Toxic Epidermal Necrolysis After Topical Intranasal Application of Mupirocin

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ABSTRACT

We describe a case of toxic epidermal necrolysis after intranasal application of mupirocin in a 76-year-old woman. The drug was given for eradication of methicillin-resistant *Staphylococcus aureus* (*Infect Control Hosp Epidemiol* 2003;24:459-460).

Toxic epidermal necrolysis (TEN) is characterized by an erythemato-bullous skin eruption followed by epidermal necrolysis with skin scaling and mucosal involvement. The general consequences are extended burns. Mortality is approximately 20% to 30%, increasing with age and the extent of the lesions.[1,2] The most severe complications are sepsis and ocular involvement. The mechanisms responsible for the accelerated apoptosis of the keratinocytes remain unclear, but, besides multiple factors, drugs are clearly implicated. Many agents are deemed responsible for TEN. Among the most frequently cited are nonsteroidal anti-inflammatory drugs, sulfonamides, and anticonvulsants.[3] Until now, TEN occurring after topical intranasal applications of mupirocin has never been described.

CASE REPORT

A 76-year-old woman with a tracheostomy after operation for an oropharyngeal carcinoma was admitted to our hospital for ventilatory weaning. Her usual medications were prednisone, ipratropium bromide, salbutamol, citalopram, hydrochlorothiazide, lisinopril, aspirin, and acetaminophen. She had been treated with the same medication regimen for several weeks before entering our hospital. She was allergic to penicillin and had asthma.

Eighteen days later, sputum cultures yielded methicillin-resistant *Staphylococcus aureus*. The patient was isolated, bathed with chlorhexidine once a day, and treated with mupirocin intranasally twice a day. Two days later, a skin eruption of a maculo-erythematous type appeared around the nares, evolving rapidly into bullae and extending to the cheeks and neck, accompanied by a fever (temperature, 38°C and higher). The patient had been given two baths with chlorhexidine and four intranasal applications of mupirocin before the onset of the rash. Despite the discontinuation of intranasal mupirocin and the chlorhexidine baths, the skin lesions progressed in the form of large bullae involving the face and upper trunk, covering approximately 20% of the body surface area. A positive Nikolsky sign confirmed the clinical diagnosis of TEN. With the consent of the patient, considering her dismal oncologic prognosis and bedridden state, no life support was started. Five days after the eruption of the dermal lesions, the patient died of sepsis.

DISCUSSION

In this patient, TEN appeared after the application of mupirocin for eradication of methicillin-resistant *S. aureus*. It is highly probable that mupirocin, introduced 2 days before the appearance of the skin disease, was the cause because, except for chlorhexidine skin antisepsis given at the same time, no other medication had been introduced during the 4 preceding weeks. In particular, acetaminophen, often cited as a cause of TEN,[4] had been given for many weeks for the patient's chronic pain due to the oropharyngeal carcinoma. The cutaneous application of chlorhexidine has been followed by anaphylactoid and immediate or delayed skin reactions of eczematous or urticarial type, but has never been implicated as a cause of bullous lesions.[5,6] Mupirocin is usually well tolerated, but can occasionally induce burn-type lesions, rash, edema, and exudation.[7]

In 1987, Daly reported a case of vesicular dermatitis following the topical administration of mupirocin in a patient suffering from a chronic stasis dermatitis.[8] Mupirocin contains polyethylene glycol as an excipient, a product well known for its allergenic properties.[8-10] In our case, however, mupirocin for nasal use contained no polyethylene glycol, which is ill tolerated by the mucosal surfaces (ie, causing irritation, dryness, and pruritus), but did contain paraffin and glycerin esters.

Our patient developed TEN 48 hours after topical intranasal applications of mupirocin. It seems reasonable to imply a highly probable relationship between TEN and the application of mupirocin, although such a phenomenon has never been described in the literature. Our patient was atopic, with an allergy to penicillin, and was suffering from asthma; she also had damaged facial skin and nasal mucosa due to former intubation and the presence of a nasogastric suction tube. All of these elements might have enhanced a hypersensitivity reaction to the nasal application of mupirocin, provoking TEN.

Except for a re-exposure trial, one can never be certain that a drug is responsible for TEN. Nevertheless, many arguments seem to corroborate the hypothesis that mupirocin was indeed implicated in the TEN of this patient.

