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A CASE SERIES ON STAPHYLOCOCCAL SCALDED SKIN SYNDROME

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INTRODUCTION

Staphylococcal scalded skin syndrome (SSSS) is a acute dermatological disease caused by the exfoliative toxins A (ETA) and B (ETB), of *Staphylococcus aureus (SA)*. SSSS is rare but potentially fatal disorder.[1] SSSS mainly affects young children and is characterized by Nikolsky sign. In youngsters, SSSS typically has a fair prognosis and recovers entirely with therapy.[2-4]

KEYWORDS: Staphylococcal scalded skin syndrome, Nikolsky sign.

Differential diagnosis of SSSS includes blistering and exfoliating skin illnesses, such as Steven-Johnson syndrome, Drug-induced toxic epidermal necrolysis, epidermolysis bullosa, bullous mastocytosis, herpetic lesions, and newborn pemphigus.[3,5] SSSS is characterized by periorificial face involvement, de-epithelialization of friction zones, and the lack of mucosal involvement. Nonetheless, in toxic epidermal necrolysis (Lyell's syndrome), visible mucosa as well as respiratory, gastrointestinal, and urinary tract mucosa are significantly affected.[5] A search for the primary site of infection should be included in both the history and examination, as well as a history of recent medication exposure, since this may more likely indicate TEN. A skin biopsy will differentiate between SSSS and TEN as well as guide further treatment.[6] Streptococcal impetigo is distinguishable from staphylococcal impetigo (localized SSSS) by its distinctive thick, filthy, golden crusting that quickly reforms when removed. However, clinically, this difference is sometimes difficult to discern, especially because the two species can coexist.[1] In this case series, we discuss the clinical presentation and treatment course of

five children with SSSS. It will give an outline of the diagnostic and therapeutic challenges encountered in SSSS.

CASE 1

A 16-days old female neonate weighing 2.98 kg presented with lesions all over the body along with skin peeling for six days. The skin lesions started on the face and then spread to the neck, upper chest, joints, elbow and ankle. Skin lesions on the neck got ruptured for which local care was given. The child had umbilical bleeding on day 6th of life, which then improved on treatment after two days. The patient had no history of seizures. On examination, the baby was conscious and alert but irritable. Physical examination revealed desquamation all over the body. Skin denudation was also observed. The skin was yellow up to the abdomen. During admission, the vitals recorded were pulse rate of 142 beats/min, respiratory rate of 56 breaths /min, oxygen saturation 96% and temperature 37°C. Laboratory test showed elevated C Reactive Protein (CRP)-12.3mg/dl, total bilirubin-6.0mg/dl, lymphocytes-48%, platelet count-4.9lakh/ul. Leucocyte count and neutrophils were within the normal limits. She was started on intravenous antibiotics, Ampicillin 150mg (50mg/kg/dose) thrice daily, and Gentamycin 12mg (5mg/kg/day) once daily in view of elevated CRP. The baby had a fever along with mild tachypnea and retraction on the next day. Treatment with oxygen via nasal cannula was started. Nebulisations such as Budesonide twice daily and 3% saline solution thrice daily was also added. Acetaminophen drops one drop per oral was administered to lower the body temperature. Her samples were sent for culture and coagulase-negative staphylococcus (CONS) was isolated from the blood. Nasal swab culture was notable for moderate growth of Staphylococcus aureus. The culture and sensitivity test of pus was done, and no pathogen was identified. An antibiotic sensitivity test was done which showed resistance to Amoxycillin, Ampicillin, Benzylpenicillin, Clindamycin, Erythromycin, and sensitivity to Amoxicillin/ Clavulanic acid, Cefuroxime, Trimethoprim/Sulfamethoxazole, Cefazolin, Gentamycin, Cloxacillin. Consultation with the dermatologist was obtained and she was diagnosed with SSSS. So Ampicillin injection was changed to Augpen (Amoxicillin +Clavulanate) injection 70 mg twice daily (50-100mg/kg/day) on the second day and continued for seven days. Gentamycin injection was administered for five days. The baby was initially on intravenous fluids but gradually she started to tolerate oral feeds well and had adequate urine output. She was prescribed Cetaphil moisturizing lotions for local application (L/A) onto the skin and denuded areas. Within one week, skin lesions showed signs of healing but exfoliations were present. Multivitamins such

as Zincovit drops 0.5ml per oral twice daily, Z and D drops 0.5ml once daily, and Calshine P drops 0.5ml once daily were also given. Her symptoms improved and became clinically better. Skin lesions were noted to be entirely resolved, and the CRP count decreased to 3.6 gm/dl at the time of discharge. The length of hospital stay was nine days, and the child was discharged in a stable condition with A to Z drops 0.5ml once daily for one month, Calshine P Drops 0.5 ml once daily for one year. Cetaphil moisturizing lotion twice daily was also continued for L/A onto the skin.

