Linezolid induced lactic acidosis and hepatic failure

Evangelos Potolidis, Eleftheria Gousi, Dimitrios Delios, Eleftheria Bei, Charalampos Mandros

To the Editors,

Linezolid is oxazolidinone antibiotic, widely used to treat infections from multidrug-resistant gram positive microorganisms by compromising bacterial ribosome function [1]. Gastrointestinal disturbances, megalosuppression, serotonin syndrome, optic neuropathy and lactic acidosis comprise the constellation of the well known linezolid associated adverse effects [2, 3]. Given the similarities between bacterial and mitochondrial ribosome, this linezolid-induced lactic acidosis is well expected [4]. This potentially serious side effect occurred mainly during long-term treatment, as depicted from the maximum four-week treatment FDA approval. We describe a patient who developed lactic acidosis and hepatic failure during a few days period of linezolid administration.

A 70-year-old female was admitted to the hospital due to fever and hypotension. The patient had a past history of hypertension and osteoarthrithis. On evaluation she appeared tired and restless. The blood pressure was 90/65 mmHg, pulse 124 beats per minute, temperature 37.9°C, respiratory rate 28 breaths per minute and Glasgow coma scale 15/15. The abdomen was distended with normal bowel sounds, cardiac sounds and lungs were clear and all other examinations were normal. Chest X-ray was also normal and computed tomography (CT) scan of the abdomen was ordered due to abdominal findings and concomitant hypotension. Abdominal CT scan was normal and rapid test for influenza was negative. Specimens of blood and urine were sent for culture and cerebral fluid was drawn. Cerebral fluid was negative. The blood tests revealed elevated WBC to be 15x10³/mm³ and increased C-reactive protein levels. Other routine tests were normal including liver enzymes. Soon after, the patient became hemodynamically unstable. Therefore linezolid was administered (600 mg b.d.) and ceftazidim (2 g t.d.s.). Fluids and vasopressors were given and the patient was temporarily admitted to the intensive care unit. Urine culture revealed urinary tract infection due to pseudomonas. Blood cultures were negative. Cardiac ultrasound was normal. Chest X-ray was performed on the second day because of breathing discomfort and revealed a left upper lobe pneumonia. CT scan of chest confirmed the inflammatory process of the left upper lung lobe. On the third day, the patient was afibrile, hemodynamically stable with normal urine output. On the sixth day, the patient suffered from abdominal discomfort. On examination, the patient was alert but appeared uncomfortable. Vital signs were normal. Abdomen X-ray and ultrasound (USG) scan were normal. Blood tests revealed total bilirubin 2.2 mg/dL (0.3–1.2 mg/dL), indirect bilirubin 1.7 mg/dL, SGOT 234 IU/L (5–40 IU/L), SGPT 222 IU/L (5–40 IU/L), yGT 100 IU/L (10–50 IU/L), LDH 443 IU/L (130–245 IU/L) and INR 2.8 (<1.2). Further laboratory investigations depicted a high anion gap metabolic acidosis with bicarbonate 6 mEq/L (24 mEq/L), anion gap 48 mEq/L (12 mEq) (normal range in brackets), elevated lactate levels 20 mmol/L and renal failure (normal range 0g given in brackets) (Cr 2.3 mg/dL (0.9–1.6 mg/dL)). Methanol was not detected. On the next day, the possibility of linezolid toxicity was considered and the drug was withdrawn. The patient was switched to clarithromycin 500 mg twice daily and ceftazidim resulting in a normalization of liver enzymes, lactate levels, prothrombin time and renal function.

Lactic acidosis is the most common cause of metabolic acidosis in hospitalized patients. Type A lactic acidosis (due to tissue hypoperfusion) is observed in septic shock, hypovolemia and cardiopulmonary arrest.

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Metformin and nucleoside reverse transcriptase inhibitors are able to cause type B lactic acidosis (mitochondrial dysfunction). As previously mentioned, linezolid has the potential to inhibit mitochondrial ribosomes. The resulting deficiency of the thirteen mitochondrial DNA encoded proteins results in mitochondrial malfunction. Interestingly this effect is observed predominately after prolonged drug exposure. Additionally, lactic acidosis is reported to be dose dependent. In patients treated with the standard 600 mg dose every 12 h, overexposure was documented in 12% cases. It has been suggested that overexposure occurs especially in patients cotreated with drugs which may act as P-glycoprotein inhibitors (omeprazole, amiodarone). The implementation of therapeutic drug monitoring may be helpful limiting such cases [5]. Patients with mitochondrial diseases such as MELAS syndrome (mitochondrial encephalomyopathy, lactic acidosis and stroke like episodes) are prone to lactic acidosis after linezolid treatment [6].

Our patient developed lactic acidosis and liver dysfunction during treatment with linezolid. Undoubtedly linezolid is a valuable drug with a good safety profile. Clinicians need to be aware of linezolid-induced lactic acidosis.

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Authors declare no conflict of interest.

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