Acute Lung Infiltrates in a Child With Chronic Granulomatous Disease: Is It Voriconazole-Induced Lung Injury?

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Voriconazole has been used in clinical practice for approximately 15 years. Since its introduction, many adverse effects related to the use of voriconazole have been reported. Photosensitivity, hepatotoxicity, and visual disturbances are commonly reported side effects. Hallucinations, insomnia, periostitis, encephalopathy, peripheral neuropathy, alopecia, nail changes, and cutaneous malignancy are relatively less common side effects of voriconazole.^{1–3} All these adverse effects are related to prolonged use of the drug, and little is known about its idiosyncratic reactions.

A 3-year-old boy, diagnosed to have chronic granulomatous disease (CGD), presented with fever, cough, and respiratory distress for 10 days. On examination, he had tachypnea, tachycardia, SpO₂ of 96%, and bilateral chest crepitations. The rest of the physical examination was unremarkable. Laboratory investigations revealed hemoglobin 67 g/L, white cell counts $22.2 \times 10^9/L$ (polymorphs 52%; lymphocytes 40%), erythrocyte sedimentation rate 76 mm in the first hour, and C-reactive protein 50 mg/L. Blood culture was sterile. The chest x-ray showed non-homogenous opacities in bilateral lung fields. Serum galactomannan index was 0.27 (normal < 0.5), but serum β -D-glucan was 229 pg/mL (normal < 60 pg/mL). A possibility of fungal pneumonia was considered, and treatment with intravenous amphotericin B (4 mg/kg/day) was initiated. In addition, he was also given intravenous vancomycin (15 mg/kg/dose, 8 hourly) and oral levofloxacin (10 mg/kg/dose, 12 hourly). By day 4 of the hospital stay, fever and respiratory distress subsided and a chest x-ray done on day 10 of the hospital stay showed minimal infiltrates and hyperinflation (Figure A). Injection

amphotericin B was discontinued, and oral voriconazole (9 mg/kg/dose, 12 hourly) was initiated. After 3 doses of voriconazole, he developed sudden onset respiratory distress with hypoxia. A chest x-ray showed infiltrates in bilateral lung fields (Figure B). Two-dimensional echocardiography revealed no abnormality. Rapid improvement of respiratory distress and resolution of chest infiltrates (Figure C) was noted 5 days following discontinuation of voriconazole.

Acute lung injury secondary to voriconazole has rarely been reported.⁴ The mechanism of this toxicity is not known but may be an idiosyncratic reaction. Our patient also showed features of acute lung injury following oral voriconazole. Because the lung injury resolved following discontinuation of voriconazole and since the Naranjo Adverse Drug Reaction Score⁵ suggested that this adverse effect was probably due to the drug, a diagnosis of voriconazole-induced lung injury was made. This is perhaps the first case reported of acute lung injury secondary to voriconazole in the pediatric age group.

Sandesh Guleria, MD
Ankur Kumar Jindal, MD
Deepti Suri, MD
Amit Rawat, MD

ARTICLE INFORMATION

Affiliations Pediatric Allergy Immunology Unit, Advanced Pediatrics Centre, Postgraduate Institute of Medical Education and Research, Chandigarh, India (SG, AKJ, DS); Pediatric Allergy Immunology Unit, Advanced Pediatrics Centre, Postgraduate Institute of Medical Education & Research (AR)

Figure. Chest x-rays of the patient. A, Chest x-ray 2 days prior to initiating voriconazole showing hyperinflation and minimal infiltrates. B, Chest x-ray 24 hours after initiating voriconazole showing bilateral diffuse inhomogeneous opacities (right > left). C, Chest x-ray 5 days after discontinuing voriconazole showing resolution of infiltrates.

Correspondence Sandesh Guleria, MD;
guleriasandesh662@gmail.com

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Ethical Approval and Informed Consent Given the nature of this report, it was exempt from institution review board/ethics committee review.

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