Managements of the less common paraviral exanthems in children – asymmetrical periflexural exanthem, papular-purpuric gloves and socks syndrome, eruptive pseudoangiomatosis, and eruptive hypomelanosis

Chuh A.¹, Fölster-Holst R.², Zawar V.³
¹School of Public Health and Primary Care, The Chinese University of Hong Kong and Prince of Wales Hospital, Shatin, Hong Kong
²Universitätsklinikum Schleswig-Holstein, Campus Kiel, Dermatologie, Venerologie und Allergologie, Germany
³Department of Dermatology, Godavari Foundation Medical College and Research Center, DUPMCJ, India

Summary

Although all paraviral exanthems in children are self-remitting, clinicians should be aware of the underlying viral infections leading to complications. Many reports covered the commonest paraviral exanthems, namely pityriasis rosea and Gianotti-Crosti syndrome. We reviewed here the managements of the less common paraviral exanthems in children.

For asymmetrical periflexural exanthem/unilateral laterothoracic exanthem treatments should be tailored to the stages of the rash. For children with papular purpuric gloves and socks syndrome, important differential diagnoses such as Kawasaki disease should be excluded. Where this exanthem is related to parvovirus B19 infection, the risk of aplastic reticulocytopenia should be monitored for. Clinicians should also be aware of ongoing infectivity of parvovirus B19 infection upon rash eruption, and possible exposure to pregnant women.

For children with eruptive pseudoangiomatosis, important differential diagnoses should be excluded. For eruptive hypomelanosis, the prime concern is that virological investigations should be contemplated where available, as there exists only clinical and epidemiological evidence for this novel exanthem being caused by an infectious microbe.

Key words

Acyclovir, Gianotti-Crosti syndrome, human herpesvirus-7, human herpesvirus-6, papular acrodermatitis, pityriasis rosea.

Paraviral exanthems (PE) are skin eruptions suspected to be caused by viruses (26). The commonest PE are pityriasis rosea (PR), Gianotti-Crosti syndrome (GCS, also known as papular acrodermatitis of childhood), asymmetrical periflexural exanthem (APE) (29), unilateral laterothoracic exanthem (ULE) (5, 6), papular-purpuric gloves and socks syndrome (PPGSS) (25), eruptive pseudoangiomatosis (EP) (7), and eruptive hypomelanosis (EH) (9, 11, 30).

APE could be the same or a very similar disease as ULE (Taïeb A., personal communication, 2015), with the latter nomenclature likely to be more appropriate owing to the valid description of the rash distribution (Bodemer C., personal communication, 2015). Currently, many investigators and clinicians believe that APE and ULE are synonyms. Unilateral mediothoracic exanthem (UME) is likely to be a rare variant of ULE owing to clinical manifestations and lesional histopathological changes (10, 16). EH is a novel paraviral exanthem (9, 11, 30).

Reports are proliferating for the managements of PR and GCS. It is usually considered
that the management of the other PE would be only symptomatic relief, while waiting for spontaneous remission. Important management parameters can be omitted. In this article, we hope to cover the non-generic aspects on the managements of the less common PE.

**Asymmetric periflexural exanthem / unilateral laterothoracic exanthem**

ULE (5, 6), APE (29), and their rare variant UME (10, 16) are likely to be the same or very similar exanthems. Almost all of the 300 reported patients were young children. Up to now, only 12 adult patients with APE/ULE/UME have been reported (23).

Typical lesions in APE/ULE are small erythematous papules with hypopigmented peri-lesional halos. The larger lesions are macules, scaly, or coalescent plaques. The eruption usually starts near one axillary region, spreading centrifugally, then becoming more widespread (29), and finally remits spontaneously in around four weeks (5, 29).

APE/ULE is often associated with Epstein Barr virus and parvovirus B19 infections (22). Other associated viruses include parainfluenza viruses and adenoviruses.

The differential diagnoses of APE/ULE depend on the geographical location of the child and the background incidence of other dermatological diseases. Prominent differential diagnoses include atopic dermatitis, allergic contact dermatitis, drug eruptions, unilateral blaschkitis (3), PR, GCS, papular urticaria, miliaria, scarlet fever (21), and ectoparasitic infestations. The initial asymmetric monomorphous papules and the subsequent clinical stages in otherwise healthy children are the major diagnostic clues to APE/ULE.

