

Letters to the Editor

Pleural Diffusion of Voriconazole in a Patient with *Aspergillus fumigatus* Empyema Thoracis

Fungal empyema is an emerging clinical entity associated with a high mortality rate (1). We describe a case of a patient with empyema thoracis due to *Aspergillus fumigatus* successfully treated by chest tube drainage associated with voriconazole (VZ). Pleural concentrations of VZ demonstrated adequate pleural diffusion of this drug.

An 82-year-old patient was admitted for weight loss and a left pleural air-fluid level. He did not take immunosuppressive drugs. One year prior to the current admission, he underwent video-assisted thoracoscopy for an unexplained left pleural effusion. Pathological and microbiological analyses of the pleura were negative. One month after the video-assisted thoracoscopy, he developed a left pleural empyema due to *Staphylococcus epidermidis*. Plasma C-reactive protein (CRP) was 95 mg/liter (normal, <5 mg/liter). The patient underwent chest tube drainage and 6 weeks of oxacillin. A chest X ray showed disappearance of the pleural fluid. CRP decreased to 48 mg/liter. Ten months later, he was readmitted for persistent fatigue and weight loss. A chest X ray and a thorax computerized tomography scan showed reappearance of an air-fluid level in the left pleural space with pleural thickening. CRP was 116 mg/liter. The pleural fluid was macroscopically purulent. Microscopic examination showed 99% polymorphonuclear cells and mold cells that were identified as *A. fumigatus*. The patient underwent chest tube drainage and pleural irrigation once a day with a saline-iodine solution. Ten days later, a sample of pleural fluid showed persistence of *A. fumigatus*. Antifungal therapy was initiated with VZ, 200 mg twice daily from day 0 to day 14 (for 70 kg of body weight). The dose was then increased to 300 mg twice daily. On days 12 and 22, plasma and pleural

VZ levels were measured 2 h after oral intake (C_{2h}) and at trough (C_{tr}) (Table 1) by solid-phase extraction followed by reversed-phase liquid chromatography with UV detection. Progressively, the physical status of the patient improved. Microbiological analysis of the pleural fluid at the same time as VZ measurements was negative. The chest tube was removed, and the patient was discharged from the hospital. He continued taking VZ at 300 mg twice daily. Six months later, the patient was well and had gained 5 kg. The air-fluid level had completely disappeared on the chest X ray, and CRP was 9 mg/liter.

In patients with empyema, the pleural surface is thicker and more acid. The pleural diffusion of antibiotics is highly variable (3). VZ, an expanded-spectrum azole antifungal, is approved for the treatment of patients with invasive aspergillosis. Recommended steady-state concentrations in plasma range from 2 to 3 mg/liter (2). The penetration of pleural fluid by VZ has not been previously studied. We demonstrated in a patient with empyema due to *A. fumigatus* that VZ penetrated the pleural fluid, sterilized the pleural cavity, and was therefore the probable direct cause of his cure.

REFERENCES

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TABLE 1. VZ levels in plasma and pleural fluid

Day (dose)	VZ concn (mg/liter) in:			
	Plasma		Pleural fluid	
	C_{2h}	C_{tr}	C_{2h}	C_{tr}
12 (200 mg twice a day)	1.24	0.95	0.8	0.9
22 (300 mg twice a day)	3.1	1.4	1.4	1.2

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