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Life-threatening toxic epidermal necrolysis during voriconazole therapy for invasive aspergillosis after chemotherapy

In patients with invasive aspergillosis, initial therapy with voriconazole led to better responses and improved survival and

resulted in fewer severe side effects than the standard approach of initial therapy with amphotericin B [1]. We report a case of life-threatening toxic epidermal necrolysis related with the use of voriconazole in a patient with pulmonary invasive aspergillosis.

A 39-year-old man affected by breast cancer with brain and lung metastases developed a pulmonary aspergillosis during chemotherapy (Cisplatin 60 mg/m^2 day 1, 21, Epirubicin 50 mg/m^2 day 1, 21 and continuous infusion 5-fluorouracil 200 mg/m^2 day 1–21). We started voriconazole treatment with two doses of 6 mg per kilogram of body weight on day 1, then 4 mg per kilogram twice daily for seven days followed by 200 mg orally twice daily. Concomitant drugs were phenythoine 100 mg twice daily and subcutaneously dexamethasone 4 mg once daily (the two drugs were both assumed since 14 weeks). Chemotherapy was discontinued. Five days after the oral voriconazole was started, the patient noticed a rash, and all drugs were discontinued. Within three days, he had fever and diffuse erythema of the trunk, extremities, and face, with blistering skin lesions and positive Nikolsky's sign on erythematous areas, characteristic of toxic epidermal necrolysis. Rash and detachment toxic epidermal necrolysis involved 85% of the body surface (Figure 1). The conjunctivae were injected, and multiple bullae and ulcers were present on the lips and oropharyngeal mucosa. Skin biopsy histology showed necrosis of cells from the basal layer and *stratum spinosum* resulting in detachment of the epidermis from the dermis as toxic epidermal necrolysis. Patient had impaired alimentation, photophobia, and haematuria. Blood cultures yielded gram-negative rods later identified as *Pseudomonas aeruginosa*, sensitive to imipenem. Due to clinical conditions the patient was hospitalized in the intensive care unit. We treated the patient with human intravenous immunoglobulins at dose of 0.5 g/kg of body weight per day for four consecutive days [2], adding imipenem 4 g per day in four administrations for 10 days. The patient recovered after 2 weeks of intensive therapy.

To our knowledge, this is the first report of voriconazole related toxic epidermal necrolysis. Voriconazole is a new broad-spectrum triazole that has been demonstrated as superior over amphotericin B as initial therapy for invasive aspergillosis, in terms of response rate, survival rate, and safety. Caution should be exercised when combining voriconazole with other drugs known to cause skin reaction, such as phenythoine.

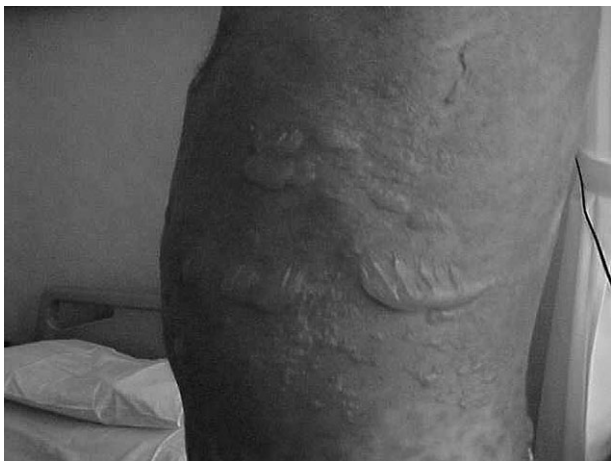

Figure 1. Rash and detachment toxic epidermal necrolysis involving 85% of the body surface following therapy with voriconazole.

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