Case Report/Case Series

Eruptive Hypomelanosis
A Novel Exanthem Associated With Viral Symptoms in Children

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Several skin eruptions—Gianotti-Crosti syndrome (GCS), pityriasis rosea (PR), asymmetric periflexural exanthem, eruptive pseudangiomatosis, papular-purpuric-gloves-and-socks-syndrome—are suspected to be caused by viruses because of a predictable course of clinical events with a prodromal phase, primary lesions with or without secondary lesions in single or successive eruptions, and spontaneous resolution; epidemiological characteristics; and histopathological and virological findings. Differing clinical presentations of viral exanthems and virally triggered (“paraviral”) eruptions need to be recognized in order to appropriately evaluate, diagnose, and counsel patients. Although no specific treatment for many viral exanthems is known, recognition of exanthems allows clinicians to differentiate such from other treatable cutaneous diseases.

Nine children aged 2 to 9 years developed eruptions of hypopigmented macules following coryzal symptoms. Other diagnostic considerations, such as pityriasis alba, pityriasis versicolor, and progressive macular hypomelanosis, were excluded. This novel clinical presentation, eruptive hypomelanosis, may represent a paraviral exanthem with a prodromal coryzal phase, sudden eruption of fairly monomorphic lesions, and predictable time course with spontaneous resolution.

Report of Cases

Description of the Case Series
Six of the 9 patients were boys, and 3 were girls (Table). Their average age was 4.3 years. All children had Fitzpatrick skin types IV to V. Only 1 child had a history of contact with 2 other children with similar skin eruptions. One girl had history of allergic rhinitis, and another girl had a family history of atopic dermatitis and urticaria.

The time between prodrome and onset of eruption ranged from 5 days to 2 weeks (median, 8.5 days). The onset of eruption was sudden (within 3-4 days) in 7 children, with 1 child having successive eruptions in 1 week, and 1 child having spread of successive eruptions over 10 days.

Clinical Findings
The common sites of involvement were the arms, forearms, and thighs in 6 children, the knees in 3 children; and elbows, dorsa of hands, legs, and dorsa of the feet in 2 children. The distribution of the eruption was symmetrical for all 9 children. None of the children had pruritus. Nearly all lesions were hypopigmented macules without erythema. The macular lesions were 3 to 8 mm in diameter with fairly distinct margins.

Five children had systemic involvement with axillary lymphadenitis (in 4) and an inflamed throat (in 2). The time between onset and resolutions of the eruption ranged from 2 to 8 weeks (median, 24.5 days).

Patient 1
This child, who was younger than 5 years, presented with a sudden appearance of nonpruritic eruptions over her forearms and thighs. She experienced coryza 2 weeks prior to the eruption. There was no personal or family history of atopy. Drug history was unremarkable.

Examination revealed monomorphic, circular, hypopigmented, and similar-sized macules with fine powdery scales prominently over the patient’s forearms (Figure 1) and on her thighs. Wood’s light examination revealed no fluorescence. Her throat was inflamed, and the cervical lymph nodes were moderately enlarged. Chest and abdominal examinations revealed no abnormality.
nosis became faint over the next 3 weeks without any scales. The hypomelanosis had almost stopped progressing. The hypomelanosis in the next 3 wk.