CASE 2

A 2-year-old male infant weighing 10 kg presented with complaints of facial and scrotal edema for two days. Facial puffiness started in and around the eyes which then progressed to the perioral, perinasal, ears and then to the umbilical area. During this time, he experienced many episodes of pain associated with erythema in the axillary and infra-axillary areas. The area was tender, and a local rise in temperature was present. He had scrotal edema along with decreased urine output since one day. He was also suffering from nasal discharge. His appetite was decreased and was not taking oral feeds. The mother complained that the child cried when she tried to lift him. He had a history of respiratory tract infection three weeks back. His parents denied cough, loose stools, abdominal pain, or any preceding history of urinary tract symptoms. On local examination, generalized erythema was noted all over the body including neck, ear lobe, axillae and genital areas. Nikolsky's sign was negative. On his abdomen, he had soft, tender skin around the umbilicus, infra-axillary and right and left hypochondriac areas. His temperature was 37.8^0C, pulse rate 80beats/min, respiratory rate 30breaths/min, and blood pressure 90/60mmHg. Laboratory tests showed : leukocyte count-12300cells/ul, lymphocytes-57%, neutrophils-37%, eosinophils-08%, Erythrocyte sedimentation rate (ESR)-12mm/hr, CRP- 2.5mg/L. Peripheral blood smear showed a normocytic normochromic blood picture. On the day of admission, urine routine and culture was done to rule out urinary tract infection. The urine routine was normal and no organisms were isolated. But the child was irritable and sick looking. The redness in the umbilical area started to increase and perioral crusting was noted. The swelling and inflammation progressed to the right and left thighs. The local rise in temperature and tenderness was also noted. His leucocyte count increased to 16600cells/ul on the second day and then to 17500cells/ul on the third day. He also had fever spikes during this time (37.8^0C). He was referred to a dermatologist for further evaluation. A diagnosis of SSSS was made. Paracetamol suppository 170mg was given rectally to reduce the temperature. He was treated

empirically with Vancomycin injection slow intravenous 150mg (15mg/kg/dose) thrice daily for five days to reduce the infection. The dermatologist added Hydroxyzine syrup (10mg/5ml) 2.5ml twice daily to reduce the allergic skin reactions, and other topical treatments to the affected area including Calosoft lotion thrice daily, T Bact ointment once daily, and Eumesone cream during night time. He was started on intravenous fluids and other supportive treatments including multivitamins syrup Bevon 2.5ml once daily. Nasoclear nasal spray (Sodium chloride) one spray in each nostril four times daily was prescribed to relieve his nasal congestion. The child developed a conjunctival discharge, for that ophthalmology consultation was done, and the child was prescribed Tobramycin eye drops thrice daily, Eyemist Gel (Hydroxypropylmethylcellulose) twice daily on both eyes for three days. The child became clinically better within a few days of treatment, the erythema subsided with no fever spikes and the edema begins to improve. The child started to take oral feeds, his bowel and bladder habit became normal. His pain subsided, became active and playful at the time of discharge. After eight days of hospital stay, the child was discharged in a good general condition on syrup Hydroxyzine 2.5 ml at bedtime for two weeks, T Bact ointment and Aveeno stain relief moisturizing lotion twice daily for local application.

