

## CASE REPORT



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## An experience with colistin applied in treatment of immunocompromised patients with peritonitis on peritoneal dialysis

Iskustvo sa primenom kolistina u lečenju peritonitisa kod imunokompromitovanih bolesnika na peritoneumskoj dijalizi

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### Abstract

**Introduction.** Immunocompromised patients, such as those with multiple myeloma on peritoneal dialysis, are particularly susceptible to the occurrence of peritonitis. **Case report.** We presented a 56-year-old female patient with a 10-year history of multiple myeloma. The patient was on peritoneal dialysis since 2010. During 2012 the patient had the first episode of peritonitis that was successfully managed, but in 2013 the second episode of peritonitis occurred. Analysis of dialysate culture and exit site swab revealed the presence of multiresistant *Acinetobacter* spp., which was susceptible only to colistin. Prompt colistin therapy was administered at the doses of 100,000 units/day during six days, which resulted in complete recovery of the patient, as well as improvement of local abdominal findings. Gram-negative bacteria (genus *Acinetobacter*) are common causative agents in hospital-acquired infections. Studies confirmed susceptibility of *Acinetobacter* to colistin, which was also the case with the presented patient. Intravenous administration of colistin resulted in a complete remission of this severe, life-threatening peritonitis. **Conclusion.** Patients with multiple myeloma and renal failure are highly prone to severe life-threatening infections.

### Key words:

multiple myeloma; peritoneal dialysis; peritonitis; colistin.

### Apstrakt

**Uvod.** Imunokompromitovani bolesnici, kao što su bolesnici sa multiplim mijelomom na peritoneumskoj dijalizi, posebno su skloni nastanku peritonitisa. **Prikaz bolesnika.** Prikazali smo bolesnicu, staru 56 godina, koja je bolovala od multiplog mijeloma 10 godina. Od 2010. god. lečila se metodom peritoneumske dijalize. Prvu epizodu peritonitisa koja je uspešno sanirana, imala je tokom 2012. U 2013. ponovo je došlo do razvoja peritonitisa. Analizom kulture dijalizata i brisom izlaznog mesta peritoneumskog katetera izolovan je multirezistentni *Acinetobacter* spp, osetljiv samo na kolistin. Primenom kolistina u dozi od 100 000 jedinica/dan tokom šest dana došlo je do potpunog poboljšanja opšteg stanja bolesnice, kao i lokalnog nalaza na trbuhu. Gram-negativna bakterija (*Acinetobacter* spp) čest je uzročnik hospitalnih infekcija. Istraživanja potvrđuju osetljivost *Acinetobacter* spp. na kolistin, što je slučaj kod prikazane bolesnice. Intravenska primena kolistina rezultovala je potpunim oporavkom od teškog, po život opasnog, peritonitisa. **Zaključak.** Bolesnici sa multiplim mijelomom i bubrežnom insuficijencijom imaju povećanu sklonost ka nastanku teških, po život opasnih, infekcija.

### Ključne reči:

multipli mijelom; dijaliza, peritoneumska; peritonitis; kolistin.

### Introduction

Multiple myeloma is a progressive malignant disease of plasma cells featuring the production of pathological paraproteins. Multiple myeloma cells come from pathologically altered plasma cells, which produce abnormal amounts of

paraproteins. Accumulated paraproteins interfere with the production of normal antibodies in the bone marrow, and activation of natural killer cells stimulates increased osteoclast recruitment and activity finally resulting in bone defects. The process of remodelling and destruction of bone tissue leads to the release of calcium into blood, which can cause severe

kidney disorders<sup>1</sup>. High amounts of paraproteins are associated with a significant increase in total blood protein levels resulting in renal function disorders in some 50% of patients. Light chains and amyloid frequently cause chronic renal failure rather than the acute one, thus indicating administration of renal replacement therapy, i.e. hemodialysis or peritoneal dialysis. Renal failure secondary to myeloma carries poor prognosis to patients. Such patients are highly prone to severe, mostly lethal infectious complications induced by Gram-negative bacteria<sup>2,3</sup>.