Table. Clinical Summary of 9 Patients With Suspected Eruptive Hypomelanosis

<table>
<thead>
<tr>
<th>Patient, No./Age, y/Sex</th>
<th>Time Between Prodrome and Onset of Eruption</th>
<th>Distribution of Skin Lesions</th>
<th>Systemic Involvements</th>
<th>Treatment</th>
<th>Time Course of the Eruption</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/≤5/F</td>
<td>2 wk</td>
<td>Forearms and thighs, symmetrical</td>
<td>Nil</td>
<td>Nil</td>
<td>Spontaneous arrest of progression in 3 wk and gradual fading of hypomelanosis in the next 3 wk</td>
</tr>
<tr>
<td>2/≤5/M</td>
<td>2 wk</td>
<td>Cheeks, arms, forearms, dorsa of hands, pubic areas, thighs, legs, dorsi of feet symmetrical</td>
<td>Throat inflamed, marginally enlarged bilateral mandibular, axillary, and inguinal lymph nodes</td>
<td>Emollients</td>
<td>Spontaneous arrest of progression in 2 wk and gradual fading of hypomelanosis in the next 3 wk</td>
</tr>
<tr>
<td>3/≤5/M</td>
<td>1 wk</td>
<td>Forearms and thighs, symmetrical</td>
<td>Nil</td>
<td>Nil</td>
<td>Spontaneous arrest of progression in 2 wk</td>
</tr>
<tr>
<td>4/5-10/M</td>
<td>1 wk</td>
<td>Arms and forearms, symmetrical</td>
<td>Bilateral axillary lymphadenitis</td>
<td>Clotrimazole cream, emollients</td>
<td>Spontaneous arrest of progression in 4 wk and gradual fading of hypomelanosis in the next 4 wk</td>
</tr>
<tr>
<td>5/5-10/M</td>
<td>5 d</td>
<td>Arms, forearms, thighs, knees, legs, symmetrical</td>
<td>Throat inflamed</td>
<td>Ketoconazole cream, emollients</td>
<td>Spontaneous complete resolution in 2 wk</td>
</tr>
<tr>
<td>6/5-10/F</td>
<td>10 d</td>
<td>Arms, thighs, symmetrical</td>
<td>Bilateral cervical, axillary, and inguinal lymphadenitis</td>
<td>Emollients</td>
<td>Spontaneous complete resolution in 3 wk</td>
</tr>
<tr>
<td>7/≤5/M</td>
<td>2 wk</td>
<td>Elbows and knees, sparsely on arms and thighs, symmetrical</td>
<td>Nil</td>
<td>Emollients</td>
<td>Spontaneous complete resolution in 2 wk</td>
</tr>
<tr>
<td>8/5-10/M</td>
<td>1 wk</td>
<td>Elbows, dorsi of hands, knees, dorsi of feet, symmetrical</td>
<td>Nil</td>
<td>Emollients</td>
<td>Spontaneous arrest of progression in 2 wk and rapid fading of hypomelanosis in the next 2 wk</td>
</tr>
<tr>
<td>9/≤5/F</td>
<td>1 wk</td>
<td>Extensor surfaces of arms, flexor surfaces of forearms, symmetrical</td>
<td>Bilateral axillary lymphadenitis</td>
<td>Emollients</td>
<td>Spontaneous near-complete resolution in 2 wk</td>
</tr>
</tbody>
</table>

No active intervention was initiated. Three weeks later, the skin lesions had almost stopped progressing. The hypomelanosis became faint over the next 3 weeks without any scales.

Patient 2

This boy had sudden onset of skin lesions over his face and extremities 2 days prior to presenting for care and had experienced coryza and low-grade fever 2 weeks prior to presentation. He had no history of similar eruptions and had no personal or family history of atopy. There was no antecedent drug history. Examination revealed an otherwise healthy child with round, similar sized, margined, and hypopigmented macules with slight scaling over his face and all extremities. The macules started at his pubic area and upper thighs. Lesions then progressed downwards to his lower thighs, knees, legs, and dorsa of feet. Additional lesions erupted on his arms, forearms, and dorsa of hands. His cheeks were involved up to the jaw line (Figure 2). Early lesions had minimal scaling. Subsequent lesions were only macules.

Bilateral submandibular, axillary, and inguinal lymph nodes were marginally enlarged. The patient’s throat was inflamed. Other systematic examinations revealed no abnormalities. Wood’s light examination revealed no evidence of pityriasis versicolor (PV).

White petrolatum jelly was prescribed. The eruption spontaneously stopped progressing 2 weeks after the onset. The residual hypomelanosis completely remitted over the next 3 weeks.

Additional clinical photographs from our work as submitted in the original version of the manuscript are shown in the Supplement as eFigures 1, 2, 3, and 4.

Investigations

For all 9 patients, results from complete blood cell counts were normal except for patients 2 and 9, who showed slight lymphocytosis. Findings from blood glucose, urinalysis, and liver function tests revealed no abnormality. Results from venereal disease research laboratory tests and human immunodeficiency virus antibodies were negative. Wood’s lamp examination and lesional skin scrapings for potassium hydroxide (KOH) preparation smear were performed for all patients without evidence of PV. Skin biopsy was possible only in patient 7 (Figure 3). The biopsy, which was performed 3 days after onset of the eruption, revealed slight orthohyperkeratosis, slight epidermal spongiosis, and nonspecific upper dermal patchy inflammatory lymphocytic infiltrates. There was no evidence of fungal or yeast infection.
Discussion

The term eruptive hypomelanosis conveys the sudden onset, in single or successive eruptions, of hypopigmented macules that was observed in our patients. The differential diagnoses included pityriasis alba (PA), PV, progressive macular hypomelanosis, and postinflammatory hypopigmentation. The lesions were extrafacial, symmetric, of very similar sizes, and were of acute onset without any personal or family history of atopic diathesis. None of our patients had applied topical corticosteroids. Postinflammatory hypopigmentation owing to atopic dermatitis or as a variant of PA with extrafacial involvement would have relatively ill-defined margins and be more persistent than the disease in our patients; therefore, those 2 diagnoses are unlikely.5 However, owing to the scaliness and the biopsy findings of spongiosis with a lymphocytic infiltrate, the hypopigmentation seen in our patients is likely to be analogous to the postinflammatory hypopigmentation seen in PA. Pityriasis versicolor is less common before the initiation of sebaceous gland function in puberty. When PV does occur prior to puberty, it is more likely to have atypical distributions, such as the face, neck, and arms. Hypopigmented lesions of PV tend to be sharply demarcated, can be fairly monomorphic, and may persist for months after effective treatment. However, the negative results from KOH examinations of scrapings from scaly lesions in our patients render this diagnosis unlikely.

