



CLINICAL CASE

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Pulmonary nocardiosis treated with tedizolid

Nocardiosis pulmonar tratada con tedizolid

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Introduction

Nocardiosis is an acute or chronic infection, often disseminated, suppurative, or granulomatous, which is caused by several microorganisms of the genus *Nocardia*. It mainly affects immunocompromised patients. The typical clinical picture is pneumonia, but skin and central nervous system (CNS) infections are also common. Associated mortality rates are high, ranging from 14% to 40% increasing to 60-100% when CNS disseminated infection occurs.

Pulmonary nocardiosis remains a difficult diagnostic entity because of its clinical and radiological nonspecificity. Diagnosis is established from the identification of *Nocardia* species in tissues or cultures of samples obtained from the lesions. The choice of treatment should be based on antibiogram.

Trimethoprim-sulfamethoxazole (TMP/SMX) is the antimicrobial of choice to treat pulmonary nocardiosis. Other antimicrobial agents with activity against *Nocardia* species include amikacin, imipenem, meropenem, ceftriaxone, cefotaxime, minocycline, levofloxacin, linezolid, tigecycline, and amoxicillin/clavulanic acid. In order to minimize the risk of relapse, treatment duration is generally from 6 months to 12 months¹.

Tedizolid is an oxazolidinone-class antibiotic with activity against gram-positive microorganisms. It is indicated in skin and soft tissue infections at a recommended dosage of 200 mg oral or IV once daily for six days^{2,3}. Experience of tedizolid in the treatment of pulmonary nocardiosis is anecdotal but promising, due to its good in vitro activity⁴ and excellent oral bioavailability, despite limited evidence on prolonged treatment.

We describe the efficacy and safety of prolonged treatment with tedizolid in a case of pulmonary nocardiosis.

Case description

A 47-year-old woman with COPD treated with β_2 adrenergic agonists combined with inhaled corticosteroids. There was no other history of interest and renal function was normal. She had returned from Venezuela, where she had a clinical picture of at least 10-months duration of cough with scarce hemoptoic expectoration, asthenia, and weight loss of at least 10 kg, accompanied by dyspnea with moderate exercise. Chest CT scan showed a cavitary-abscess lesion in the left lower lobe suggestive of infectious disease. The scan also showed small homogeneous hilar/mediastinal adenopathies, probably inflammatory, as well as calcified and non-calcified granulomas in the right upper lobe. Biopsy ruled out neoplasia and only confirmed an acute inflammatory component: thus, a diagnosis of pulmonary nocardiosis without infiltration was assumed. In March 2018, we began outpatient treatment with TMP/SMX. However, on April 21, 2018, treatment was suspended after she developed a diffuse erythematous nonpruritic painless rash, jaundice of the skin and eyes, and choloria.

On May 8, 2018, she was admitted to our hospital with TMP/SMX hepatotoxicity and persistent pulmonary lesion. We were unable to isolate and determine the *Nocardia* species, so antibiotic coverage was begun with imipenem and amikacin. The patient developed a skin rash after the administration of amikacin, which was replaced by linezolid 600 mg/12 h. On 23 May, 2018, the patient was discharged under a Home Hospitalization program and treated with intravenous imipenem, oral linezolid, and her usual inhaled treatment. On June 15, 2018, she developed anemia, thrombocytopenia, and neutropenia. We decided to maintain treatment with imipenem but suspend linezolid until hematologic recovery.

