A Case of Optic Neuropathy after Short-Term Linezolid Use in a Patient with Acute Lymphocytic Leukemia

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A patient undergoing chemotherapy for treatment of acute lymphocytic leukemia developed septicemia that was treated with linezolid for 16 days. The patient subsequently reported reduced vision in both eyes and was found to have bilateral optic neuropathy. After the discontinuation of linezolid treatment, both the optic neuropathy and visual impairment resolved without sequelae.

Linezolid is part of a new class of antibiotics (oxazolidinones) with activity against methicillin-resistant Staphylococcus species, penicillin-resistant Streptococcus species, and vancomycin-resistant enterococci [1]. There have been several reported cases of linezolid-associated toxic optic neuropathy [2]. All of these reported cases have all been associated with the long-term use of linezolid (5–10 months), except for 1 recent reported case of an irreversible optic neuropathy that occurred after 16 days of linezolid treatment [3]. We describe a case of linezolid-associated toxic optic neuropathy that also occurred as a consequence of short-term linezolid treatment (16 days) of vancomycin-resistant Enterococcus infection. In contrast to the case reported by Azamfirei et al. [3], optic nerve edema and visual function both improved after cessation of the linezolid treatment.

Case presentation. A 29-year-old woman received a diagnosis of acute lymphocytic leukemia a few weeks before admission to the hospital with increasing dyspnea and malaise. She received chemotherapy 4 days after hospital admission (UK-ALL XII induction protocol); her regimen included vincristine, daunorubicin, intramuscular L-asparaginase, and intrathecal methotrexate. On day 33 after hospital admission, she became pyrexial with some associated neck stiffness. CT findings were unremarkable, but her C-reactive protein level was increased at 131 mg/dL (normal range, 0–6 mg/dL). Blood cultures and a lumbar puncture were performed, and treatment with piperacillin with tazobactam and gentamicin was commenced. Coagulase-negative Staphylococcus species was cultured from her lumbar puncture sample, and the following day, she developed a chest infection and became increasingly unstable. Her antimicrobial treatments were changed to meropenem, vancomycin, and rifampicin, but her respiratory condition continued to deteriorate. She was admitted to the intensive care unit and required intubation on day 38. Vancomycin-resistant enterococci were discovered in sputum and urine specimens; rifampicin treatment was stopped at this point, and linezolid was substituted for vancomycin.

When the patient regained consciousness, she noticed reduced vision in both eyes. On examination, she had visual acuities of 6/36 in the right eye and 6/6 in the left eye, which was associated with reduced color vision in the right eye on testing with Ishihara plates and a right-relative afferent pupillary defect. Fundoscopy revealed bilateral optic nerve edema that was worse in the right eye, and she received a diagnosis of bilateral optic neuropathy. The short-term use of linezolid was suspected to be the cause, possibly exacerbated by the previous course of rifampicin. By this stage, linezolid treatment had been stopped, and there was a gradual improvement in her visual acuity to 6/6 in both eyes during the following 4 weeks and a complete resolution of optic nerve swelling and function within 6 weeks.

Discussion. Toxic optic neuropathies are usually bilateral and can be associated with a number of antimicrobials, including ethambutol and isoniazid; more than one-third of drug-induced toxic neuropathies are attributable to antibiotic therapy [4]. There have been several cases describing linezolid-induced toxic optic neuropathy, reviewed elsewhere [2]. All of these cases were associated with the long-term use of linezolid (5–10 months, which is in excess of the maximum treatment duration of 28 days stipulated in its product license); in the case presented here, optic neuropathy occurred after only 16 days of therapy. One other case report of linezolid-induced
toxic optic neuropathy after short-term therapy exists, but it was associated with irreversible blindness in a patient with muscular dystrophy [3]. Recovery of reduced vision has, however, been previously reported after cessation of antimicrobial treatment [7].

Linezolid is part of the oxazolidinone class of antibiotics that inhibit bacterial protein synthesis by binding to the 70S ribosomal initiation complex [8]. Although this complex is not present in mammalian cells, a recent study has demonstrated reduced mitochondrial respiratory chain enzyme activity in experimental animals and in a patient receiving linezolid therapy who developed optic neuropathy [9]; this finding suggests that mammalian mitochondria are vulnerable [2]. The process involved in linezolid-induced toxic optic neuropathy may be similar to the respiratory chain dysfunction observed in mitochondrial optic neuropathies (e.g., Leber hereditary optic neuropathy), although the exact mechanism of action is unclear. It has previously been suggested that coadministration of ciprofloxacin or rifampicin may potentiate the toxicity of linezolid, although no mechanism has been postulated, and this patient did not receive rifampicin and linezolid concurrently [10].

It is unlikely that this bilateral optic neuropathy was attributable to another cause. Possible infective causes include *Candida* infection and cryptococcal arachnoiditis, but optic nerve involvement only occurs in candidal infection in cases of *Candida* endophthalmitis [5], of which there were no clinical signs, and the patient was serum cryptococcal antigen negative throughout the hospitalization. There was also no evidence of viral retinitis or cerebral abscess, both of which can cause visual loss in immunosuppressed individuals. CNS leukemia can cause an infiltrative optic neuropathy [6], but CT and lumbar puncture findings did not support this diagnosis.

This case confirms the earlier report that linezolid can also cause optic neuropathy after a short treatment course [3]. However, in contrast to the other report [3], this case indicates that the optic neuropathy may be reversible and that visual recovery is associated with cessation of linezolid therapy.

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**References**