CASE REPORT

Colistin neurotoxicity: revisited

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SUMMARY

The revival of polymyxin antibiotics with the advent of multidrug resistant gram-negative bacteria in the recent decade has led to renewed interest in toxicity of this indispensable drug. We report a postoperative case of burst abdomen where colistin was started in view of *Pseudomonas* organism sensitive to colistin. Subsequently, the patient went into respiratory depression and encephalopathy after starting the treatment. She recovered promptly after stopping the drug.

BACKGROUND

The revival of polymyxin with the advent of multidrug resistant gram-negative bacteria in the recent decade has led to renewed interest in its toxicity. The use of polymyxin declined because of its considerable toxicity, mainly nephrotoxicity and neurotoxicity. Nephrotoxicity levels of polymyxins are higher as compared to neurotoxic effects, which are usually mild and resolve after prompt discontinuation of the drug responsible for them. Furthermore, cases of neuromuscular blockade and apnoea have not been reported in the recent literature. The diagnosis of colistin-mediated neurotoxicity should be considered in patients with altered mental status of unknown aetiology.

CASE PRESENTATION

A 20-year-old woman presented on postoperative day 15 of caesarean section performed for obstructed labour, with high grade fever associated with chills and rigours along with a foul smelling purulent discharge from stitch line for the past 4 days. On examination, her pulse rate was 120 bpm, blood pressure was 100/60 mm of Hg, temperature was 102° F and respiratory rate was 20/min. Abdominal examination revealed a gaping abdominal wound with purulent discharge through which the patient's subinvolved uterus was visible. A gaping and infected episiotomy wound was also present, however, vaginal examination did not reveal any pelvic collection.

Blood transfusion was given in view of severe anaemia and the patient was started on triple antibiotics (injection ceftriaxone, metronidazole and gentamicin). The patient underwent repair of the abdominal as well as episiotomy wounds. Cultures from stitch line and urine grew *Pseudomonas aeruginosa* resistant to all antibiotics, including ceftriaxone, ciprofloxacin, gentamicin, ceftazidime, vancomycin, meropenam etc, with the exception of colistin; thus, colistin was started at a dose of 1 million IU intravenously 8 hourly. The other antibiotics were stopped. After 4 days of colistin, the

patient developed hallucinations followed by drowsiness, and later responded only to painful stimuli, with rigours and twitching in the upper limbs, and flexed body posture, with a Glasgow coma scale of E2V1M2, after 5 days of initiation of colistin. All investigations including for electrolytes and sugars, and chest X-ray were repeated and found to be within normal limits. There was no exposure to any toxic agents, muscle relaxants or narcotics that might have caused encephalopathy. Pelvic vein and deep vein Doppler flow was also normal. Colistin was stopped as it was considered to be the attributing factor. Subsequently, over 12 h of stopping the treatment, the patient needed only supportive treatment in the form of intravenous fluids and continuous vital monitoring in the intensive care setting as, during this period, there was prompt improvement in the patient's neurological status; she fully recovered in 48 h.

OUTCOME AND FOLLOW-UP

The patient was discharged in stable condition with healthy stitch line after 10 days.

DISCUSSION

Colistin belongs to a class of polymyxins derived from *Bacillus polymyxa*. It exerts its bactericidal effect by displacing the divalent cations magnesium and calcium, which stabilise anionic lipopolysaccharide molecules in the outer membrane of gram-negative bacteria, thereby disrupting cell permeability.¹ Despite proven efficacy against gram-negative bacilli, it was abandoned in the 1960s due to concerns of neurotoxicity and nephrotoxicity.² However, recently, with the emergence of multidrug resistant gram-negative bacilli that are resistant to almost all classes of available antibiotics, Polymyxins have regained importance and, for the past few years, intravenous colistin, particularly in the form of colistin methanesulfate, has been used for treatment of serious *Pseudomonas aeruginosa* and *Acinetobacter baumannii* infections of various types, such as pneumonia, urinary tract infections and septicæmia.

