Piperacillin/tazobactam-induced acute delirium in a peritoneal dialysis patient

Sir,

Penicillins are β-lactam antimicrobial agents. They act by binding to penicillin-binding proteins on the bacterial cytoplasmic membrane and then interfere with the cell wall physiology. Piperacillin belongs to the group of acylamino-penicillins which has additional coverage for Pseudomonas aeruginosa and other Gram-negative bacilli. However, antimicrobial degradation can occur with β-lactamase-producing bacteria, causing drug resistance. With the addition of the β-lactamase inhibitor tazobactum, Tazocin® (piperacillin/tazobactum) is active against β-lactamase-producing bacteria that are resistant to acylamino-penicillin.

We present a case of hallucinations and mental confusion in a continuous ambulatory peritoneal dialysis (CAPD) patient after receiving piperacillin/tazobactam for 7 days for the treatment of pneumonia. The drug-induced encephalopathy resolved with the discontinuation of the drug and continued peritoneal dialysis.

Case. A 47-year-old end-stage renal disease male patient, who had been on CAPD for 1 year, was admitted to hospital for cough, right pleuritic chest pain and fever for 2 days. The clinical picture was suggestive of lobar pneumonia, with chest X-ray showing consolidation of the right lower lobe. Laboratory results showed leukocytosis with white cell count $19.2 \times 10^9/l$. He had a residual renal creatinine clearance of $\sim 3$ ml/min, and empirical intravenous (i.v.) piperacillin/tazobactam was started at a dose of 4 g/500 mg every 12 h. Meanwhile, he continued CAPD with four 2 l exchanges per day. His fever came down on day 7 and piperacillin/tazobactam was continued. However, on the following evening, he began to experience auditory hallucinations, progressive mental confusion and abnormal behaviour. Electrolyte disturbances were excluded with normal sodium, potassium, calcium and magnesium levels. Computed tomography of the brain and electroencephalogram were unremarkable. Lumbar puncture yielded cerebrospinal fluid with normal biochemistry and cell counts. Drug-induced encephalopathy was suspected and piperacillin/tazobactam was stopped. 2 days after the onset of symptoms. His mental state gradually improved over the next 3 days and his pneumonia was resolving as well. He remained stable and was discharged 4 days later.

Discussion. Neurological complications following the use of i.v. piperacillin have been identified in the elderly or in patients with renal insufficiency. The most frequently seen manifestations were dizziness and headache. Induction of seizure has also been reported and was considered a shared property among penicillins [1,2]. In patients with end-stage renal failure on peritoneal dialysis or haemodialysis, antibiotic-induced confusion has been seen from time to time. The most frequently involved drugs include cephalosporins, cefepime and clarithromycin, while acute delirium induced by piperacillin is very rare. In our case, encephalopathy was seen after 7 days of i.v. piperacillin/tazobactum given at 8 g/1 g/day in two divided doses. The dosage was appropriate for patients >50 kg with a creatinine clearance <20 ml/min. No structural lesions were identified and there were no electrolyte disturbances in our patient, as piperacillin had been shown to induce hypomagnesaemia, hypokalaemia and to a lesser degree hypocalcaemia [3]. Piperacillin/tazobactum injection was stopped immediately and our patient’s mental condition gradually returned to normal over 3 days, which strongly suggested a causative relationship. The exact mechanism for penicillin-induced encephalopathy is unknown, but it is now believed to be mediated through GABAergic inhibition. Penicillins inhibit GABAergic transmission not only at the GABA receptor, but also at the benzodiazepine receptor [4]. It has been shown that penicillin reduces the number of benzodiazepine receptors through a direct effect on this receptor, which is a part of the major inhibitory system in the brain, the GABAergic macromolecular receptor complex. Also, this decrease in benzodiazepine receptors is thought to play a significant role in penicillin-induced encephalopathy [5]. Our case well illustrated that piperacillin/tazobactum can cause acute confusion even with an apparently appropriate dosage; and special attention should be paid in dialysis patients with no or minimal residual renal function, as this may potentiate its toxicity.

Conflict of interest statement. None declared.

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DOI: 10.1093/ndt/gfh048