Painful polyneuropathy secondary to prolonged treatment with linezolid: Presentation of a case

Polineuropatía dolorosa secundaria a tratamiento prolongado con linezolid: a propósito de un caso

Dear Editor:

Polyneuropathy is a common disease that requires an exhaustive aetiological study. Even so, the cause goes undiscovered on some occasions. Toxic neuropathies represent a small percentage of this group’s diseases; some cases may be reversible, which makes identifying them all the more important. At present, the appearance of new drugs such as linezolid means that we have to be especially alert in order to detect potential neurotoxic side effects that had not been described before those drugs were marketed.

Our patient was a 24-year-old female smoker (20 cigarettes per day) with no other history of drug use. She was being treated with paroxetine for depressive disorder and used a vaginal ring; there was no other relevant medical or surgical history. She was referred to the hospital by her primary care doctor, who had observed positive Mantoux and bacilloscopy in a contact tracing study; her partner had recently been diagnosed with pleuropulmonary TB. Upon admission, the patient was completely asymptomatic and reported no fever, wasting syndrome, or respiratory problems. We began treatment with isoniazid, rifampicin, and pyrazinamide. After checking for good tolerance to the treatment (the patient only showed a slight increase in urine acid caused by the pyrazinamide) and a negative bacilloscopy, the patient was discharged. Since the sputum culture was positive for Mycobacterium chelonae, tuberculostatic treatment was replaced with clarithromycin, ethambutol, and linezolid dosed at 1200mg daily. Three months after the treatment modification, she was readmitted for symptoms of dyspepsia, diarrhoea, and major asthenia. Analytical tests revealed normocytic

In conclusion, we would like to suggest considering treatment with an epidural blood patch even when more than 24 hours have passed since the onset of CNP. This treatment may significantly accelerate the patient’s recovery.

References


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anaemia (haemoglobin 6.8 mg/dl and 20.1% haematocrit). The patient also reported a painful dyseaesthetic sensation in both feet. Examination revealed superficial tactile hypoesthesia of the feet with Achilles tendon areflexia, patellar tendon hyporeflexia, mildly ataxic wide-based gait, and very slight heel-knee asymmetry. Results from the nerve conduction study were compatible with predominantly sensory and axonal neuropathy of the lower extremities. Analyses for vitamin B₁₂, folate, and folic acid, cryoglobulins, immuno- noelectrophoresis, serology studies (for Borrelia, Brucella, syphilis, hepatitis B and C, cytomegalovirus, HIV, herpetic simplex, and varicella zoster) and TSH were all normal. We also performed a visual evoked potential test and brain and cervical MRI scans; there were no pathological findings. Anaemia and digestive symptoms were studied with the aid of coprocultures, fibrogastrscopy, marked leukocyte scintigraphy, and bone marrow biopsy, all of which returned normal results. In principle, all symptoms are compatible with the side effects of linezolid treatment. The digestive problems and the anaemia both abated after suspension of the drug. The painful polyneuropathy of the lower limbs required invasive treatment in the pain unit. An epidural catheter with an infusion of levobupivacaine remained in place for approximately 1 month. A year later, the patient required treatment with oxcarbazepine, duloxetine and delayed-release tramadol. Although ethambutol was also administered in this case and may also cause peripheral neuropathy, the clinical manifestations with anaemia and gastrointestinal problems have already been described as side effects of linezolid. This leads us to believe that the polyneuropathy was secondary to linezolid, although we cannot rule out the possibility of a synergistic effect exerted by both drugs.

