

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

F Simsek, T Yildirmak, G Cetmeli, N Iris, A Kanturk

Citation

F Simsek, T Yildirmak, G Cetmeli, N Iris, A Kanturk. *Successful treatment of pan - resistant pseudomonas Aeruginosa meningitis with intrathecal polymyxin b therapy*. The Internet Journal of Infectious Diseases. 2008 Volume 7 Number 2.

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 successfully 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 drainage 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 administered 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 under controlled external drainage was ended. Her treatment was completed and she was discharged. She visited our out-patient department monthly 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 causative

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 successfully 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 drainage was initiated. The patient developed pain and

consciousness. CSF(cerebrospinal fluid) findings were WBC: 1300/mm³(%80 PMN,

%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 21 st 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 6 th 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 3 rd and 4 th generation cephalosporins,

antipseudomonal penicilin + 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 montly 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 succesful results(5). There are several case reports about the

treatment of meningitis with intrathecal or intraventricular

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 membran 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 membrans 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 sceleteal 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.

References

1. Hanberger H, Garcia- Rodriquez JA, et al. Antibiotic susceptibility among aerobic gram negative bacilli in intesive care units in European countries. JAMA 1999; 281(1):67-71
2. Yucesoy M, Yulug N, Kocagöz S, et al. Antimicrobial resistance of gram negative isolates from ICU in Turkey: Comparisonto

previous three years.

J Chemother 2000; 12(4): 294-8

3. Gunseren F, Mamikoglu L, et al. A surveillance study of antimicrobial

resistance of gram negative isolated from ICU in eight hospitals in Turkey. J

Antimic Chemother 2000; 43: 373-8

4. Turhan Ö, Saba R, İnan D, et al. Colistin as therapy for multi-drug resistant

Pseudomonas aeruginosa meningitis. Flora 2001; 6(2);131-33

5. Segal- Mauer S, Mariano N, Qavi A, et al. Successful treatment of ceftazidime-

resistant Klebsiella pneumoniae ventriculitis with intravenous meropenem and

intraventricular polymyxin B: case report and review. Clin Infectious Dis 1999;

28:1134-8

6. Falagas ME, Kasiakau SKN. Colistin: the revival of polymyxins for the

management of multi-drug resistant gram-negative bacterial infections. Clin.

Infect. Dis 2005;40:1333-1341

7. Falagas ME, Bliziotis IA, Vincent HT. Intraventricular or intrathecal use of

polymyxins in patients with gram-negative meningitis: a systemic review of the

available evidence. J of Antimic Agents 2007; 29: 9-25

8. Tunkel AR. Topical antibacterials. In: Mandell GL, Douglas R, Bennett JE eds.

Principles and practice of infectious diseases. New York: Medical

Publications, 1995: 381-7

9. Polymyxins. In: Finch RG, Greenwood D, Norrby SR, Whitley RJ. Antibiotic

and Chemotherapy. 2003 ; 34: 407-411

Author Information

Funda Simsek, M.D.

Department of Infectious Diseases and Clinical Microbiology, Okmeydani Resarch and Teaching Hospital

Taner Yildirmak, M.D.

Department of Infectious Diseases and Clinical Microbiology, Okmeydani Resarch and Teaching Hospital

Gul Cetmeli, M.D.

Department of Infectious Diseases and Clinical Microbiology, Okmeydani Resarch and Teaching Hospital

Nur Efe Iris, M.D.

Department of Infectious Diseases and Clinical Microbiology, Okmeydani Resarch and Teaching Hospital

Arzu Kanturk, M.D.

Department of Infectious Diseases and Clinical Microbiology, Okmeydani Resarch and Teaching Hospital