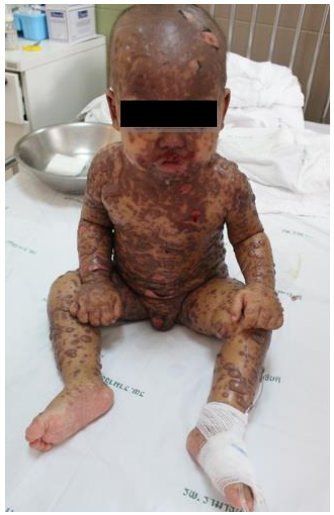
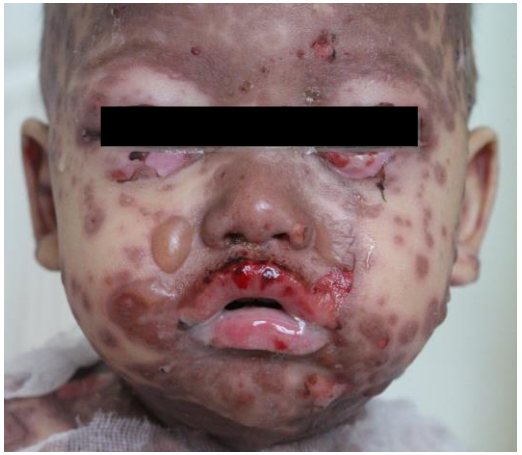
Case 13
A 1-year-old infant from Samut Prakan
Chief complaint: Whole body rash for 3 days



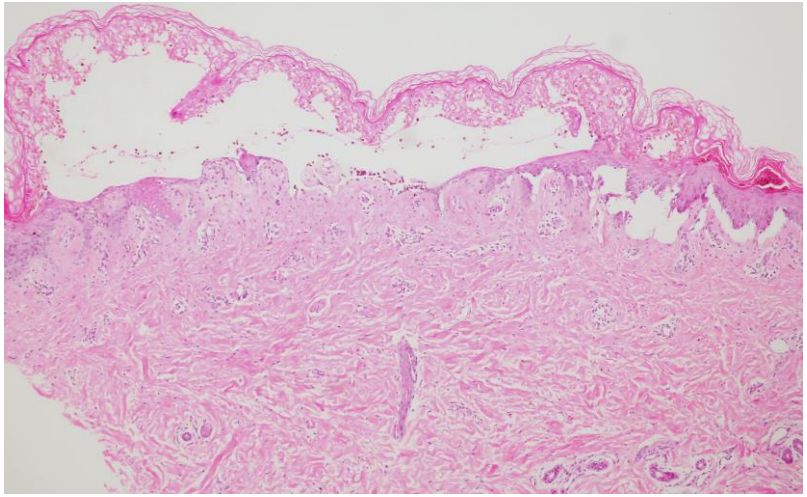


Present illness: Six days previously, the infant developed fever and erythematous rash on his lip, palms and soles. He received amoxicillin and lidocaine viscus from private hospital. Three days later, he still had a fever and developed multiple bullous lesions with some denuded areas scatter on whole body. Then he was admitted in private hospital and received intravenous cloxacillin with no improvement of rash. The bullous lesions with areas of denuded skin became worse, so he was referred to Ramathibodi Hospital.

Past history: No underlying disease. Term newborn with normal growth and development.

Physical examination:
V/S: T 38°C, PR 120 bpm, RR 28 times/min, BP 86/56 mmHg, BW 10 kg
GA: A Thai male infant, good consciousness, no pallor, no jaundice
HEENT: No pale conjunctiva, anicteric sclera
CVS: Normal S_1S_2, no murmur
RS: Normal breath sound, no adventitious sound
Abdomen: Soft, non-tender, liver and spleen not palpable
Lymphatic system: No lymphadenopathy
NS: Intact

Skin examination:
- Generalized dusky red to purplish macules and papules
- Multiple flaccid bullae and areas of denuded skin distributed on face, trunk and extremities
- Hemorrhagic erosions on lips and buccal mucosa



Histopathology (S15-008662, right thigh):

- Extensive confluent epidermal necrosis with subepidermal separation
- Mild superficial inflammatory cell infiltrate of lymphocytes and a few melanophages in the superficial dermis

Laboratory investigation:

CBC: Hct 29.4%, Hb 9 g/dL, WBC 6730/mm^3 (PMN 38% L 54% M 7 B 1%), Plt 438,000/mm^3