Linezolid is the first antibiotic in the oxazolidinone group to be effective against Gram-positive micro-organisms that are resistant to meticillin and vancomycin. The drug’s action profile and good level of tolerance among patients meant that its first main use was the treatment of chronic osteomyelitis and infections in prostheses. A treatment duration of less than 28 days was initially recommended, but prolonged use caused reversible myelosuppression in addition to other then unknown side effects, such as neutritis optical and polyneuropathy. A number of case studies have also shown linezolid to be effective in treating strains of *Mycobacterium tuberculosis* resistant to other first-line drugs. This is why continuing linezolid use more than 28 days is increasingly common, and the literature confirms a link between prolonged use and toxic neuropathy. Associating treatment with vitamin B₆ is proven to decrease the risk of blood toxicity. Although an article by Spellberg et al. claims that the drug does not seem to affect neuropathy, that article only refers to a series of 2 cases. A recently published study on treating multi-drug-resistant tuberculosis with linezolid includes 30 cases, of which 5 developed polyneuropathy. Of those 5 cases, 4 had been treated over 15–25 months, and increasing the vitamin B₆ dose improved neurological symptoms in a single case. In the last case, intractable polyneuropathy led doctors to suspend treatment in the fifth month. The same patient had poorly controlled diabetes mellitus, as did case 2 in the article by Rho et al. In both diabetic patients, painful neuropathy proved difficult to treat. Diabetes, even with no prior history of neuropathy, may be a concomitant factor that should be taken into account. The series of 85 patients published by Migliori et al. reports 3 cases of polyneuropathy. Doses of 1200 mg daily were administered in 2 of the cases; the remaining case received a daily dose of 600 mg. Furthermore, this article concludes that while drug effectiveness is the same for both doses, the rate of side effects is significantly higher for the higher dose (4 of the 28 patients on 600 mg/day had side effects vs 31 of the 57 patients on 1200 mg/day).

Lastly, we must point out that in all articles in the literature describing the characteristics of this type of neuropathy, the neuropathy was painful. We have also found a case description in which the nerve conduction study was normal, but cutaneous biopsy showed fine fibre neuropathy. Therefore, knowing that a patient experiencing neuropathic pain has been treated with linezolid is extremely relevant to the diagnosis of the neuropathy. Furthermore, this condition may become more widespread if linezolid use becomes more widespread and prolonged.

### References

Agenesis of posterior inferior cerebellar arteries in an asymptomatic adult with Dandy—Walker malformation*2

Agenesia de arterias cerebelosas postero-inferiores en adulto asintomático con malformación de Dandy Walker

Dear Editor:

Dandy—Walker malformation (DWM) is an uncommon condition characterised by agenesis or hypoplasia of the cerebellar vermis, the cerebellar hemispheres, and cystic dilation of the fourth ventricle. There are very few records of asymptomatic adults with DWM. Hypotonia and motor and mental developmental delay, together with supratentorial hydrocephalus, malformation of the corpus callosum, and macrocephaly, appear in children.1,2 This case history describes arterial agenesis associated with abnormal brain embryogenesis.

A 61-year-old female visited due to syncope. She had been taking medication for high blood pressure for 5 years (25 mg/day atenolol). Her medical history reported no motor or cognitive abnormalities. She was able to work and perform daily living activities normally. Blood tests, a 24-hour ECG, 24-hour blood pressure monitor test, a tilt test to measure response in terms of heart rate and blood pressure, and the EEG all delivered normal results. Findings from the neurological and cognitive tests were normal. Brain neuroimaging studies were performed. In Fig. 1, the sagittal brain MR image on the A side showed DWM. The supratentorial ventricles, cerebral cortex, corpus callosum, brainstem, and mesencephalic duct all appeared to be normal. On the medial slice of side A, Arrow 1 points to the entire length of the basilar artery. The cerebellar vermis is absent, and we see a small wing-shaped part of the upper cerebellum. In a paramedial slice on side B, arrows 2 and 3 indicate the anterior, superior, and inferior cerebellar parenchyma, respectively.

Angio-RM revealed that neck and supratentorial arteries were normal. Side C of Fig. 2 shows a frontal view, and side D, an oblique view, of the arteries of the posterior fossa. Arrow 1, along the final segment of the vertebral arteries, shows the lack of posterior inferior cerebellar arteries (PICA). Arrow 2 indicates the basilar trunk; Arrow 3 shows the posterior cerebral terminal branches; Arrow 4 shows the superior cerebellar collateral branches; and Arrow 5, the anterior inferior cerebellar arteries (AICA).

One year after the syncopic episode, the patient had not experienced symptom recurrence, and was able to carry out daily activities normally.

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