CASE 3

A 9-month-old male child weighing 7.9 kg presented with complaints of rash with yellow coloured scales and fever for three days. The fever was high grade and not associated with chills or rigor. The rash started on the face and progressively increased to the neck and axilla over a period of several days. He had rashes in conjunction with skin peeling three days back following which he was started on oral antibiotics. On examination, conjunctival congestion along with periorbital edema was noted. Vitals done at the time of admission showed that the child was noted to be afebrile, with a pulse rate of 100 beats/min and a respiratory rate of 30 breaths/min. His leukocyte count was 21800 cells/ul with neutrophils 40%, lymphocytes 54%, eosinophils 2% and monocytes 4%. ESR and CRP was 13mm/hr and 5.9mg/L respectively. He was provisionally diagnosed as a case of SSSS and was managed with Augmentin (Amoxicillin/Clavulanic acid) injection (50-100mg/kg/day) 160mg twice daily for five days. On the second day of admission, the child had fever spikes, and it was managed with an Acetaminophen suppository 170mg ¾ (120mg) every six hours. On the third day of admission, a culture and sensitivity test of pus, throat swab, and the nasal swab was done. Methicillin-resistant Staphylococcus aureus (MRSA) was isolated from the throat (scanty growth) and nasal swab (moderate growth) but no pathogen was isolated from pus culture.

MRSA was resistant to Penicillins, Cephalosporins, Beta-lactam/beta-lactamase inhibitor combinations and Carbapenems but sensitive to Linezolid, Vancomycin and Gentamycin.But Augmentin was continued for the patient since the skin peeling started to subside and child got better. He received Tobramycin eye drops, one drop thrice daily was given on both eyes for ophthalmic care. Zincovit drops (multivitamin and mineral supplement) 1ml twice daily was given. Dermatology consultation was done for skin rash and peeling. The dermatologist advised to continue the parenteral antibiotics and prescribed Hydroxyzine syrup (10mg/5ml) 4ml at night, FM Derma Ointment (Fluticasone Propionate + Mupirocin) for L/A to the face at night and Desowen Lotion (Desonide) mixed with Cetaphil moisturizing lotion for L/A to the body at night for skincare. After six days of treatment, the symptoms improved, fever reduced, the skin peeling decreased, and got discharged in a stable condition. And also, the ESR value (2mm/hr) and CRP (2.1mg/L) came to normal. After five days of parenteral therapy, the antibiotic was converted to its oral dosage form, Augmentin syrup (228mg/5ml) 2.5ml for a total of ten days. On discharge, treatment with FM Derma Ointment, Desowen Lotion, Cetaphil moisturizing lotion was continued for one week.

CASE 4

A 3.5-year-old male child weighing 10 kg was presented to the hospital complaining about skin rash for one day. The child had a history of cough, vomiting, loose stools with blood and mucous one week back and was given syrup Taxim O (Cefixime) for five days in view of dysentery. Symptomatically the child improved, but after two days the child developed a perioral rash with crusting. He also had itching over the skin and eyes. Parents reported that the child became irritable and complained of pain on being picked up. On examination, the skin was tender and multiple rashes were seen in the axilla, flexures, perineal, inguinal and intertriginous areas. The rash was itchy and scaly in nature. In addition, he had a congested throat, and his pulmonary examination revealed bilateral crepitations. Vital signs done at the time of admission showed that the child had no fever, with a pulse rate of 90 beats/min, and a respiratory rate of 30 breaths /min. Routine laboratory tests including complete blood count, hepatic and renal function tests were within the normal limits. But the ESR value was elevated to 35mm/hr. A culture and sensitivity test of blood was done, and no pathogen was isolated from blood culture. Dermatologist consultation was done and he was provisionally diagnosed as a case of SSSS. He was managed with Augmentin (Amoxicillin/Clavulanic acid) injection 200mg (50-100mg/kg/day) thrice daily for seven days. He was started on intravenous fluids. Topical treatment with Mupirocin ointment every six hours and

Fluticasone ointment twice a day for three days followed by once daily for four more days was provided to the affected areas. Even though new rashes appeared over the hands during hospital admission, they subsided with continuous antibiotic and steroid therapy. Cetirizine syrup (5mg/5ml) 2.5ml twice a day was given to alleviate itching. He was also advised to apply Oilatum lotion (skin moisturizing agent) to the whole body twice daily. One drop of Tobramycin eye drops was given four times a day for three days to treat itchy eyes. Later ophthalmologist consultation was done since the child developed eye discharge during hospitalization. The ophthalmologist stopped Tobramycin and started Eyemist gel (Hydropropylmethylcellulose) twice a day and Tobastar F eye drops (Tobramycin + Fluorometholone) one drop, four times a day for three days. Mucinox (Oxymetazoline hydrochloride) spray was administered twice a day in the initial two days to treat nasal congestion. The child was discharged after a course of parenteral antibiotic for one week, and he was advised to take Syrup Bevon (multivitamin, multi-mineral and antioxidant) 2.5ml once daily, Oilatum lotion L/A twice daily and Mupirocin ointment L/A for one month. He was also instructed to taper the frequency of Eyemist eye gel to once daily for five days and Tobastar F eye drops to one drop, thrice a day for three days then to twice daily for three days and finally to once daily for three more days. At that time, the child was symptomatically better, vitals were stable and the chest became clear.

