

Antipyretics Induced Erythema Multiforme

**N.K. Dubey
Deepak Jajoo
Ajay Gupta
Daya Sharma**

Reactions to drugs are quite common and are generally mild and are hence not reported. However, occasionally life threatening reactions including Steven Johnson's syndrome and toxic epidermal necrolysis may occur. Drugs incriminated include sulphonamide, barbiturates, antituberculars, antibiotics, pyrazolone derivatives and non esteroidal anti-inflammatory drugs(1-7). We report one case each of Steven Johnson's syndrome and toxic epidermal necrolysis following administration of paracetamol and novalgin, respectively. Although these drugs are commonly used in practice, reported cases following paracetamol are few(8-9) and none reported with analgin (Novalgin).

Case Reports

Case 1: A 9 year old girl was admitted with complaints of fever of 4 days duration. For the last one day, she had shown rashes all over body, ulcers in mouth

From the Department of Pediatrics, Lady Harding Medical College and Associated Kalazvati Saran Children's Hospital, New Delhi.

Reprint requests: Dr. N.K. Dubey, A-II/25, Vasant Vihar, New Delhi 110 058.

Received for publication: February 24, 1993;

Accepted: November 30, 1994

with difficulty in swallowing and redness of eyes. The patient was treated by a private practitioner with injection novalgin on second day of fever. As the fever persisted, Ciprofloxacin was added on third day and a dose of injection novalgin repeated. Few hours later, the patient developed rashes all over body and was referred.

On examination, the patient was acutely sick and irritable with a temperature of 103°F. The pulse rate was 140/min, respiratory rate 40/min and blood pressure 120/70 mm Hg. The skin showed multiple large areas of erythema, few of them with large bullae and tendency to confluence. Multiple large denuded erythematous areas were also seen over the face, neck, trunk and extremities. No lesions were noticed on palms and soles. The Niklosky's sign was positive only over the areas of erythema. Multiple ulcers with surrounding areas of erythema were present in mouth; oropharynx and nostrils. There was marked conjunctival congestion, but cornea and anterior chamber was normal. A diagnosis of toxic epidermal necrolysis was made. The patient was treated symptomatically with intravenous fluid and antibiotics with care of skin, eye and oropharynx.

Laboratory investigations revealed a Hb of 12.4 g/dl and, total leucocyte count of 5600/mm³ (polymorphs 81%). Blood, urine and skin swab cultures were sterile. Chest X-ray showed right upper zone consolidation which cleared after antibiotics. At follow up 45 days later, the child had no sequelae and her vision was normal.

Case 2: A 5 year old male child was

brought with history of fever for 5 days. During the next two days, the patient developed rashes all over the body and ulcers in the mouth. The patient received paracetamol, chloroquin, chloromycetin and metoclopramide for fever.

On examination, the child was febrile (temperature 102.8°F). The pulse rate was 130/min, respiratory rate 36/min and blood pressure 110/68 mm Hg. The skin showed numerous discrete erythematous areas; many of which were surmounted by vesicles and bullae, over the face, neck, trunk, and extremities. Few vesicles had ruptured leaving behind denuded areas. Some target lesions were also noticed. Vesicles were small in size 3 cm x 3 cm. Niklosky's sign was negative. Multiple ulcers with surrounding erythema and pseudomembrane formation were present in mouth and pharynx. Conjunctiva was congested but cornea, anterior chamber and pupils were normal. A diagnosis of Steven Johnson's syndrome was made and the patient treated symptomatically. During one of the episodes of pyrexia, the child was given paracetamol following which the skin lesion exacerbated. Paracetamol was withdrawn and the child progressed normally. The child was discharged 30 days later with the advice not to take paracetamol.

Discussion

Erythema multiforme minor, Steven Johnson's syndrome and toxic epidermal necrolysis represent a spectrum of the same disease of which erythema multiforme minor is the mildest one. The etiology is not very well known but occurs as an adverse reaction to medication. Infection specially *Herpes simplex*,

all kind of vaccines, transplantation and certain malignancies like leukemia and lymphoma can also lead to erythema multiforme. Nearly 60-80% of Steven Johnson's syndrome and 80-90% of the toxic epidermal necrolysis reported are due to drugs(10,11).

