Successful treatment of pan - resistant pseudomonas Aeruginosa meningitis with intrathecal polymyxin b therapy

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Citation

Abstract
Serious treatment problems are experienced in nosocomial infections caused by multi-drug resistant Pseudomonas aeruginosa especially in intensive care units. We report a case of multi-drug resistant Pseudomonas aeruginosa meningitis treated succesfully with intrathecal polymyxin B. As the 26 year old female patient operated in the department of neurosurgery with the diagnosis of hemangioblastoma developed hydrocephalus 14 days after the operation, external dreinage was initiated. The patient developed pain and consciousness. CSF findings were WBC 1800/mm3 (%90 PMN, %10 lymphocyte), glucose 21 mg/dl, protein 87 mg/dl. In the CSF obtained from the external drainage, there was growth of Pseudomonas aeruginosa. It was only sensitive to carbapenems and meropenem was initiated at a dose 3x2 gr iv. CSF findings and the patient’s clinical condition did not improve and the growth of Pseudomonas aeruginosa continued under meropenem treatment. Pseudomonas aeruginosa has developed resistance to carbapenems and meropenem was stopped. It was only sensitive to polymyxin B was investigated with disc diffusion method and the diameter of inhibition was found to be 15 mm. Polymyxin B administrated intrathecally every other day until two weeks. In the following CSF controls, findings improved and there was no growth. The patient’s hydrocephalus was taken undercontrolled external dreinage was ended. Her treatment was completed and she was discharged. She visited our out-patient department montly about one year.

CASE REPORT
Nosocomial infections caused by multidrug-resistant bacteria are creating an important health problem. Antibiotic resistance has increased at a frightening pace during last two decades, especially in intensive care units. According to European data Escherichia coli, Pseudomonas aeruginosa, Enterobacter spp., Klebsiella spp. and Acinetobacter spp. are the dominating bacteria in those units(1). Some causitive agents are being isolated most commonly in our country data and these are all important for their multi drug resistance(2). Serious treatment problems are experienced in nosocomial infections caused by multi-drug resistant Pseudomonas aeruginosa especially in intensive care units(3). We report a case of multi-drug resistant Pseudomonas aeruginosa meningitis treated succesfully with intrathecal polymyxin B.

As the 26 year old female patient operated in the department of neurosurgery with the diagnosis of hemangioblastoma developed hydrocephalus 14 days after the operation, external dreinage was initiated. The patient developed pain and consciousness. CSF(cerebrospinal fluid) findings were WBC: 1300/mm3(%80 PMN,
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%20 lymphocyte), CSF glucose: 31 mg/dl, protein: 80 mg/dl, and the CSF cultures yielded methicillin resistant Staphylococcus aureus. Vancomycin 2gr/day and rifampicin 600 mg/day combination administrated. On the 21st day of treatment, the patient’s general condition improved. In control LP CSF findings were WBC: 21/mm3, glucose: 54 mg/dl, protein 54 mg/dl. On the 6th day after the cessation of the treatment, she developed fever and nuchal stiffness her general condition deteriorated, CSF and blood cultures were repeated. CSF findings were WBC 1800/mm3 (%90 PMN, %10 lymphocyte), glucose 21 mg/dl, protein 87 mg/dl. In the CSF obtained from the external drainage, there was growth of Pseudomonas aeruginosa. It was found to be resistant to 3rd and 4th generation cephalosporins, antipseudomonal penicillin + beta lactamase inhibitor combinations, to quinolons and aminoglycoside group antibiotics with disc diffusion method. It was only sensitive to carbapenems and meropenem was initiated at a dose 3x2 gr iv. CSF findings and the patient’s clinical condition did not improve and the growth of Pseudomonas aeruginosa continued under meropenem treatment. Pseudomonas aeruginosa has developed resistance to carbapenems and meropenem was stopped. It was only sensitive to polymyxin B was investigated with disc diffusion method and the diameter of inhibition was found to be 15 mm. In the disc diffusion, if the inhibition zone of Polymyxin B >15 mm, it is accepted as sensitive. As Polymyxin B preparations were not available in Turkey, they were brought from abroad. The patient’s family was informed about the treatment and written consent was obtained. As there were no penetration to CSF in iv administration, the treatment was initiated intrathecally at a dose of 50,000 U/day for three days. Afterwards, it was administrated every other day until two weeks. In the following CSF controls, findings improved and there was no growth. The patient’s hydrocephalus was taken undercontrolled external drainage was ended. Her treatment was completed and she was discharged. She visited our out-patient department monthly about one year.

DISCUSSION
Resistant Pseudomonas aeruginosa meningitis that was treated by Colistine was reported in Turkey(4). Segal et al utilized iv meropenem and intraventricular polymyxin B in the treatment of cephalosporin resistant Klebsiella pneumoniae ventriculitis obtained successful results(5). There are several case reports about the treatment of meningitis with intrathecal or intraventricular...
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use of polymyxins in patients with gram-negative meningitis(6).

Our knowledge concerning in the utilization of polymyxin B is limited. As the case for colistin we do not have preparations of polymyxin B in our country either. We do not observed any side effect during the treatment and the drug was well tolerated by the patient. Polymyxin B is a polypeptide group antibiotic that has been isolated from Bacillus polymyxa. Polymyxins are active against selected gram negative bacteria, including Acinetobacter species, Pseudomonas aeruginosa, Klebsiella spp., Enterobacter spp(7). By interacting with the membr phospholipids of the bacteria and increasing cellular permeability, it has bactericidal effects on cell membrane through detergent action. The microorganism that are resistant to polymyxin B possess cell walls that inhibit the entrance of the drug to cell membrane. There is no cross resistance to other antimicrobials and resistance rarely develops during treatment. As polymyxin B is bound to cell membranes with high affinity( in local administration) systemic reactions are very rare. In systemic applications it might cause nephrotoxicity( albuminuria, nitrogenemia) and neurotoxicity( facial paralysis, peripheral paresthesia, ataxia). During intrathecal administration there are findings of meningeal irritation such as fever, headache(increase of proteins and cells in CSF), rashes, drug fever and trombophlebits. Polymyxin B excreted though the kidneys. It is not absorbed from the gastrointestinal tract. It does not cross blood-brain barrier, thus cannot enter CSF. It has limited transmission to body fluids and organs such as lungs, liver, kidney and sceletal muscle. Polymyxin B has intravenous, intrathecal and topical route of administration in treatment. For the intrathecal administrations performed in adults patients and above two years of age after the first 3-4 days a single daily dose of 50 000 units/day is given every other day and the treatment is completed in two weeks(8,9).

The case has been presented for the purpose of emphasizing the role of polymyxin B in the treatment of pan-resistant Pseudomonas aeruginosa meningitis for which the treatment choices are limited.

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