In the experience of the authors, most children with APE/ULS are asymptomatic, and no intervention of any kind is necessary. When treatment is warranted, the non-generic aspect is that different treatments might be indicated for its four overlapping stages (5, 6, 29).

After a coryzal prodrome, the first “eczematous stage” debuts as erythematous papules at unilateral axilla and the adjacent lateral thoracic cage. It is very difficult to diagnose APE/ULE in this stage. When it has been diagnosed, the mainstay of treatment are potent anti-pruritic measures, such as topical mometasone counting on its anti-inflammatory effects (4).

In the second “coalescence stage” (5, 6, 29), lesions are spreading out to the trunk and proximal aspect of the unilateral upper and lower extremities. The primary lesions would have turned brownish, for which no treatment might be necessary. Topical mometasone could be applied to the new lesions.

During the third “regression stage” (5, 6, 29), previous lesions are brownish. Moisturisers as lotions could be applied to the trunk and limbs, sparing the unilateral axilla and the unilateral inguinal crease in the parts of the world with high relative humidity to prevent intertrigo.

Scales appear in the final “desquamation stage”. Emollients as creams would be appropriate. If the local weather is dry, ointment might be indicated, again sparing the flexures.

**Papular-purpuric gloves and socks syndrome**

PPGSS can occur in infants, children and adults. It is typically preceded by fever, fatigue, and coryzal symptoms. Hands and feet of the patient then become erythematous and swollen. A sharp demarcation at the levels of gloves and socks is characteristic (25). Lesions in PPGSS are usually pruritic, and sometimes painful (28). Satellite lesions over the more proximal regions of limbs are common. Spontaneous remission occurs two to four weeks after rash onset.

PPGSS is particularly associated with parvovirus B19 infection (24, 27, 28). Other associated viruses include cytomegalovirus, coxsackie virus, hepatitis B virus, HIV, and rubella virus.

Differential diagnoses of PPGSS include rickettsial diseases, hand-foot-mouth disease, Kawasaki disease, serum sickness, GCS, and hand-foot syndrome due to chemotherapy. The course of the disease and the sharp demarcation of the erythema at gloves and socks levels will substantiate the diagnosis of PPGSS.

There exists three particularly non-generic aspects of managing children with PPGSS. The
Managements of the less common paraviral exanthems in children

first is that for children with congenital hemoglobinopathies and PPGSS due to parvovirus B19 infection, complete blood count should be monitored to detect aplastic reticulocytopenia at an early stage of this complication.

The second non-generic aspect is that PPGSS can be very acute with high fever and fatigue. Investigations would be necessary to exclude its differential diagnoses, the commonest ones being hand-foot-mouth disease and Kawasaki disease. Signs of Kawasaki disease should be actively looked for in these children. In this phase, antipyretics can be prescribed for the symptomatic remission.

In the next stage, hands and feet would become swollen with erythema. However, for some patients, swollen hands and feet appear concomitantly with the febrile and fatigue phase. Pruritus over the hands and feet is the rule, and can be alleviated with systemic histamine-antagonists such as chlorpheniramine or loratidine. We have found that topical calamine lotion to be applied to the hands and feet would be fit complements to the oral anti-histamine treatments for most children with PPGSS.

In this stage, pain can be severe for children. Systemic paracetamol would be adequate. Non-steroidal anti-inflammatory agents might not be necessary. The use of aspirin should particularly be avoided to minimize the risk of Reye syndrome.

The third non-generic aspect of management is one of infectivity. For erythema infectiosum, the infectivity of parvovirus B19 is very low once the erythematous cheeks and reticular lesions on the trunk are seen in children. However, this is not the case for PPGSS, with the children still being infectious when the skin rash appears. Therefore, arrangements for isolation and contact tracing for pregnant women, as parvovirus B19 infection in pregnancy could lead to severe fetal anemia, non-autoimmune fetal hydrops, and miscarriage.

Eruptive pseudoangiomatosis

Most patients with EP are children. They experience a prodrome of fever, fatigue, or mild diarrhea. The eruption appears four to seven days later, as monomorphous erythematous papules of around 2.5 mm in size, on the face, trunk, and the four extremities. Telangiectasia can be seen on close observation or via an epiluminescence dermatoscope. Lesions are blanchable, and are sometimes surrounded by hypopigmented halos. Spontaneous remission then occurs around four weeks after rash onset.