### Case report

A 56-year-old female patient had a 10-year history of multiple myeloma. In 2005, end-stage chronic renal failure was confirmed, so the patient was subjected to the chronic hemodialysis (HD) program. In 2010, because of the exhaustion of vascular access, the patient underwent laparoscopic placement of a peritoneal dialysis catheter (PD) catheter<sup>4</sup> and was transferred to continuous ambulatory peritoneal dialysis (PD-CAPD) therapy. After the initiation of PD, the patient exhibited moderate umbilical hernia. During 2012, the patient had the first peritonitis episode with severe clinical presentation, which was successfully managed. The patient was in complete remission until February 2013, when headaches, swelling and redness in the right eye and spinal column occurred. Relevant diagnostic procedures (endocranial magnetic resonance imaging, sternal puncture, serum immunoelectrophoresis test) revealed the relapse of underlying disease, manifested as the extranodal retrobulbar mass in the right eye accompanied by skull bone infiltration (Figures 1a, b). Corticosteroid therapy was administered according to the

therapy was initiated – at first III and IV generation cephalosporins, subsequently after 48 hours vancomycin and aminoglycosides and antianaerobic antibiotics, but no clinical improvement was observed. During further course of the disease, the patient developed phlegmon of the anterior abdominal wall in the region of the umbilical hernia and her overall condition worsened. The patient was examined several times by the abdominal surgeon, and computed tomography of the abdomen was performed confirming the existence of phlegmon without signs of incarcerated hernia indicating continuation of conservative therapy. After 72 hours, multiresistant *Acinetobacter* spp., which was susceptible only to colistin, was isolated from dialysate culture and exit site swab. Considering highly severe clinical status of the patient, peritoneal catheter was removed and the patient transferred to HD by placing a double-lumen catheter into the right jugular vein. Prompt colistin intravenous therapy was administered at the doses of 100,000 units/day i.v. during six days which resulted in rapid improvement of general condition of the patient as well as of local abdominal finding (Figure 2a, b) and laboratory results (PCT 0.91 ng/mL, CRP 19 mg/L). Further therapy of relapsed underlying disease was planned and continued by the hematologist.

### Discussion

Peritonitis is the most common, most severe and most dangerous complication in PD patients. Most frequent causative agents are Gram-positive bacteria (*Staphylococcus* spp, *Staphylococcus aureus*, *Enterococcus*). Peritoneal dialysis-associated peritonitis is mostly characterized by milder clinical manifestations as compared to the postoperative peritonitis



Fig. 1a – Magnetic resonance of the head – retrobulbar localization of right eye multiple myeloma.

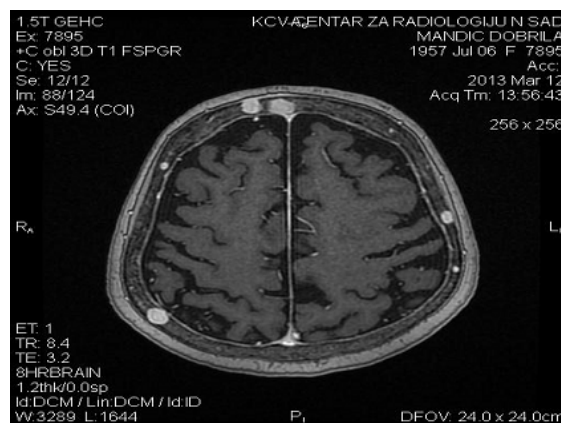


Fig. 1b – Magnetic resonance of the head – multiple myeloma infiltrates in the skull bones.