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Transmission of Methicillin-Resistant *Staphylococcus aureus* in the Neonatal Intensive Care Unit From a Patient With Community-Acquired Disease

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ABSTRACT

Methicillin-resistant *Staphylococcus aureus* (MRSA) has traditionally been a nosocomial pathogen. However, several recent studies have noted community-acquired MRSA among young, healthy patients with no risk factors or healthcare system exposure. We report the transmission of a strain of community-acquired MRSA in our neonatal intensive care unit (*Infect Control Hosp Epidemiol* 2003;24:460-461).

Staphylococcus aureus is a major cause of nosocomial and community-acquired infections. Since the first report of methicillin-resistant *Staphylococcus aureus* (MRSA) in 1960,[1] MRSA has spread throughout the world. Traditionally, MRSA infections have been acquired almost exclusively in hospitals, long-term–care facilities, and similar institutional settings. When cases of MRSA infection have been identified in the community, investigation usually reveals prior contact with the healthcare system such as a history of recent hospitalization, close contact with a person who has been hospitalized, or other risk factors such as previous antimicrobial drug therapy.[2,3] We report transmission of an isolate of community-acquired MRSA in our neonatal intensive care unit.

CASE REPORT

A 22-year-old pregnant African American woman was admitted to our hospital with a history of prolonged rupture of membranes for 6 days and for chorioamnionitis. The patient had no prior history of hospitalization, surgery, work or residence in a long-term–care facility, or injection drug use. She underwent a primary transverse cesarean section on the day of admission because of arrest of dilatation. The patient received ampicillin for group B *Streptococcus* prophylaxis. The neonate born was admitted to the neonatal intensive care unit with an Apgar score of 6 after 5 minutes, a body temperature of 39°C, and the need for oxygen. The blood cultures performed for the neonate on the first day of life were positive for MRSA and *Enterococcus faecalis*. The mother was given clindamycin and gentamicin due to extensive blood loss and fever, which were changed after 24 hours to metronidazole and levofloxacin due to acute renal failure. The fever did not resolve and blood cultures performed for the mother on the second day of admission were positive for MRSA. The two isolates were sensitive only to gentamicin, rifampicin, and vancomycin. The mother and neonate were each treated with vancomycin and responded well to therapy.

Routine weekly surveillance cultures for MRSA in the neonatal intensive care unit 7 days after the admission of the neonate revealed nasal MRSA colonization in a different neonate who had been admitted to the NICU 3 weeks previously. Surveillance cultures of this second neonate had been negative prior to the admission of the neonate with MRSA sepsis.

RESULTS

Pulsed-field gel electrophoresis (PFGE) was performed after digestion with *Sma*I on MRSA isolates of all three patients. All strains had an identical PFGE banding pattern, suggesting one clonal PFGE subtype (Figure). This PFGE pattern differed significantly from that of MRSA strains previously recovered in the neonatal intensive care unit or adult inpatient areas of our hospital. Our findings suggest transmission of community-acquired MRSA in the neonatal intensive care unit.

DISCUSSION

The SENTRY Antimicrobial Surveillance Program found an increase of MRSA among both nosocomial and community-onset strains (from 34% in 1997 to 45% in 1999 for nosocomial MRSA, and from 21% in 1997 to 27% in 1999 for community-acquired MRSA) in the United States.[4] The increase in community-acquired MRSA infections among patients admitted to hospitals has the potential to increase the prevalence and risk of nosocomial infections due to MRSA.[5] Patients with community-acquired MRSA likely have not had prior contact with the healthcare system, and therefore may not be suspected of having MRSA infection or colonization. This may result in a delay of the implementation of contact isolation precautions for MRSA as recommended by the Centers for Disease Control and Prevention.[6]

The mother had had prior contact with the healthcare system due to prenatal care. More detailed questioning after the result of the blood culture was known also revealed that she had been caring for an individual with a chronic wound infection. Whether that individual was MRSA positive remained unknown. Considering the antimicrobial susceptibility pattern of the strain and the PFGE result, it seems possible that the strain was acquired from the individual with the chronic wound infection.

The impact on the number of nosocomial MRSA infections in a particular hospital will be influenced by the prevalence of MRSA acquisition in the community,