10. Douglas CWI, Heath J, Hampton KK, Preston FE: Identity of viridans streptococci isolated from cases of infective endocarditis. Journal of Medical Microbiology 1993, 39: 179–182.

Toxic Epidermal Necrolysis Associated with *Mycoplasma pneumoniae* Infection

Toxic epidermal necrolysis (or Lyell syndrome) is a life-threatening skin disease characterized by extensive detachment and necrosis of the epidermis and mucous membrane erosions (1). The relationship between toxic epidermal necrolysis and Stevens-Johnson syndrome remains unclear. Unlike Stevens-Johnson syndrome, drugs are the only well-documented etiology of toxic epidermal necrolysis. We report here a case of toxic epidermal necrolysis associated with *Mycoplasma pneumoniae* infection.

A 16-year-old girl was referred on 10 March 1992 to the dermatological intensive care unit because of toxic epidermal necrolysis. She first developed pharyngitis and nonproductive cough on 5 March. The skin lesions had begun on 6 March, with oral erosions. At admission, physical examination revealed generalized blisters, with positive Nikolsky sign and confluent areas of sloughing epidermis. Areas of skin denudation covered 45 % of the body surface. She presented with conjunctivitis and widespread erosions of the lips, mouth and genitalia. She also had a moderate pericardial effusion and severe respiratory distress syndrome with diffuse bilateral pulmonary infiltrates, and required intubation and ventilatory support. Histological examination of a skin biopsy showed full-thickness necrosis of the epidermis, characteristic of toxic epidermal necrolysis. Serological investigations (enzyme immunoassay) revealed a high titer (> 1/1,000) for *Mycoplasma pneumoniae* antibodies (including IgM antibodies) and cold agglutinins. Serological tests for HIV, viral hepatitis, parvovirus B19, Coxsakieviruses, herpes virus, rubella, measles virus, legionella and chlamydiae were negative or showed low residual titers. *Mycoplasma pneumoniae* pneumonitis was suspected, and ciprofloxacin (1 g/day) was administered. The cutaneous lesions, pericardial effusion and pulmonary lesions gradually resolved, and the patient was extubated after one month.

An inquiry revealed that she had taken several drugs before the onset of toxic epidermal necrolysis: mefenamic acid, phloroglucinol, bacterial extracts and a combination of acetylcysteine, thuaminoheptane and benzalkonium. It was doubtful whether toxic epidermal necrolysis could be attributed to any of these drugs according to the French Pharmacovigilance algorithm because of nonsuggestive chronologic relationship (2). In addition, the patient took these drugs only occasionally and a few months prior to occurrence of toxic epidermal necrolysis.

In contrast with the doubtful relationship of the drug history to toxic epidermal necrolysis, *Mycoplasma pneumoniae* infection was associated with high antibody titers for IgM antibodies and cold agglutinins. The pericardial effusion and severe pulmonary involvement were probably related to mycoplasma infection. Pulmonary lesions of unknown mechanisms have been previously described in the course of toxic epidermal necrolysis. To the best of our knowledge, pericardial effusion has never been reported before. In this particular case, the *Mycoplasma pneumoniae* infection seemed more likely to be responsible for the disease than the drugs, unless one postulates some interaction between the infection and previously well-tolerated drugs. That kind of interaction has been well documented for some viral infections, especially with Epstein-Barr virus and cytomegalovirus. To our knowledge it has never been suspected before in infection with *Mycoplasma pneumoniae.*

Mucocutaneous lesions occur in approximately 25 % of *Mycoplasma pneumoniae* infections (3). They are more often macular and papulovesicular rashes. Several cases of erythema multiforme or Stevens-Johnson syndrome have also been reported (4).

The classification of Stevens-Johnson syndrome remains disputed, and its boundaries with toxic epidermal necrolysis are not well defined. A classification was recently proposed separating Stevens-Johnson syndrome from toxic epidermal necrolysis on the basis of the extent of skin denudation (5). According to that classification, the denomination of Stevens-Johnson syndrome should be restricted to cases with blisters and erosions involving less than 10 % of the body surface area. Cases with detachment on more than 30 % should be classified as toxic epidermal necrolysis and those with 10 to 30 % as Stevens-Johnson/toxic epidermal necrolysis overlaps. In none of the previously published cases relating

Stevens-Johnson syndrome to *Mycoplasma pneumoniae* infection were blisters and epidermal detachment extensive enough to suggest a diagnosis of toxic epidermal necrolysis and to endanger the lives of patients.