CASE-5

A 1-year 15day old male baby of 8.5kg was referred from a local hospital for evaluation of fever, dry cough, congested throat and mucoid nasal discharge along with skin peeling for one day. The fever was mild, on and off type relieved on antipyretics. The parents noticed pus discharge on the diaper. On the day of admission, the child presented a blister on his scalp and the skin peeling had added to his symptoms. On examination, the patient had flaccid bullae over the forehead and all over the face including the eyes, nose, mouth, lips and behind the ears. Blanching erythema was also seen all over his skin. Nikolsky's sign was positive. The child was irritable at the time of admission. The child was apparently asymptomatic till one day before. His vitals were stable and laboratory test showed elevated CRP-7.64mg/dl, leukocyte count-18600 cells/ul, and platelet count-6.2lakh/ul. His peripheral blood smear showed normocytic normochromic to mildly hypochromic blood picture with neutrophilic leukocytosis and mild thrombocytopenia. A culture and sensitivity test of blood was done, and no isolated organisms were found. He was started on Augmentin injection intravenous 180mg (20mg/kg/dose) twice daily for seven days because of elevated leukocyte

count and CRP value. Azithromycin syrup (200mg/5ml) 2.5ml once daily was given to relieve chest symptoms. On the next day, his body temperature started to increase with maximum reading 38^0C. The lesions progressed to all over the body with itching and redness. Subsequently, he was referred to a dermatologist to investigate this and he was provisionally diagnosed with SSSS. So, treatment with Azithromycin syrup was stopped and Amikacin injection 125mg (15mg/kg/dose) intravenous once daily was started and continued for five days. He was started on T-bact ointment L/A twice daily, Calosoft lotion L/A twice daily and Hydroxyzine syrup (10mg/5ml) 2ml twice daily. The patient was commenced on symptomatic management with Acetaminophen syrup (250mg/5ml) 3ml once daily, Mucolite drops (Ambroxol) 2ml thrice daily, and Nasoclear nasal spray (Sodium chloride) two spray in each nostril four times daily, Mucinac 3ml thrice daily, 3% saline nebulization four times daily, Asthalin nebulization thrice daily. Multivitamins such as Z and D drops 1ml once daily, Bevon syrup 2.5 ml twice daily, and A to Z drops 0.5ml once daily were also added. He also had conjunctival discharge during his hospital stay. The skin lesions showed signs of healing and no new blisters appeared after antibiotics treatment. His CRP and leukocyte count decreased to 2mg/dl and 10400cells/ul respectively. After seven days of treatment with a combination of systemic and topical medications, the child seemed to be relatively stable and was discharged. The baby was active and feeding well at the time of discharge. His CRP, leukocyte count and platelet count decreased to 2mg/dl, 10,400cells/ul and 4.7lakh/ul respectively. He continued taking medications such as Mucolite drops 1ml twice daily for five days, Z and D drops 1ml for eight days, Bevon syrup 2.5ml twice daily, A to Z drops 0.5ml once daily for one month and Cetaphil moisturizing lotion for local application.