KEYWORDS

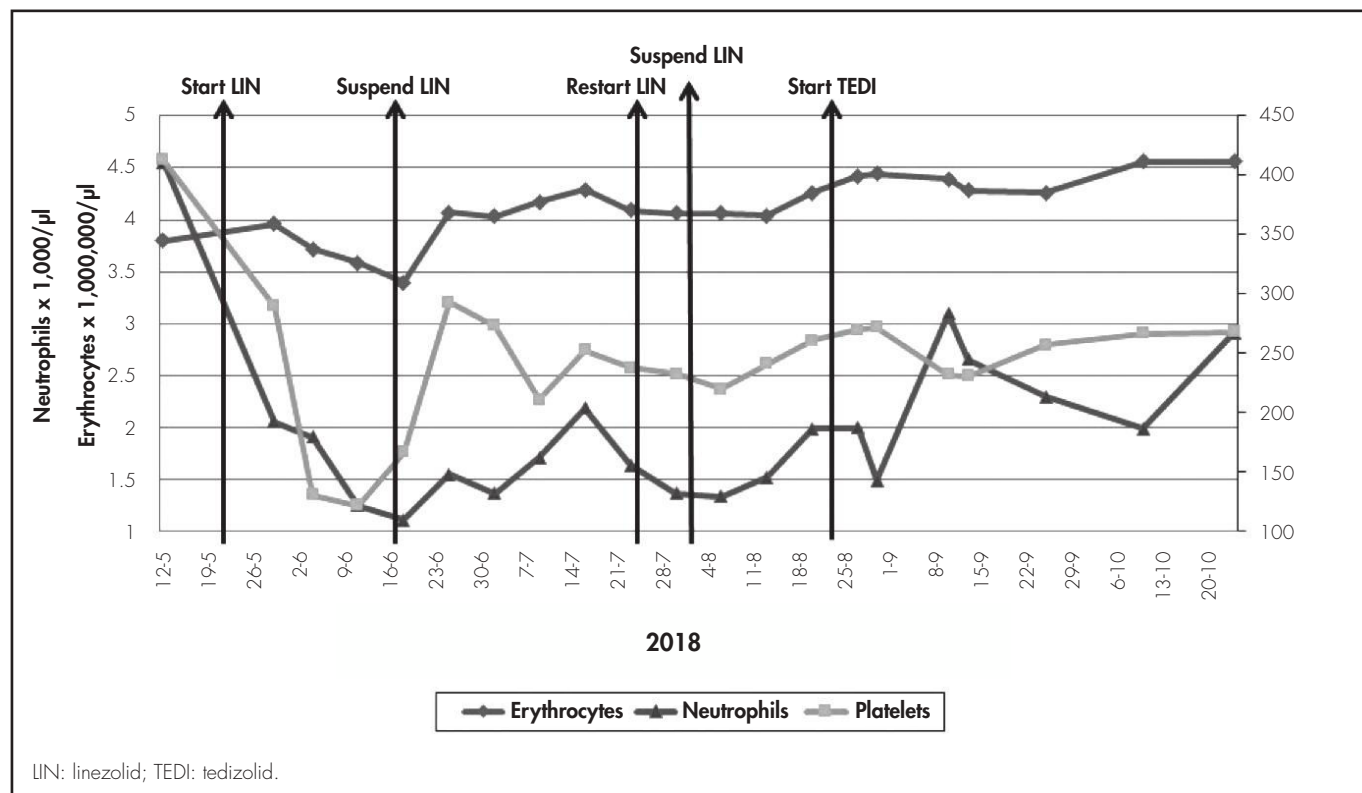
Oxazolidinones; Nocardiosis; Long Term Treatment; Tedizolid; Adverse reactions.

PALABRAS CLAVE

Oxazolidinonas; Nocardiosis; Larga duración; Tedizolid; Efectos adversos.



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Figure 1. Temporal variation of blood cell count during treatment with oxazolidinones.

On July 24, 2018, linezolid was restarted at a reduced dose of 600 mg/24 h; however, she developed new hematological disorders and so it was discontinued again. The patient continued on treatment with imipenem alone until August 23, 2018, when it was changed to oral tedizolid 200 mg/24 h. The patient had good tolerance to tedizolid and developed no adverse effects. Subsequent analyses showed gradual hematologic recovery until normal values were reached.

Two months after starting treatment with tedizolid (six months of total treatment), the patient was free of respiratory symptoms and hematologic values were within normal ranges (Figure 1). The last CT scan showed improvement with a scar-like lesion without liquid content or signs of abscess.

Discussion

We have described a case of the successful use of tedizolid for two months for the treatment of pulmonary nocardiosis in the setting of limited therapeutic options after ruling out the alternatives of choice due to the development of toxicity.

Oxazolidinones are interesting alternatives because of their good *in vitro* activity against most *Nocardia* species and their high oral bioavailability. Although there is limited clinical experience of the use of linezolid, its potential is hindered by the development of myelotoxicity in long-term treatments⁵. Tedizolid *in vitro* activity against *Nocardia* species is similar to or superior to that of linezolid⁴, although there is only anecdotal experience of the use of tedizolid in the treatment of nocardiosis. *Matin et al.* described a clinical case of the successful treatment of a patient with cerebral nocardiosis who completed six months of treatment with tedizolid and TMP/SMX without developing hematologic toxicity⁶.

Myelosuppression may be the limiting aspect of prolonged treatment with tedizolid. Two pivotal studies limited treatment duration to six days^{2,3}.

In a pooled analysis of these two studies, the incidence of hematologic abnormalities of tedizolid vs that of linezolid was expressed as the percentage of patients with counts below the lower limit of normal during the treatment period: thrombocytopenia (6.4% vs 12.5%; $P=0.0016$), neutropenia (1.9% vs 3.3%; $P>0.5$), and anemia (28.9% vs 31.3%; $P>0.5$)⁷. More recently, data from the Food and Drug Administration Adverse Event Reporting System suggested that linezolid and tedizolid had similar rates of thrombocytopenia⁸.

There are no studies on the efficacy and safety of prolonged treatment with tedizolid and experience is limited to the very few clinical cases that have been described. One study analysed a series of 24 patients who received tedizolid for mycobacterial infections. Median treatment duration was 101 days (range, 15-369 days). Adverse effects included the following: 5/24 patients experienced peripheral neuropathy, 3/24 muscle rigidity associated with the use of metoprolol suggestive of serotonin toxicity, 1/24 thrombocytopenia, 1/24 anemia, and 1/24 leukopenia⁹. A clinical case study reported treatment with tedizolid over a period of 18 months for a recurrent *Staphylococcus aureus* infection without evidence of the development of hematologic abnormalities¹⁰.

This case study of a patient with nocardiosis describes the experience of the effective use of tedizolid without the development of myelotoxicity.

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Conflict of interests

No conflict of interests.

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