A few cases of toxic epidermal necrolysis have been related to other infections such as viral hepatitis (6) and rubella. In an epidemiologic study of toxic epidermal necrolysis in France, 10 of 253 patients denied taking any drugs before the onset of the disease. Of these ten patients, two had some serological findings suggesting recent *Mycoplasma pneumoniae* infection (7). Our case report and the previous epidemiologic study suggest that *Mycoplasma pneumoniae* infection may be related to toxic epidermal necrolysis. Whether the infection is a direct cause or a precipitating factor remains difficult to ascertain.

S. Fournier[1]*, S. Bastuji-Garin[2], H. Mentec[3], J. Revuz[2], J.C. Roujeau[2]

[1] Service de Maladies Infectieuses, Hôpital de l'Institut Pasteur, Université Paris V, 211 rue de Vaugirard, 75015 Paris, France.
[2] Service de Dermatologie, and [3]Service de Réanimation Médicale, Hôpital Henri Mondor, Université Paris XII, Créteil, France.

References

1. Bianchine JR, Malaraeg PV, Lasagna L, Azamoff DL, Brunk F, Hvidberg EF, Owen JA: Drugs as etiologic factors in the Stevens-Johnson syndrome. American Journal of Medicine 1968, 44: 390–405.
2. Moore N, Biour M, Paux G, Loupi E, Begaud B, Boismare F, Royer RJ: Adverse drug reaction monitoring: doing it the French way. Lancet 1985, ii: 1056–1058.
3. Cassel GH, Cole BC: Mycoplasma as agents of human disease. New England Journal of Medicine 1981, 204: 80–89.
4. Ludlam GB, Bridges JB, Benn EC: Association of Stevens-Johnson syndrome with antibody for *Mycoplasma pneumoniae*. Lancet 1964, i: 958–959.
5. Bastuji-Garin S, Rzany B, Stern RS, Shear NH, Naldi L, Roujeau JC: Clinical classification of cases of toxic epidermal necrolysis, Stevens-Johnson syndrome, and erythema multiforme. Archives of Dermatology 1993, 129: 92–96.
6. Werblovsky-Constantini N, Livshin R, Burstein M, Zeligwski A, Tur-Kaspa R: Toxic epidermal necrolysis associated with acute cholestatic viral hepatitis A. Journal of Clinical Gastroenterology 1989, 11: 691–693.
7. Roujeau JC, Guillaume JC, Fabre JP, Penso D, Fléchet ML, Girre JP: *Toxic epidermal necrolysis (Lyell syndrome)*. Incidence and drug etiology in France, 1981–1985. Archives of Dermatology 1990, 126: 37–42.

Fluconazole in the Treatment of Three Cases of Mucormycosis

Mucormycosis is a severe, often fulminating infectious disease caused by fungi of the order *Mucorales*. It can present in various clinical forms, the most common being rhinocerebral mucormycosis (1). The disease usually affects patients with underlying disorders that impair the immune system. Treatment of this highly fatal infection includes control of the underlying disease, surgical debridement and systemic antifungal therapy (2). We report on three patients diagnosed as having rhinocerebral mucormycosis and effectively treated with fluconazole.

Case 1 was a 20-year-old woman who had been diagnosed to have aplastic anemia in 1990. She was given various immunosuppressive drugs including cyclosporin and antilymphocyte globulin. In 1993 her aplastic anemia transformed into paroxysmal nocturnal hemoglobinuria, and she was treated with corticosteroids. In March 1993 she presented with pain and swelling in her left eye. Her blood glucose level was 240 mg/dl. She was admitted to the hospital with diagnosis of secondary diabetes and possible sinus infection. The results of a physical examination were normal except for the swelling and pain around the left eye, ptosis of the left eye and a temperature of about 38°C. Laboratory investigations revealed hemoglobin level 7.2 g; leukocyte count 2,200/mm^3 (absolute neutrophil count 1,000/mm^3); and platelets 12,000/mm^3. Steroids were discontinued, and insulin and antibiotics started. A CT scan of the facial sinuses disclosed left ethmoidal sinusitis. A fungus resembling a mucoraceous species was detected in a biopsy specimen of the drainage from the deep, left nasal cavity. The patient was put on fluconazole 200 mg b.i.d. intravenously. The fever resolved in three weeks. The absolute neutrophil count remained at a low level of 1,500/mm^3. Fluconazole treatment was continued for six weeks until the pain and swelling of the eye completely disappeared. A dose of 200 mg of fluconazole orally was continued for another two weeks, then