Steven Johnson's syndrome is characterized by the blistering of atleast two mucosal surfaces alongwith the cutaneous lesion. The cutaneous lesion begins as maculopapular rash with rapid and marked blistering. The rash is widespread over face, neck, trunk and extremities but remains discrete. Scalp is not affected. Constitutional symptoms like fever, myalgia and prostration are quite common. The oral cavity is involved in all the cases. Multiple large erosion often covered with grey pseudomembrane are found in oral cavity and on lips which may be covered with hemorrhagic crust. Eye involvement is in the form of catarrhal or purulent conjunctivitis*In severe forms, uveitis and corneal ulcers may occur. Other mucous membrane involvement manifests as rhinitis, vulvovaginitis balanitis, etc.(8-10).

In toxic epidermal necrolysis, the lesion start as large erythematous patch. The skin underneath is tender. The lesion blisters rapidly and individual bullae enlarges, forming palm sized or larger lesions. As the blister roof ruptures, large flap of skin peels away leaving weeping denuded area, giving an appearance of second degree burn. Mucous membrane involvement is like Steven Johnson's syndrome but less severe(9,10). Management is symptomatic with IV fluid and other supportive therapy. The patient should be isolated

and systemic antibiotics are indicated on earliest suspicion of infection. The skin should be covered with antibiotic ointment and mouth wash given for oral cavity. Artificial tear for eyes are recommended along with antibiotic drops and ointments. The use of steroids is controversial. It can be used in toxic patients, presenting within 48 hours of appearance of rash. They are contraindicated in nontoxic patients and where skin denudation is >20% (12). Common complications include pneumonia, keratitis, corneal perforation and esophagitis leading to stricture. Rarely myocarditis, hepatitis and renal involvement may occur. Mortality due to Steven Johnson's syndrome and toxic epidermal necrolysis is 5-10 and 20-70%, respectively. Permanent sequelae are rare if managed properly (13,14).

REFERENCES

1. Bottiger LE, Strandberg I, Holms BE. Drug induced febrile mucocutaneous syndrome. *Acta Med Scand* 1975, 198: 229-233.
2. Bianchini JR, Macaraeg P, Lasagna L, *et al.* Drugs are etiological factor in Steven Johnson syndrome. *Am Med* 1968,44:390-450.
3. Stern RS, Bigby M. An expanded profile of cutaneous reactions to non steroidal anti-inflammatory drugs. *JAMA* 1984, 252:1433-1437.
4. Bjornburg A. Fifteen cases of toxic epidermal necrolysis (Lyell), *Acta Derm Venerol* 1973, 53:149.
5. Nanda A, Kaur S. Drugs induced toxic epidermal necrolysis. *Arch Dermatol* 1990,125:26.
6. Madalene CY Heng. Drug induced toxic epidermal necrolysis. *Brit J Derm* 1985,113: 597-600.
7. Guillaume J-C, JRoujeau J-C, Revug J. Dominique penso Rene Touraine. The culprit drugs in 87 cases of toxic epidermal necrolysis (Lyell's syndrome). *Arch Dermatol* 1987,123:1166-1170.
8. Ting HC, Adam BA. Erythema multiforme. Epidemiology, Clinical characteristics and natural history of fifty nine patients. *Aust Dermat* 1984, 25: 83-88.
9. Roujeau J-C, Guillaume J-C, Paul J, *et al.* Toxic epidermal necrolysis. *Arch Dermatol* 1990,126: 37-42.
10. Huff JC, William LW, Marcia T, Denver CO. Erythema multiforme: A critical review of characteristics, diagnostic criteria and causes. *J Am Acad Dermatol* 1983, 6: 763-775.
11. Chan H-L, Stern RS, Kenneth A, *et al.* The incidence of erythema multiforme, SJS and Ten. *Arch Dermatol* 1990,126: 43-47.
12. Lawrence F, Eichenfield P., Honig J. Blistering disorder in childhood. *Pediatr Clin North Am* 1991, 38: 959-976.
13. Morley WN. Diseases of skin. Text Book of Pediatrics, 3rd edn, Vol 2. Eds Forfar JO, Arneil GC. Edinburgh, Churchill Livingstone, 1985, pp 1658-1659.
14. Prendiville JS, Hebert AA, Gross C, *et al.* Management of SJS and TEN in children. *J Pediatr* 1989,115: 881-884.