Nigerian Journal of Paediatrics 1993; 20(2): 45-8

Recurrent Erythema Multiforme

EE EKANEM[+] AND AA ASINDI[++]

Summary

Ekanem EE and Asindi AA. Recurrent Erythema Multiforme. *Nigerian Journal of Paediatrics* **1993; 20: 45.** The case of a three-and-half-year old male child with the severe form of erythema multiforme (EM) major (Stevens-Johnson syndrome) is described. From the past medical history, the child had seven previous attacks of a similar disease in the immediate past 24 months. The first four attacks of the disease were considered, by their description, to be mild EM minor, as the lesions were limited to the skin, while the next four recurrences, including the present one, were regarded as severe, with extensive involvement of the skin, mucosae of the mouth, nose, eyes and urethral orifice, that required hospitalization. Each recurrent episode of the disease was causally related to self-medication with pyrimethamine-sulfadoxine (*Fansidar*). With the current frequent and indiscriminate use of *Fansidar* and other sulphonamide-containing substances as alternatives for chloroquine-resistant malaria, physicians should be alerted to the possibility of an upsurge in the prevalence and recurrent attacks of EM, minor or major, in malaria-endemic areas of the developing world.

Introduction

ERYTHEMA multiforme (EM) is an acute cutaneous eruption consisting of a lesion which starts as anannular red papule with a dark centre. This target lesion undergoes changes similar to those of a bruise. In a severe case, the lesion develops into a vesicle, or a bulla which later breaks down to expose a raw weeping area that resembles thermal burn. Resolution of the lesion usually occurs with crusting or scaling before healing takes place. The condition has been causally linked with microorganism infection [1-3] and ingestion of certain drugs, including the sulphonamides. [4 5] Recurrences have reportedly been precipitated in the same individual by viruses and drug ingestion, but such recurrent episodes have rarely exceeded three in number. In view of this, it is considered that the present case of a child with eight episodes of EM within a period of 24 months, is unique and thus worth documenting.

College of Medical Sciences
University of Calabar, Calabar

Department of Paediatrics
+ Lecturer
++ Reader

Correspondence: AA Asindi

Case Report

A three-and-half-year old male child was referred from a private hospital to the University of Calabar Teaching Hospital (UCTH) in March 1992, with a four-day history of generalized

pruritic skin eruption that was associated with some burning sensation. According to the mother, the skin lesion had initially erupted in the form of blisters which later broke to expose raw, weeping and crusted areas. Four days prior to the onset of the eruption, the child had fever with rigors and cough, for which the mother administered *chloroquine, sulphatriad* and *pyrimethamine-sulfadoxine* (*Fansidar*). Past medical history revealed that the child apparently had seven previous episodes of similar condition during the preceding 24 months. Each of the first four episodes was associated with antecedent fever and pruritus for which the child received *Fansidar* before the rash erupted; during each of the episodes, the mouth and the eyes were not affected and he was treated on out-patient basis at the same referring hospital. The lesions in the three next episodes were more extensive than those of the first four, with involvement of the mucosa of the mouth. Again, there was an antecedent fever and the mother had treated the child for "malaria" with *Fansidar*. The last two of these three attacks were associated with bleeding from the skin, discharging eyes and ulcers in the mouth, leading to difficulty with feeding. At each of these three episodes, the child was admitted into the same private hospital and treated with intravenous infusion, antibiotics and steroids; blood transfusion was undertaken during the last two admissions.

The eighth recurrence for which he was admitted to UCTH was, according to the mother, the worst ever. The interval between the eight episodes varied from one to three months with each of the seven previous attacks lasting seven to twelve days and followed by complete recovery.

The patient was the first child of parents who were civil servants. The mother denied knowledge of any case of drug allergy in any other member of the family.

On admission, physical examination revealed a well-nourished, but very acutely ill child. He was ferbile (temperature, 38 C); the eyes were injected, but there was no discharge. There were generalized skin eruptions, some of which had broken down exposing extensive raw, weeping and crusted areas. These eruptions were present on the trunk, limbs, face, mucosae of the mouth, nose and urethral opening. Besides a pulse rate of 136/min., the cardiovascular and the respiratory systems were normal; the blood pressure (BP) was 100/60 mmHg and repeated measurements of the BP remained normal. Except for some degree of irritability, the central nervous system was also normal.

Investigations included full blood count, urinalysis, serum urea, electrolytes and creatinine, all of which were normal. Blood culture was sterile.

Treatment consisted of intramuscular gentamicin 5mg/kg/day in three divided doses, procaine penicillin 300,000 units daily, both for one week; oral prednisone 2mg/kg/day for one week after which the drug was tapered off over another seven days. Dressing was applied to the skin lesion. By the end of two weeks hospitalization, the patient had improved enough to be discharged.

