervention is necessary — Correct. No acute intervention is necessary with PGE1-associated migratory polycyclic eruptions. This eruption will clear within days after discontinuation of PGE1, as seen in our case (Fig 2).[2]

Question 2: What will histopathologic analysis of this condition demonstrate?

A. Leukocytoclastic vasculitis with a typically negative direct immunofluorescence

B. Neutrophilic dermal infiltrate with marked leukocytoclasia and papillary edema

C. Perivascular lymphocytic infiltrate with scattered eosinophils and focal overlying vacuolar interface change

D. Sparse mononuclear infiltrate

E. Vacuolar alteration at the dermoepidermal junction with a superficial perivascular and periadnexal lymphocytic predominant infiltrate

Answer:

A. Leukocytoclastic vasculitis with a typically negative direct immunofluorescence — Incorrect. This histopathologic finding can be seen in acute hemorrhagic edema of infancy.[1]

B. Neutrophilic dermal infiltrate with marked leukocytoclasia and papillary edema — Incorrect. This histopathologic finding occurs in Sweet syndrome.[1]

C. Perivascular lymphocytic infiltrate with scattered eosinophils and focal overlying vacuolar interface change — Incorrect. This histopathologic finding occurs in morbilliform drug eruption.

D. Sparse mononuclear infiltrate — Correct. Histopathology demonstrates a very sparse mononuclear infiltrate in the dermis which is consistent with urticaria.[3] Clinico-pathologic correlation (specifically the history of PGE1 administration) is needed for diagnosis of this condition.

E. Vacuolar alteration at the dermoepidermal junction with a superficial perivascular and periadnexal lymphocytic predominant infiltrate — Incorrect. This histopathologic finding can be found in neonatal lupus erythematosus.[4]

Question 3: What is the most probable mechanism of action of this eruption?

A. Activating KIT mutation leading to increased mast cell growth and maturation

B. Binding of drug-derived antigen to mast cell and basophil IgE receptors

C. Deficiency of the C1 inhibitor resulting in generation of bradykinin

D. Histamine-mediated vasodilation and capillary permeability

E. Type III hypersensitivity reaction with deposition of immune complexes

Answer:

A. Activating KIT mutation leading to increased mast cell growth and maturation — Incorrect. This mutation is found in mastocytosis, presenting with flushing, itching, and monomorphic reddish-brown macules.

B. Binding of drug-derived antigen to mast cell and basophil IgE receptors — Incorrect. This describes simple acute allergic urticaria. PGE1 urticaria is nonallergic as the intensity of eruption occurs in a dose-dependent manner.[3,5] There is a strong temporal relationship between rash presentation and PGE1 administration. Most cases occur due to increased PGE1 doses after transition to ECMO. Increased PGE1 dosing is thought to be due to ECMO-related blood volume expansion, decreased pulmonary metabolism, and bypass-induced endothelial damage.[2,5]

C. Deficiency of the C1 inhibitor resulting in generation of bradykinin — Incorrect. Hereditary angioedema occurs via this mechanism, presenting with asymptomatic swelling of the deep dermal or subcutaneous tissues.

D. Histamine-mediated vasodilation and capillary permeability — Correct. The proposed mechanism involves nonallergic urticaria, whereby PGE1 triggers direct degranulation of histamine from mast cells and basophils, causing vasodilation and increased capillary permeability.[2,3] Pretreatment with antihistamines can partially suppress the rash, suggesting it is unlikely the sole mediator.[2] Other proposed mechanisms include the coagulation cascade and increased levels of neuropeptide substance P.[2] Hypoxic events may also play a role in color changes, but the exact mechanism remains unknown.[5]

E. Type III hypersensitivity reaction with deposition of immune complexes — Incorrect. This is seen in urticarial vasculitis, presenting with painful and pruritic plaques often associated with angioedema, purpura, and arthralgias. It also typically has a longer duration than common urticaria.

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Abbreviations used:

ECMO: extracorporeal membrane oxygenation
PGE1: prostaglandin E1

Conflicts of interest

None disclosed.

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