relevant protocol (40 mg/day iv, 1–4; 9–12; 17–20 days). After completing the therapy, abdominal pain, dialysate turbidity and peritonitis were observed and designated as a second peritonitis episode. Laboratory analysis revealed elevated levels of procalcitonin (PCT) in the serum (18.39 ng/mL) and in dialysate (4.65 ng/mL), serum C-reactive protein (CRP) (186.3 mg/L) and leukocyte count in dialysate ( $4850 \times 10^6/L$ ). Bacteriological examination of dialysate and the catheter exit point was in progress. Empiric antimicrobial

therapy and responds well to outpatient treatment. Peritonitis caused by Gram-negative bacteria is rare, and may result from touch contamination of dialysis system, exit site or tunnel infection, possible inflammatory process in the abdomen, constipation, etc. Most common pathogens include *Escherichia coli*, *Klebsiella*, *Proteus*, more rarely *Campylobacter*, *Citrobacter*, *Acinetobacter* etc. Gram-negative peritonitis is particularly troublesome and severe resulting mostly in technique failure, catheter removal or even lethal out-



**Fig. 2a – Phlegmon of the front abdominal wall before the therapy.**



**Fig. 2b – The front abdominal wall after the therapy.**

come<sup>5,6</sup>. Immunocompromised patients are particularly susceptible. Multiple myeloma is a disease characterised by a high incidence of severe complications, especially when renal function is disturbed and patients are subjected to any of dialysis methods (HD or PD)<sup>7,8</sup>. Survival rates in such patients after 1- and 3-year therapy range from 50% and 25%, respectively<sup>9</sup>. Peritoneal dialysis is not the preferred program in patients with multiple myeloma and end-stage chronic renal failure, and only few cases were reported from dialysis centres in North America and Europe<sup>2-4</sup>. Between 1998 and 2013, three patients with multiple myeloma underwent PD at our Center<sup>10</sup>. Extramedullar localizations of multiple myeloma are uncommon and rare cases have been described in the lungs, the larynx, skull bones and the bladder. We presented a rare case of retrobulbar localization in the right eye and skull bone infiltration. Gram-negative bacteria are common causative agents in hospital-acquired infections<sup>11</sup>. Bacterial species of the genus *Acinetobacter*, which may be seen as a part of normal bioflora of the human skin, mucosa and secretions is of particular importance. It is responsible for severe nosocomial infections, particularly in immunocompromised patients. The organism is especially difficult to treat because of its ability to survive and persist in hospital environment, as well as its resistance to the broad variety of antibiotics<sup>12-14</sup>. The presented patient was immunocompromised due to the underlying disease, particularly after receiving corticosteroid therapy and subsequent peritonitis episodes. Initial empiric antimicrobial treatment of peritonitis (cephalosporins, vancomycin, aminoglycosides) revealed no clinical improvement, since the isolated *Acinetobacter* organism was resistant to all tested antibiotics, except colistin<sup>8,15</sup>. This caused serious problems in clinical practise and further peritonitis complication manifested as

phlegmon in the front abdominal wall. The increased incidence of multiresistant strains of *Acinetobacter* has been reported in Serbia as well as in Italy, Greece, Slovakia, China and USA<sup>16,17</sup>. Considering the multiple resistance to the range of antimicrobials, carbapenems are the drug of choice in the therapy of such infections; however, the increasing resistance to this class of antibiotics is evident. Studies conducted in Bulgaria and Korea confirmed susceptibility of *Acinetobacter* to colistin, which was also the case in the presented patient<sup>17</sup>. The drug is highly toxic and thus rarely administered at clinics. However, in the presented patient, intravenous administration of colistin at the doses adjusted to the rate of renal failure resulted in complete remission of this severe, life-threatening peritonitis without any adverse effects. Such severe episodes of Gram-negative peritonitis in PD patients often lead to removal of PD catheter and transfer to HD therapy, which was the case in the presented patient<sup>18</sup>. After complete recovery from inflammation, the treatment of the relapsed underlying disease was planned<sup>19</sup> taking into consideration that such cases of multiple myeloma accompanied with renal failure and extramedullar localization have very poor prognosis and severe disease course.

### Conclusion

Patients with multiple myeloma and renal failure are highly prone to severe life-threatening infections. Immunocompromised patients on peritoneal dialysis often develop peritonitis associated with multiresistant bacteria (*Acinetobacter* spp.), which is a highly severe complication of peritoneal dialysis, and only the prompt diagnosis and immediate administration of an appropriate therapy are the prerequisites for a positive outcome of such conditions.

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