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Case Report

Recurrent varicella complicated with staphylococcal scalded skin syndrome in an immunocompromised child

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ABSTRACT

Immunocompromised children are at increased risk of recurrence and reactivation of varicella and its various complications. Staphylococcal scalded skin syndrome (SSSS) is an exfoliative dermatitis caused by toxicogenic strains of *Staphylococcus aureus*. Recurrent varicella lesions can predispose to *S. aureus* infection, and in the immunocompromised patients, SSSS can rapidly lead to multi-organ failure and death. A 3-year-old male child, on immunosuppressive therapy for acute lymphoblastic leukemia, presented with recurrent varicella infection. After initial improvement, there was deterioration due to the development of secondary bacterial infection and SSSS. He also developed septic shock and disseminated intravascular coagulation. The child recovered with antimicrobial therapy combined with aggressive supportive care. SSSS may present as a complication of varicella infection and is of special importance in immunocompromised. Even with such a rare combination of lethal conditions in the background of immunosuppression, where both diagnosis and treatment is a great challenge, early institution of appropriate therapy may lead to successful outcome.

Key words: *Acute leukemia, Febrile neutropenia, Immunocompromised, Pediatric, Staphylococcus aureus*

Primary varicella infection (chicken pox) is an acute but benign disease in childhood. Varicella virus can also become latent in the ganglion of nerve cells, both sensory and motor, after primary infection, and when the cell-mediated immunity and neutralizing antibodies are unable to keep it under control, it gets reactivated as herpes zoster. Malignancy, immunosuppressive drugs or radiation, trauma, stress often trigger reactivation [1]. Immunocompromised children are not only at an increased risk of reactivation of varicella, the complication rate, and mortality is also increased by many folds [2].

Staphylococcal scalded skin syndrome (SSSS) is a toxin-mediated, blistering dermatitis caused by infection with some particular toxin producing strains of *Staphylococcus aureus*. This syndrome may present in a wide variety of skin manifestation ranging from bullous impetigo, scarlatiniform rash, to a generalized desquamative process; again, it might be very deceptive in the presence of underlying immunodeficiency and other skin conditions. Mortality in childhood SSSS is <10%; however, in the setting of immunosuppression, it can rapidly lead to multi-organ failure and death [3].

The two above-mentioned conditions can complement each other as loss of skin barrier from recurrent varicella lesions may provide a favorable medium for *S. aureus* to thrive and produce toxins [4].

We report a case of SSSS complicating recurrent varicella infection in a pediatric oncology patient, treated successfully with a combination of early and appropriate antiviral and antibacterial agents coupled with aggressive supportive care.

With the advances in modern medicine, increasing number of immunosuppressed children are being cared for by pediatricians. These children being prone to such atypical clinical course of diseases are expected to pose significant challenges. Our case may help in early suspicion of similar cases where the prompt diagnosis, based mainly on clinical judgment coupled with aggressive management is the key to a successful outcome.

CASE REPORT

A 3-year-old male child, diagnosed as a case of B-cell acute lymphoblastic leukemia 6 months back was receiving treatment with standard chemotherapy protocol, currently on "repeat induction" cycle. He received the last dose of chemotherapy with L-asparaginase 1 week back. The child was admitted with complaints of fever for 4 days, generalized rash, with peeling of skin and bleeding from skin lesions. The lesions started as small vesicles over the abdomen and rapidly spread over the whole body with blister formation. There was a history of chicken pox 3 months back and he was not immunized with the varicella-zoster

vaccine (VZV). On examination, there were vesicobullous lesions spread all over the body, including palms and soles with surrounding erythema (Fig. 1a) and multiple flaccid blisters (Fig. 1b). There was no involvement of mucosal surfaces. Child's vital parameters and systemic examination were within normal limits. Dermatological consultation was sought and a diagnosis of reactivation of varicella was considered as Tzanck smear revealed multinucleated giant cells with intranuclear inclusions. Investigations revealed an absolute neutrophil count of zero with thrombocytopenia (platelet count 32,000/mm^3) and anemia (hemoglobin 8.3 g/dl), though renal and liver function parameters were within normal limits. He was started on IV antibiotics (injection piperacillin-tazobactam and injection amikacin) and injection acyclovir. There was clinical improvement (decrease in fever and no new skin lesions) over next 72 h. However, after another 24 hours, there was a recurrence of fever and worsening of skin lesions with the development of large bullae filled with clear fluid on the nape of the neck and upper back. The child also had areas of erosion over the body with serosanguinous exudates. Over next 24 h, he also developed septic shock manifesting with tachycardia, tachypnea, bounding pulses, and wide pulse pressure requiring intravenous (IV) fluid boluses followed by inotropic support with noradrenaline. He also developed abnormal bleeding in the form of malena and the laboratory investigations (platelet count 5,000/mm^3, prothrombin time 21 s, INR 1.9, activated partial thromboplastin time 58 s, fibrinogen degradation products 53 mcg/ml, d-dimer >0.5 mcg/ml) were suggestive of disseminated intravascular coagulation (DIC). It was managed with fresh frozen plasma (FFP) transfusion. A diagnosis of secondary infection with possible SSSS was considered. As the initial blood culture was sterile, empirical up gradation of antibiotics was done to include clindamycin. Acyclovir was continued along with aggressive supportive measures in the form of inotrope, growth factor (granulocyte colony stimulating factor), and blood component therapy (packed red blood cell and single donor platelet). Skin lesions were managed with sterile wrappings and semi-permeable dressings along with topical antistaphylococcal antibiotic (mupirocin). Repeat blood culture was also sterile, but skin swab culture showed abundant growth of methicillin-sensitive *S. aureus* (MSSA). Skin punch biopsy and histopathological examination demonstrated intraepidermal cleavage under stratum corneum with little inflammatory infiltrate, confirming the diagnosis of SSSS. Over next 48 h, he showed signs of improvement and inotrope could be tapered and stopped. He became afebrile after another 3 days. He was given IV antibiotics and acyclovir for 14 days followed by acyclovir prophylaxis. Reepithelization of the denuded skin began 2 weeks after admission, and the child could be discharged after 4 weeks. Complete reepithelization of the skin occurred in 6 weeks. Now, after 1 year of follow-up, the child is currently on maintenance cycle of chemotherapy and did not have further reactivation of varicella infection.