The initial patients reported by Cherry et al. (7), were associated with echovirus infections. However, evidence of such infections was not found in subsequent children with EP.

EP causes almost no complication in children. Some of the larger lesions may burst upon physical pressure, leading to bleeding.

The non-generic aspect of the management of EP lies in its diagnosis. It is very easily missed with its differential diagnoses including spider nevi, cherry angiomas, multiple pyogenic granulomas, and bacillary angiomatosis.

The course of the exanthem and the blanchable monomorphous papules would suggest the diagnosis being EP.

Eruptive hypomelanosis

EH is a novel paraviral exanthem (9, 11, 30). Most reported patients are young children below the age of six. After a prodromal coryzal stage, monomorphous hypopigmented macules of around 2-5 mm would be seen mainly on the extensor surface of the limbs. Systemic involvement including pharyngitis and lymphadenitis is common.

This exanthem is usually asymptomatic. The prime concern is to perform virological investigations where available, as virus has been not yet identified as the cause of EH.

Discussion

Investigations on the treatment of PR in children and in adults have been dynamic over the past two decades, because of several factors. Firstly, much virological evidence was reported on the association of PR and human herpesvirus (HHV)-7 and -6 (HHV-6) infections, particularly
endogenous reactivation of HHV-7 (18, 19). This led to a series of clinical trials evaluating the efficacy of low-dose and high-dose oral acyclovir to treat PR (20). Secondly, there was an initial enthusiasm on the efficacy of oral erythromycin in treating PR. This led to subsequent trials on the use of newer macrolides such as azithromycin and clarithromycin to treat PR (1, 2).

Thirdly, it was reported that the rash severity of PR is not closely correlated with impacts of PR on the quality of life (QOL) of patients (15) and that most patients with PR might not need any treatment (13). This is particularly true for children, for whom PR (14) and GCS (8) exert little impact on their QOL.

These findings might apply to less common PE as well. Virological investigations are of course necessary for these PE. Although severe complications are not observable at the present stage of knowledge, the underlying viral infections could stay as lifelong latent infections, and could manifest complications decades later when the hosts become immunocompromised. Furthermore, the gravity of chromosomal integration of HHV-6 or other viruses is yet to be assessed.

Treatments of these exanthems are unlikely to be a straightforward find-cause-and-treat-the-cause.

The efficacy, or lack of efficacy, of erythromycin and other macrolide in PR did not originate from hypotheses on bacteria causing PR, then employing antibiotics for anti-bacterial action. We have previously shown that PR is highly unlikely to be associated with Chlamydia pneumoniae, C. trachomatis, Legionella longbeachae, L. micdadei, L. pneumophila, and Mycoplasma pneumoniae infections (12), which are likely to be sensitive to macrolides. In the case of any modification on the course of PR, such changes are likely to be related to the anti-inflammatory and immuno-modulating effects of the macrolide concerned.

Along similar paths, it was known decades ago that HHV-6 and HHV-7 lack thymidine kinase for the phosphorylation of acyclovir, and would not be particularly sensitive to acyclovir (17). Whether acyclovir, or other antiviral agents, is effective on PR or other exanthems related to HHV-6 or -7 should be determined by results in clinical trials.

As aforementioned, PE casts low impacts for children as PR (14) and GCS (8). Clinical trials to establish efficacies of specific treatment modalities might not be warranted in the current stage of knowledge.

We have thus highlighted the most prominent non-generic aspects in the management of these PE. We hope that future studies on these less common PE would be based on patient-assessed outcomes, and that non-generic aspects of management of these less common PE would be addressed.

Address to:
Dr Antonio Chuh
Shops 5 and 6, The Imperial Terrace
356 Queen’s Road West, G/F
Hong Kong
Telephone: 852-25590420
Facsimile: 852-22394009
Email: antonio.chuh@yahoo.com.hk
References

18) Drago F., Broccolo F., Ciccarese G. et Al. - Persistent pityriasis rosea: an unusual form of pityriasis rosea with persistent active HHV-6 and HHV-7 infection. Dermatology 230, 23-6, 2015.