CARBAPENEM-RESISTANT ACINETOBACTER BAUMANNII POSTOPERATIVE MENINGITIS

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CARBAPENEM-RESISTANT *ACINETOBACTER BAUMANII* POSTOPERATIVE MENINGITIS *(ABSTRACT):* *Acinetobacter baumannii* is an opportunistic pathogen of increasing relevance in hospital infections during the last 15 years.This organism causes a wide range of infection .Extensive use of antibiotics within hospitals has contribute to the emergence of multidrug-resistent *A.baumannii* strains that exhibit resistance to a wide range of antibiotics ,including carbapenems.We report the case of an 37 years old man diagnosed with Acinetobacter multidrug-resistant post-neurosurgical meningitis with fatal outcome.

KEY WORDS: POSTOPERATIVE MENINGITIS, MULTIDRUG-RESISTANT *ACINETOBACTER BAUMANNII*.

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INTRODUCTION

Acinetobacter baumannii is an opportunistic germ of clinical importance in continuous boost for the last 15 years, which can determine a big number of infections: sepsis, pneumonias, plague infections, urinary tract infections and post-operation meningitis, especially in the patients of the intensive care units [1].

The emergence of resistance of Acinetobacter to a wide range of antibiotics makes these infections almost impossible to treat.

CASE PRESENTATION

We would like to present the case of a patient of 37 years old, hospitalized twice in our clinic through transfer from the Neurosurgery Hospital in February and April 2005. This youngster was the victim of a labor accident in February 2005, which resulted into craniocerebral injury, right frontal and orbital sinus, for which it was preceded surgically.

Postoperative, after 24 hours, the patient presents fever, the lumbar puncture showing pleiocitosis thus being transferred to the Clinic of Infectious Diseases, with the suspicion of bacterial meningitis.

At his first hospitalization (in February 2005): patient was in vegetative status, tube fed. The lumbar puncture presents milky cephalorachidian liquid, with 1500 elements/mmc, with PN prevalence. The fever occurrence immediately after the surgery indicates the suspicion of post-traumatic meningitis and not a nozocomial meningitis and it was initiated a treatment in association with 3rd generation Cefalosporine and Ciprofloxacin. In his 8th day of hospitalization the patient presents convulsions at the level of his right hemicorpus.

* received date: 10.10.2010
accepted date: 08.12.2010

He is evaluated again in the Neurosurgical Clinic and a new surgical intervention is done to solve the cranionasal fistula and in order to evacuate a left parietal hematoma. The evolution is aggravated by incidence of a stercoral peritonitis through the rectum rupture for which it was surgically performed a temporary colostomy. During all this time he received treatment with 3rd generation Cefalosporine, Fluoroquinolone and Metronidazol. The patient becomes feverish, the lumbar puncture presents milky cephalorachidian liquid (LCR), and the cerebral CT examination indicates: bilateral hemispheric diffuse edema, contrast clutch with aspect of epidural and epicranial biconvex lens at the level of the left frontal craniotomy area (aspect of meningo-encefalitis and non-surgical epiduritis at that specific moment). The patient returns to our clinic for further investigations and treatment.

At the moment of the hospitalization the patient was in a serious general condition, with obstruction in the tracheo-bronchial area, requires oxygen and frequent aspiration of the tracheo-bronchial areas. The lumbar puncture presents milky purulent cephalorachidian liquid (LCR), with intense inflammatory reaction. At the direct examination there was observed Gram-negative diplococci and coco bacillus. Given the patient status, the multiple surgical interventions and the anterior prolonged treatment with antibiotics it was supposed the implications of several germs with multiple resistance to antibiotics and it was proceeded to the treatment with Vancomycin 1g/day and Meropeneme 3g/day The cultures obtained from the cephalorachidian liquid were positive for *Acinetobacter baumannii* and the resistance profile of the stem had raised serious problems when choosing the accurate treatment. Acinetobacter baumannii provided resistance to ampicilline, amoxicilline-clavulanic acid , ticarcilline, ticarcilline- clavulanic acid , 3rd generation cephalosporin ,quinolones, trimethoprim-sulfamethoxazole , aminoglycozides ,imipenem,meropenem, and cefoxitin.