DISCUSSION

Staphlococcal Scalded Skin Syndrome is a skin condition that mostly affects the age group under five and is more prevalent in developing countries. Young children are primarily affected because the desmoglein-1 content in their skin is comparatively small than that of adult skin.[3] The factors that contribute to the onset of ssss in neonate are absence of immunity against the toxin and immature kidney function. The functional Immaturity of the kidney causes lower toxin clearance. The percentage of ET-A antibody carriers drops from 88 percent to 30 percent right away after birth which rise again between 4 months to 2 years of age.[5]

The severity of staphylococcal scalded skin syndrome varies, by a few localised blisters at the infection site to a severe exfoliation that affects nearly the entire body. The Staphylococal toxin acts at a distant location, causing a red rash as well as the separation of the epidermis underneath the granular cell layer. The ETA, ETB and ETD produced by *Staphylococcus aureus* act as a glutamate-specifific serine protease enzymes that cleaves desmoglein-1 protein, which when inactivated result in desquamation and blisters.[7-9] Toxins are spread by hematogenous circulation and reaches stratum granulosum of the skin. The SSSS mortality rate in children is estimated to be around 4%[2] where as in adult, due to underlined immunodeficiency the mortality rate is up to 50%.[3]

SSSS emerges after a premonitory symptom of disease such as pharyngitis or conjunctivitis.[9] Four of our patients showed conjunctivitis and were treated with Tobramycin eye drop and eyemist gel. The patient subsequently develops an erythematous rash that looks like sandpaper and evolves to local or generalized epidermal exfoliation. The patients skin seems to be burned, thus the name "scalded skin syndrome." And also known as "Ritter diseases" or "Staphylococcal epidermal necrolysis". Children with the disease have a generalized malaise, fever and skin tenderness. Erythema commonly begins on the scalp and skin creases and spreads across the body within 48 hours. The patient's skin wrinkles as a result of flaccid sterile bullae, and positive Nikolsky sign.[9] Nikolsky sign was only expressed by our last patient. Four of our patients had fever and were managed with Acetaminophen. Our 2nd and 5th patient had a generalized erythema all over the body and children showed skin peeling that commonly begins from the face. The patient's flexures tend to exfoliate, resulting in perioral and periocular crusting, as well as radial fissuring.[9] Three children showed alike symptoms such as perioral crusting, erythema, blisters and flaccid bulbae. Mucus membranes are not affected, hence there is no intraoral involvement.[9] The lesions in neonates are commonly found around the umbilicus or the perineum, while in elder children they usually seen on the extremities.[1]

Hypothermia, dehydration, and secondary infections are the potentially dangerous consequences that may occur in newborns and young children due to the loss of protective epidermis.[1,3] Intravenous fluids were administered to three of our patient to prevent dehydration. Although inflammatory indicators are not a reliable predictor for SSSS severity, but a subsequent increase from the baseline value is a good signal of secondary infection.[6] Here also three patients showed the evidence of secondary infection and an Aminoglycoside

(Amikacin,15mg/kg/dose, OD /Gentamycin, 5mg/kg/day OD) was added to their treatment regimen. Exfoliation of ssss is seldom an issue since the extent of epidermal cleavage is shallow, which implies scarring is rare.[1]

The diagnosis of SSSS is generally based on the objective & subjective data, and it is confirmed by the presence of S. aureus in the wound, conjunctival, pharyngeal, or nasal swabs.[5] The culture and sensitivity reports of pus, throat and nasal swabs were also used in our patient to diagnose SSSS. Staphylococcus aureus generating exfoliative toxin can sporadically isolated from blood cultures. Blood cultures in children are frequently negative as the toxins are formed in a distant location.[1] Here, Blood culture was done among three children, but organisms were isolated from only one and other two cultures showed no growth. The Cultures taken from undamaged bullae of SSSS patients are often absent for S. aureus generating ETs. It appears that toxins generated at a distant site of infection appear to reach the skin via the circulation as a cause of toxaemia, thus generating SSSS eruptions.[5]

The drug therapy of SSSS includes intravenous antibiotics that cover *Staphylococcus aureus* and adjuvant therapy with topical agent like fusidic acid and/or mupirocin. Here in 5 cases, four patients was treated with intravenous antibiotic, amoxicillin clavulanic acid for seven days and other one was treated with Vancomycin (15mg/kg/dose) 8th hourly for 5 days. Topical antibiotic (mupirocin) therapy was prescribed for all patients as organisms may be present in the lessions. Moisturizing lotion was also commonly prescribed in all patient. Topical cortico-steroids were given to three patients. The treatment was effective and patients became symptomatically better within 6 - 9 days of therapy.

CONCLUSION

This case series emphasize the potential severity and importance of the disease condition and its management. It is crucial for Pediatrician and dermatologist to take a prompt action in differential diagnosis of the condition. The treatment should be focused on skin care, fluid & electrolyte balance and prevention of complications.

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