Patients 1 and 5 used topical antifungal agents effective against Malassezia species, which did not halt the progress of the disease. The rate of appearance of several new lesions in healthy individuals at the areas not preferential for PV was striking. The diameters of individual lesions in our patients were fairly uniform, unlike lesions PV, which have varying sizes. Thus, PV seems very unlikely for our patients. For these same reasons, pityriasis versicolor alba7 is also unlikely.

Progressive macular hypomelanosis, which may occur in adolescent children, is unlikely in our patients because it is chronic and typically occurs in adults and lasts for months to years.8,9 Spontaneous remission within a few weeks was seen in all patients. Lesions in progressive macular hypomelanosis are typically ill-defined, whereas most lesions in our patients had fairly distinct margins. Eruptive hypomelanosis may be related to a viral infection because of a prodromal coryzal phase 1 to 2 weeks preceding the lesions, the eruptive nature with 1 or more successive eruptions of lesions, the fairly uniform sizes of lesions, and spontaneous resolution without action intervention.

Interestingly, patient 2 had a distribution akin to GCS, another paraviral exanthem. Although the lesions were acrolocated and facial, this patient lacked the typical papulovesicular element that is essential for the diagnosis of GCS. Hypomelanotic eruptions as primary lesions are not known in GCS.10,11 Secondary hypomelanosis in some children with GCS occurs only after the primary papulovesicular eruptions. Thus, GCS is not an appropriate label for the overall clinical picture of patient 2. However, for patients 1, 2, 3, and 6, who did not have scaling, this is likely to be related to prior inflammation, which
might be part of an acral dermatitis as in GCS-like viral eruptions. Unfortunately, the necessary resources for complete evaluation of the associated viruses, such as hepatitis B virus, Epstein-Barr virus, and the enteroviruses, were not available.

Another young girl (patient 6) presented with eruptive, hypomelanotic, symmetrical, and well-demarcated macules on periaxillary areas extending to the extensor aspect of the arms and extensor aspect of the thighs, with fine scaling at few places. The distribution was similar to that of PR, another paraviral exanthem. However, there was no herald plaque and no collarette scales (although herald patch is not necessary for a diagnosis of PR). There was no typical distribution of lesions orientating along the skin creases—previously described as the Christmas-tree pattern—on the trunk. Postinflammatory hypopigmentation may be seen after resolution of PR. However, hypomelanotic eruptions as primary lesions are not known in PR. Thus, PR was an inappropriate label for this patient. (Unfortunately, however, the authors do not have clinical photographs of patient 6 to present herein.)

For PR in dark-skinned children, hypopigmented lesions, usually following popular ones with involvement of the arms and legs, have been described. These PR eruptions run a shorter course. In another study, of 113 Indian children with hypopigmentory disorders, 4 were diagnosed as having PR, which involved the extremities as well as the trunk. The likelihood of developing postinflammatory hypopigmentation after PR is higher for dark-skinned patients. However, the first and foremost clinical manifestation was hypopigmentary macules without other intervening eruptions. Scaling was seen on some of the hypopigmented macules of this exanthema, but the hypopigmentation was evident before the scaling was clinically visible.

Conclusions

Eruptive hypomelanosis is likely to be a primary viral exanthem in its own right, like PR. The possibility of postinflammatory hypopigmentation as one of the underlying causes should be investigated further. Considering that the anatomical clinical distribution of the hypomelanotic eruptions in patients 2 and 6 mimic the paraviral exanthems GCS and PR, respectively, it seems that EI is a paraviral exanthem similar to GCS and PR. If similar cases are detected by other dermatologists in the future, acute and convalescent sera can be tested in parallel to detect rises of the IgG titers against a panel of viruses. Viral DNA could also be detected by polymerase chain reaction in the plasma, peripheral blood mononuclear cells, and lesional biopsy specimens. The criteria for sequence based identification by Fredericks and Relman can then be applied to substantiate whether the associations are incidental, genuine, casual, or causal. Lesional biopsy specimens could be obtained for histopathological and immunohistochemical studies. Epidemiology studies could be considered to determine the demographics of these patients, trace contact histories, elucidate association with seasonal and climate changes, and to detect temporal and spatial-temporal clustering. Eruptive hypomelanosis may be an underrecognized clinical form of paraviral exanthem, likely to be on a spectrum with GCS and PR.