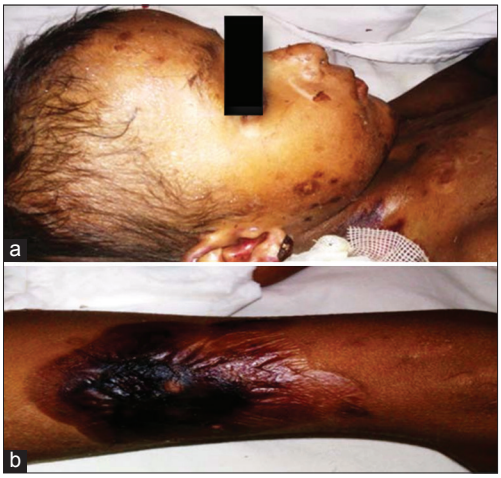

Figure 1: (a) Ruptured vesicobullous lesions of varicella with scars of previous chicken pox, (b) large hemorrhagic blister with necrotic epidermis over shin region

DISCUSSION

The incidence of infection with herpes viruses is greatly increased in immunocompromised hosts [5]; they are also at a higher risk of developing atypical/disseminated/extended infection with these viruses [2,5]. Atypical characteristics of skin lesions in immunocompromised patients include atypical locations, larger size of lesions, deeper, ulceration, satellite lesions, hemorrhagic lesion, and longer healing time [6]. The ulcerative-necrotic-gangrenous variety of zoster lesions is described exclusively in immunocompromised patients. The pathogenesis of such bullous lesions remains unclear and has been attributed to coinfecting exfoliative cytotoxin-producing organisms [7]. Our patient being persistently immunocompromised secondary to leukemia and its therapy, had recurrence/atypical reactivation of his varicella infection. Pneumonitis, hepatitis, pancreatitis, encephalitis, myocarditis, and DIC may occur with visceral dissemination in immunocompromised host [2]. Although the index child had some risk factors associated with increased risk of complications such as age <5 years and severe neutropenia [2], fortunately, he had none of the above-mentioned systemic involvement except DIC. Bacterial superinfection is the most common complication, seen in around 50% of cases of varicella, with *S. aureus* and beta-hemolytic streptococci being the most common causes [8,9]. Skin barrier disruption and virus-induced alteration of local immunity predispose to bacterial superinfection. Most of the *staphylococcus*-induced lesions in varicella are toxin-mediated [9]. Apart from symptomatic and supportive measures, management of varicella in immunocompromised, either primary or recurrent, consists of acyclovir therapy for 10-14 days [10], which our patient also received. Prevention (primary and secondary) of varicella infection in immunocompromised patients is an area of debate. The options include immunization, post-exposure prophylaxis with varicella-zoster immunoglobulin (VZIG) and antiviral agent (generally acyclovir) given either post-exposure or long-term [11]. Recommendations for VZV, a life-attenuated vaccine, in immunocompromised differ across the guidelines, though its efficacy seems to be of no concern [12]. Cost and availability limit

the use of VZIG, especially in the developing countries. Acyclovir used as a long-term prophylaxis has been shown to be effective in immunosuppressed [11]. Our patient, having a recurrence of varicella infection with a life-threatening complication was considered for the long-term prophylactic therapy.

In general, children have a prodrome of fever and malaise before developing skin lesions of SSSS. Nikolsky sign may be positive even before skin lesions are obvious. Coxsackie virus-induced blistering lesion, toxic epidermal necrolysis, drug reaction with eosinophilia, and Kaposi's varicelliform eruption or eczema herpeticum are the differential diagnoses. Time of onset and lack of mucosal involvement help in ruling out these conditions aided by a positive culture of *S. aureus* and skin biopsy. Eczema herpeticum (EH) is a disseminated herpes viral infection on a pre-existing skin disease, most commonly atopic dermatitis; but also with psoriasis, eczema, irritant contact dermatitis, burns, and seborrheic dermatitis [13]. EH is also known to have a severe course in immunocompromised children and frequently develops a secondary staphylococcal infection. However, our child did not have any pre-existing skin lesion.

IV fluid, correction of electrolyte disturbance, antibiotics, and local wound management remain the mainstay of management in SSSS. Penicillinase-resistant penicillin is the ideal first line as the majority of SSSS is caused by MSSA, though there has been increasing incidence of methicillin-resistant strains [3]. If there is no improvement or worsening, vancomycin to cover MRSA should be considered. Clindamycin and linezolid may be beneficial by toxin inhibition. Other adjuvant therapies, such as IV immunoglobulin or FFP may help in neutralizing exotoxin [3]. Our patient received FFP transfusion as he also had DIC. Dressing with saline-soaked gauze over soft silicone primary dressing of denuded skin prevents fluid loss and secondary infection. There is also a need for searching the primary site of infection with *S. aureus*, which is usually upper respiratory tract in children [3].

CONCLUSION

Immunocompromised children are at increased risk of reactivation of varicella infection and various complications thereof. SSSS can present as a complication of varicella infection, often posing a diagnostic and therapeutic challenge. Early and aggressive antimicrobial therapy along with good supportive care is the key in the management of such cases.

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