BUN 3 mg/dL, Cr 0.2 mg/dL

LFT: ALP 161 U/L, GGT 22 U/L, AST 60 U/L, ALT 31 U/L, TB 0.2 mg/dL, DB 0.1 U/L, alb 28.5 g/L

UA: normal

HSV type l and ll (oral lesion): Undetectable
HSV type l and ll (blood): Undetectable
Mycoplasma pneumonia Ab: Undetectable
Aerobic culture: Pseudomonas aeruginosa
Wound swab culture: Pseudomonas aeruginosa
Chest X-ray: Normal

Diagnosis: Toxic epidermal necrolysis

Treatment:

- Admit burn unit
- IVIG (1g/kg/dose) 10 g IV OD x 3 days
- Levofloxacin (1g/kg/dose) 100 mg IV OD
- Dressing wound with AQUACEL® Ag

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Discussion:

This infant presented with generalized dusky red to purplish macules and papules with multiple areas of denuded skin and erosions on oral mucosa. The presenting rash gave high suspicion for Stevens-Johnson syndrome (SJS)/toxic epidermal necrolysis (TEN) or erythema multiforme major. Given that our patient had received antibiotics amoxicillin and cloxacillin prior the onset of the rash and the investigation showed no herpes simplex or mycoplasma infection, this led us to suspect TEN. The skin biopsy performed on bulla of right thigh showed subepidermal separation with sheet of epidermal necrosis and intact stratum corneum in association with mild superficial perivascular infiltrate of lymphocytes. Therefore, the diagnosis in our patient is TEN from penicillins drugs. He received a course of intravenous immunoglobulin (IVIG) for 3 days after the onset of the widespread rash for 3 days. The clinical improvement was observed by 7 days after receiving IVIG. The complication in our patient was the Pseudomonas aeruginosa skin infection and septicemia. The Sequelaes were dyspigmentation, entropion and phimosis which have undergoe surgery. Human leukocyte antigen (HLA) pharmacogenetic screening was performed to prevent the administration of drugs that increased risk of TEN. The HLA result showed no specific HLA genotype for any drugs. To the best of our knowledge, there was no specific HLA genotype for penicillin-induced SJS/TEN up to now.

SJS and TEN are severe cutaneous adverse reactions to drugs that affect both adults and children. The incidence and mortality rate in children are lower than in adults.[1,2] The incidence of pediatrics SJS/TEN accounting for 10-20% of worldwide incidence (approximately 1-2 cases per million/year[3]). Due to very rare incidence of pediatrics SJS/TEN, etiological factors are based on case reports or small case series. Most cases of pediatrics SJS/TEN have been associated with medication, mainly sulphonamides and anticonvulsants, followed by penicillins and nonsteroidal anti-inflammatory drugs (NSAID) (excluding oxicams).[4]

In contrast to adults, the causative agents are mainly allopurinol, nevirapine and oxicam NSAIDs. TEN is almost caused by drugs, whereas some cases of SJS may be related to *Mycoplasma pneumoniae* infection.

The pediatrics SJS/TEN have a varying severity of clinical manifestation same as adult, including confluent purpuric macules or atypical targetoid lesions with blisters and erosion.[4] There are some cases of TEN exhibit epidermal detachment without preceding purpuric macules or atypical targetoid lesions.[5] Almost all cases have skin erosions and mucosal ulceration over the period of 1 day to 2 weeks. The prodromal symptoms of TEN are fever, malaise, anorexia, pharyngitis, headache, and rash, which may be morbiliform.[5] The diagnosis of SJS/TEN is mostly made on clinical presentation, although a skin biopsy help to confirm the diagnosis. For early TEN, histologic feature show scattered necrotic keratinocytes that resembles erythema multiforme major. The histologic findings of advanced stages of TEN display the full thickness of epidermal necrosis, subepidermal separation and scant inflammatory cell infiltration.[5]

The common complications of TEN include ocular lesions, cutaneous dyspigmentation, dental complications, genitourinary problems and pulmonary disease.[6] Ocular lesions are the most common complication.[7] Due to life threatening condition, HLA genotype screening is the important tool to prevent the administration of drugs to susceptible individuals.

Optimal supportive care is the mainstay of treatment.[6] Patients should be early admitted in burn units or ICU with strict isolation. The essential management is appropriated wound care. There is still controversy regarding the use of immunosuppressive agents or IVIG in management of TEN.[8] Some studies showed that the mean duration of disease was similar between steroid and non-steroid group. Many studies showed the use of IVIG in pediatrics SJS/TEN had more favorable outcomes in shorter average duration of disease and mean hospital stay.[9-11] Moreover, IVIG can use in case of poor responsiveness to steroid with satisfactory result.[12] Other adjuvant therapies have been tired in TEN, including plasmapheresis, tumor necrosis factor-alfa inhibitor, NAC and cyclosporine with need additional studies to confirm the efficacy.

Reference

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