Discussion

Erythema multiforme (EM) exists in two clinical forms namely, EM minor which is a mild form of the disease with lesions on the face, forearms, hands and rarely, the buccal mucosa and EM major, or Stevens-Johnson syndrome, in which the whole skin may be blistered and the lesions present also in the mucosae of the mouth, vulva, urethra and nostrils. [6] There can be no doubt from the characteristic lesions and their involvement of the skin, mucosae of the mouth, nose and urethral opening, that the

condition for which the child was admitted to UCTH, was Stevens-Johnson syndrome. The description of the previous seven episodes as given by the mother of the patient strongly suggests that all the seven recurrences were manifestations of the same disease. It would seem that with succeeding attacks, the minor form of the disease progressed into the major form. As described above, during the first four recurrences, the mouth, nose, etc., were spared; the mild nature of the disease, during those four episodes, was such that the patient was treated on outpatient basis. The next three recurrences became severer than before and the lesions involved the eyes and mouth to the extent that the child was admitted into the same private hospital that later referred the patient with the most severe and eighth attack to UCTH.

The recurrences of EM in the present case appear to be causally related to *Fansidar* which the mother had habitually administered at home for each episode of fever which she suspected to be malaria infection. Erythema multiforme major typically follows drug therapy by one to three weeks of exposure to the offending drug, but the interval may be as short as a few days or hours, particularly when the susceptible individual has been previously exposed to the drug. [6] Other well-documented aetiological associations of EM include herpes virus [1,2] and *Mycoplasma pneumoniae.*[3] Unfortunately, there were no facilities for serological studies in the present case to exclude viral, or *Mycoplasma pneumoniae* involvement. However, individuals with herpes-associated EM tend to have recurrent episodes of the disease following a recurrent attacks of herpes; furthermore, the distribution of skin lesions is frequently similar for each recurrent episode. [6] Recurrences with mycoplasma-associated EM are said to be uncommon. [3,7]

The basis for incriminating pyrimethamine-sulfadoxine in the present case, is that for each of the eight episodes of the illness, the child had ingested the drug prior to the eruption of lesions. Erythema multiforme due to virus infection is often mild, but the severe type (Stevens-Johnson syndrome) is often the result of drug sensitivity.[4,7] Such association must be recognised early and the offending drug stopped; fatalities are not uncommon when the severe form of the disease progresses to widespread epidermal necrosis with secondary bacterial infection and cardiovascular collapse. [6,8]

The present case therefore, calls for caution in the indiscriminate use of drugs. The current emergence of chloroquine-resistant malaria in Nigeria,[9] has brought in its wake, widespread use of sulphonamide-containing agents as alternatives. In many developing societies, such drugs are obtainable partly on prescription, but much more frequently, they are obtained off-the-counter without any prescription from a physician. More disturbingly, the use of *Fansidar* may not necessarily be limited to medically-diagnosed malaria, but rather to indiscriminate use by the lay person, as the case with our patient. Clinicians should, therefore, be on the alert to a possible upsurge of not just the prevalence, but also to the recurrent episodes of both the minor and major forms of erythema multiforme in areas of malaria endemicity, particularly where self-medication with sulpha-containing anti-malarial drugs is widespread.

References

1 Muff JC. Acyclovir for recurrent erythema multiforme caused by herpes simplex. *J Am Acad Dermatol* 1988; **18**: 197-9

2 Shelley WB. Herpes simplex as a cause of erythema multiforme. *JAMA* 1967; **201:** 153-6.

3 Ludlam GH, Bridges JB and Bonn EC. Association of Stevens-Johnson syndrome with antibody for *Mycoplasma pneumoniae*. *Lancet* 1964; **1:** 958-9.

4 Bianche JR. Drugs as aetiologic factors in the Stevens- Johnson syndrome. *Am J Med* 1968; **44:** 390-405.

5 Lawson DH and Paice J. Adverse reactions to trimethoprim-sulphamethoxazole. *Rev Infect Dis* 1982;**4:** 420-33.

6 Edmond BJ, Huff JC and Weston WL. Erythema Multiforme. *Pediatr Clinic N Am* 1983; **30**:631-40.

7 Rasmussen JE. Update on the Stevens-Johnson syndrome. *Cleveland Clin J Med* 1988; **55:**412-44.

8 Wuepper KD, Watson PA and Kazmierowski JA. Immune complexes in erythema multiforme and the Stevens-Johnson syndrome. *J Invest Dermatol* 1980; **74**: 368-71.

9 Ekanem OJ, Weisfield JS, Salako LA, Nohlen RL, Ezedinachi ENU, Walker O, Brenon JC, Laoye CJ and Hedberg K. Sensitivity of *Plasmodium falciparum* to chloroquine and sulfadoxine/ pyrimethamine in Nigerian children. *Bull Wld Hlth Org* 1990; **68**: 45-52.