The most common adverse effects of colistin therapy are nephrotoxicity and neurotoxicity.³ Although there have been a number of case reports about the drug's nephrotoxicity,^{4–6} little has been reported about its neurotoxicity, especially the psychiatric side effects, as noted in our case. The incidence of neurotoxicity with colistin is rare, ranging from 0% to 7%, and mostly of a mild degree.⁷ The neurological toxicity manifests as dizziness, muscle weakness, facial and peripheral paraesthesia, visual disturbances, vertigo, confusion, hallucinations, seizures, ataxia, partial deafness and neuromuscular

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blockade.^{8 9} Paraesthesias may remain undetected in the intensive care unit setting and have been reported more commonly after the intravenous rather than intramuscular route.^{10 11} Respiratory depression may occur because of a myasthenia-like syndrome as a result of neuromuscular blockade.¹² Hypoxia or concomitant use of muscle-relaxants, narcotics, sedatives, anaesthetic drugs, or corticosteroids, may precipitate neurotoxicity. It is also seen more commonly in patients with hypoalbuminaemia and concurrent use of nonsteroidal anti-inflammatory drugs.

The patient in this case report developed encephalopathy after 4 days of initiating colistin. Besides having drowsiness and confusion, she had rigours and twitching of fingers as well as hallucinations. Colistin was considered to be the most likely offending factor because the patient was not receiving anything other than colistin, with potential neurotoxicity. Furthermore, there was prompt recovery following cessation of colistin administration. Colistin causes neuromuscular blockade because of the non-competitive myoneuronal presynaptic blockade of acetylcholine release. Colistin-associated neurotoxicity has been

found to be related with the total cumulative amount of colistimethate sodium administered as against single or daily dose, which may be the reason for neurotoxicity symptoms appearing after 4 days. Neurotoxicity more commonly affects women and those with impaired renal function or myasthenia gravis.⁸

Competing interests None declared.

Patient consent Obtained.

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REFERENCES

- 1 Falagas ME, Kasiakou SK. Colistin: The revival of polymyxins for the management of multidrug-resistant gram-negative bacterial infections. *Clin Infect Dis* 2005;40:1333–41.
- 2 Nation RL, Li J. Colistin in the 21st century. *Curr Opin Infect Dis* 2009;22:535–43.
- 3 Li J, Nation RL, Milne RW, et al. Evaluation of colistin as an agent against multi-resistant gram-negative bacteria. *Int J Antimicrob Agents* 2005;25:11–25.
- 4 Cheng CY, Sheng WH, Wang JT, et al. Safety and efficacy of intravenous colistin (colistin methanesulphonate) for severe multidrug-resistant gram-negative bacterial infections. *Int J Antimicrob Agents* 2010;25:297–300.
- 5 Santamaria C, Mykietiuk A, Temporiti E, et al. Nephrotoxicity associated with the use of intravenous colistin. *Scand J Infect Dis* 2009;41:767–9.
- 6 Hartzell J, Neff R, Ake J, et al. Nephrotoxicity associated with intravenous colistin (colistimethate sodium) treatment at a tertiary care medical center. *Clin Infect Dis* 2009;48:1724–8.
- 7 Molina J, Cordero E, Pachon J. New Information about the polymyxin/colistin class of antibiotics. *Expert Opin Pharmacother* 2009;10:2811–28.
- 8 Falagas ME, Kasiakou SK. Toxicity of polymyxins: a systematic review of the evidence from old and recent studies. *Crit Care* 2006;10:R27.
- 9 Spapen H, Jacobs R, VanGorp V, et al. Renal and neurological side effects of colistin in critically ill patients. *Ann Intensive Care* 2011;1:14.
- 10 Wolinsky E, Hines JD. Neurotoxic and nephrotoxic effects of colistin in patients with renal disease. *N Engl J Med* 1972;266:759–62.
- 11 Koch-Weser J, Sidel VW, Federman EB, et al. Adverse effects of sodium colistimethate: manifestations and specific rates during 317 courses of therapy. *Ann Intern Med* 1970;72:857–68.
- 12 Duncan DA. Colistin toxicity. Neuromuscular and renal manifestations. Two cases treated by hemodialysis. *Minn Med* 1973;56:31–5.

Learning points

- The diagnosis of colistin-mediated neurotoxicity should be considered in patients with altered mental status of unknown aetiology.
- Prompt cessation of colistin therapy is indicated to avert any fatal consequences.
- Regular monitoring of renal function as well as monitoring the neurological status of patients on colistin is essential to prevent and manage the toxicities associated with colistin use.

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