The thoracic radiography proves the aspect of bronchopneumonia (Table 1). The biological analysis emphasizes an important inflammatory syndrome and severe anemia (Table 2).

Table 1
Results of imagistic exploration

IMAGISTIC EXPLORATION	RESULTS
Thoracic radiography (11.04)	intense and homogenous opacity with retractile character, left hemithorax
Abdominal ultrasonography	kidneys with extended sinus areas
Cerebral CT	cerebral edema, contrast clutch at the right frontal level

Table 2
Biological probes

	11.04	**18.04**
Haematocrit	3.300.000	2.290.000.
Hemoglobin	10	6,9
Leucocytes	30.000.	17.300.
Segmented neutrophils	90%	88%
Eosinophils		1%
Lymphocytes	5%	7%
Monocyte	5%	4%
Basophils		
Trombocytes	305.000.	246.000.
Fibrinogen	408 mg%	
VSH	120 mm/1h	

In the light of the new information, the choice for an association of efficient antibiotics had proven to be impossible. It was chosen for the association of Vancomycin and Pefloxacine but the evolution was unfavorable and the pleiocytosis persisted in the cephalorachidian liquid (LCR) (Table 3).

Table 3
Examination of the cephalorachidian liquid

11.04	Cephalorachidian liquid aspect	Elements	Sediment
	blur	uncountable	PN 95%, L 5%
14.04	blur	uncountable	PN 90%, L 7%
18.04	blur	uncountable	PN 71%, L 25%

In the 8th day of hospitalization the patient presents troubles of respiratory rhythm with desaturation, needing the transfer into the Neurosurgery Intensive Care Unit for ventilation support where he later deceases.

DISCUSSIONS

Acinetobacter baumannii is an opportunistic germ of clinical importance in continuous boost for the last 15 years, which can determine a big number of infections: sepsis, pneumonias, plague infections, urinary tract infections and post-operation meningitis, especially in the patients of the intensive care units [1]. The excessive utilization of the antibiotics in the hospitals had lead to an increase of *A.baumannii* stems with extended resistance to antibiotics, including to the new generations of extended-spectrum of Betalactamine, Aminoglycoside and Fluoroquinolone [2]. The Carbapenemes were, until recently, elective antibiotics for the treatment of the infections determined by the stems of *A.baumannii* multidrug–resistant. However *Acinetobacter* can develop a resistance to Carbapenemes through different mechanisms: decreasing the membrane permeability, supra expressing the efflux pumps and the Carbanemases production [3].

During the last years the resistance to Carbapenemes was especially attributed to the production of D class Carbapenemases (Carbapenem-hydrolysing oxacillinases) OXA -24, OXA-24, OXA- 58 and the enzymes OXA -51like and less frequent to B class metallo-betalactamases of (MBLs) type IMP, VIP and SIM [3].

Acinetobacter baumannii multidrug-resistant can trigger epidemics in the hospital departments [4,5] (as described in hospitals from Greece and Poland) where it can survive for longer periods of time.

The Carbapenemes have constituted for a long time the only hope in the treatment of the infections with *Acinetobacter* multidrug resistant and continues to be, in many areas, still active. Evidences about the resistance to Carbapenemes were mentioned all over the world [6,7]. Recently, it has been proven the increase of the infection incidence with these stems in the hospitals from USA and Europe, after the return of the militaries from Iraq and in Romania as well [8]. According to a MART-T study accomplished in four university center (Iasi, Constanta, Timisoara and the Institute ,,Matei Bals" from Bucharest) during July 2008 – December 2009, it was noticed that the volume of *Acinetobacter* stems sensible to Carbapenemes has largely decreased as compared to the year 2007: $p < 0,0001$ being identified in approximately 28% of the cases [9]. For these situations we have only a few therapeutic options and

the circumstances of central nervous system infections are more dramatic as the therapeutic arsenal is somehow reduced.

