

Ertapenem-induced delirium

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INTRODUCTION

Ertapenem is an intravenous antibiotic within the class of carbapenem antibiotics which are highly effective against severe bacterial infections. These antibiotic agents exhibit a wider spectrum of action when compared to penicillins and cephalosporins despite carbapenems being part of the beta-lactam antibiotic class.

CASE PRESENTATION

The patient is an 85-year old gentleman who developed a lower urinary tract infection and left 4th toe osteomyelitis. Ertapenem was prescribed according to the sensitivities of the cultured organisms. After two weeks of antibiotic treatment the patient developed new-onset delirium, agitation, hallucinations and throat discomfort. Ertapenem was stopped and the new symptoms resolved within 48 hours.

DISCUSSION

Delirium, agitation, hallucinations and throat discomfort are documented side-effects of ertapenem. In such cases the withdrawal of ertapenem results in a resolution of symptoms.

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INTRODUCTION AND CASE PRESENTATION

The patient is an 85-year old gentleman, a known case of peripheral vascular disease, currently a resident in a long term care facility, who developed pyuria and a wound exuding pus from the left 4th toe. Urinalysis, urine cultures, a wound swab and a left foot X-ray were taken. The urinalysis confirmed the presence of a urinary tract infection with urinalysis white blood cells of 500uL and positive urinalysis nitrites. The urine cultures showed a *Klebsiella pneumoniae* ESBL positive infection. The left 4th toe wound swab showed a methicillin resistant *Staphylococcus aureus* (MRSA) infection and 2 strains of coliforms including *Proteus* spp. The left foot X-ray showed cortical irregularity of the lateral side of the middle phalanx of the left 4th toe and osteopenia suggestive of early osteomyelitis. He had a normal renal function and an elevated C-reactive protein level of 90mg/L.

Ertapenem 1g daily intravenous and clindamycin 300mg 6-hourly per oral were prescribed according to the microbiology results and antibiotic sensitivities. After two weeks of ertapenem therapy, the patient developed new-onset delirium, agitation, throat discomfort and hallucinations which had an acute onset over a period of 24 hours. The patient had no prior neurocognitive disorders. The physical examination was unremarkable and all the parameters were within normal limits. The left 4th toe wound showed clinical improvement with decreased erythema and no further pus exudation. The pyuria had resolved and the urine was now clear. An electrolyte profile and a renal function were all within normal limits. Ertapenem treatment was immediately discontinued and these symptoms all resolved within 48 hours.

DISCUSSION

Common side-effects of ertapenem include gastro-intestinal symptoms such as nausea, vomiting and diarrhoea, thrombophlebitis and skin reactions. Delirium and hallucinations are documented side-effects of ertapenem therapy and the frequency of such adverse reactions is unknown from data to date. Another rare documented adverse reaction includes encephalopathy.¹ The Naranjo algorithm was used to assess the probability of the symptoms being secondary to an adverse drug reaction.² The score for this patient was 3 which indicated a possible adverse reaction to ertapenem with a dramatic improvement in the patient's mental status upon the discontinuation of the drug. This patient had been taking the drug for 14 days, with the symptoms occurring only at the end of the recommended 14-day course of ertapenem for the *Klebsiella pneumoniae* lower urinary tract infection.

The risk factor which may have predisposed this gentleman to these adverse reactions was his chronological age. The main patient-related risk factors for carbapenem-induced neurotoxicity are renal failure, low body weight, a history of cerebrovascular disease and advanced age.³ Carbapenem-induced neurotoxicity occurs via interactions with the γ -amino butyric acid receptor A (GABA_A).^{4,5} The interaction happens through the C-2 side-chain of the carbapenem nucleus.

Pharmacovigilance is of utmost importance in the monitoring and assessment of adverse drug reactions. It enables the identification of hazards related to pharmaceutical drugs and provides for the minimisation of harm that may occur to patients. Individual case safety reports with an identifiable patient and reporter, a suspected drug and the adverse

event are crucial in providing more information to the relevant Medicines Authority to investigate and examine adverse reactions related to the particular drug.

CONCLUSIONS

We are presenting this case report in order to highlight the possible neurologic adverse reactions of ertapenem. The identification and discontinuation of ertapenem as the cause of the delirium, hallucinations, agitation and throat discomfort in this gentleman brought about the resolution of these symptoms.

REFERENCES

1. Sutton SS, Jumper M, Cook S, Edun B, Wyatt MD. Ertapenem-induced encephalopathy in a patient with normal renal function. *J Investig Med High Impact Case Rep.* 2017; 5(1): 2324709616689376.
2. Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, et al. A method for estimating the probability of adverse drug reactions. *Clin Pharmacol Ther* 1981; 30(2): 239-245.
3. Grill MF, Maganti RK. Neurotoxic effects associated with antibiotic use: management considerations. *Br J Clin Pharmacol* 2011; 72: 381-393.
4. Hikida M, Masukawa Y, Nishiki K, Inomata N. Low neurotoxicity of LJC 10,627, a novel 1 beta-methyl carbapenem antibiotic: inhibition of gamma-aminobutyric acidA, benzodiazepine, and glycine receptor binding in relation to lack of central nervous system toxicity in rats. *Antimicrob Agents Chemother* 1993; 37(2): 199-202.
5. Sunagawa M, Matsumura H, Sumita Y, Nouda H. Structural features resulting in convulsive activity of carbapenem compounds: effect of C-2 side chain. *J Antibiot (Tokyo)* 1995; 48: 408-416.