The risk factors for the infections with *Acinetobacter* multidrug resistant to antibiotics are: prolonged hospitalization - especially in the intensive care units, invasive devices, immune depression and anterior treatment with antibiotics, including Carbapenemes.

The patient presented in this case study was hospitalized post-operation in the intensive care unit (The Neurosurgical Hospital, the Clinic of Infectious Diseases) for a period of approximately 50 days. Prolonged hospitalization - especially in the intensive care units, during wich he received multiple antimicrobials, includig 3rd generation Cefalosporine, Fluoroquinolone and carbapenems ,multiples invasive devices , result in high risk of infection with MDR – Acinetobacter. During the first period episode of meningitis occurred within 24 hours after the operation, there was no suspicion for a nozocomial etiology of the infection (reason for which it was initiated the treatment with Ceftazidime and Ciprofloxacin, which are proven to cover the etiology of a post-traumatic meningitis). During the second round of hospitalization, after several surgical interventions and hospitalizations in intensive care units, it was emphasized the possible implication of the Meticilline-resistant Staphylococcus Aureus of the resistant non-fermentative Gram-negative bacillus. It was initiated the associated treatment with Vancomycin and Meropeneme.

The cultures obtained from the cephalorachidian liquid (LCR) have isolated *Acinetobacter baumannii* with intermediate resistance to Ofloxacine and Pefloxacine and resistant to Cephalosporin, Ciprofloxacin and Carbapenemes.These strains of Acinetobacter could infect a patient ,,per primam,, or, become resistant because of antimicrobial pressure. The main characteristic of *A. baumannii* is the capability of surviving for prolonged periods in the environment, thus contributing to the transmission of the organism during outbreaks.

The intestinal tract provides also, an important reservoir for antibiotic-resistant gram-negative bacilli,including Enetrobacteriacee species, *Pseudomonas aeruginosa*, and *Acinetobacter baumannii*.Selected pressure exerted by antibiotics play a crucial role in emergence and dissemination of these pathogens [10]. In this particular case, intestinal colonization was possible during his prolonged hospitalization and antimicrobial treatments.The incidence of a stercoral peritonitis through the rectum rupture resulted in translocation of MDR –Acinetobacter ,as a second possible source of infection.

The antibiogram gives us no possibility to treat such an infection. The subsequent treatment of meningitis with Vancomycin and Pefloxacine was inefficient. In the 8th day of hospitalization the patient presents troubles of respiratory rhythm with desaturation and died.

This case is an example of worse outcome in a serious ill patient when an antibiotic therapy is no more available.

Colistin seems to be the break away solution of the moment, according to the studies proceeded in areas where there have been registered real epidemic infections with *Acinetobacter* multidrug/pan drug resistant. The microbiological studies have compared the efficiency of Colistin in mono therapy vs. associations, identifying a synergic effect for Colistin - Rifampicin, Colistin – Carbapenemes [11]. The reduced permeability of the Colistin in the cephalorachidian liquid (LCR) represents the main disadvantage for treating the infections of the central nervous system (SNC). However,

there are studies according to which these patients could beneficiate of intrathecal or intraventricular administration of Colistin, with more than 80% success rate [12].

CONCLUSIONS

Meningitis with resistant non-fermentative Gram-negative bacillus represents a permanent provocation due to treatment difficulties in the conditions of a reduced arsenal of antibiotics. The amount of *Acinetobacter baumannii* stems resistant to Carbapenemes reaches disturbing limits in Europe (Poland, Greece) but in Romania as well (where approximately 28% of the stems are sensible to Carbapenemes). The risk factors for the infections with *Acinetobacter* with multiple resistances to antibiotics are: prolonged hospitalization - especially in intensive care units, invasive devices, immune depression and anterior treatment with antibiotics, including Carbapenemes. The new options for all these infections are the synergic associations such as Colistin - Rifampicin, Colistin - Carbapenemes.

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