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One case of extensively drug-resistant (XDR) infection

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Abstract
Infections due to multidrug resistance of the infected organism have become more common in clinical settings. The non-fermenter, gram-negative bacilli cause severe hospital infections. The main non-fermenter, gram-negative bacilli (BNF) microorganisms, that cause disease in humans are Pseudomonas aeruginosa, Acinetobacterbaumannii, Burkholderia cepacia, Stenotrophomonas., Alcaligenes, Moraxella, The family of enzymes carbapenemase – KPC, NDM-1, IMP, VIM, OXA-48 – is one of the most significant health challenges. For microorganisms: Klebsiella pneumoniae, Acinetobacter baumanni, and Pseudomonas aeruginosa was launched the terms: extensively drug-resistant (XDR) and pan drug-resistant (PDR) Gram-negative microorganisms. New antibiotics is targeting some of the current most problematic Gram-negative pathogens, namely Klebsiella pneumoniae carbapenemase (KPC) - producing Enterobacteriaceae and multi-drug-resistant (MDR) *P.* aeruginosa. We presented case, when sputem microbiological analysis in patient with bilateral pnumoniae and respiratory distress syndrome, revealed extensively drug-resistant (XDR) gram-negative microorganism. Also chest computer tomography diagnosed lung cavitation,For antibacterial treatment was used new class of antibiotics, named Ceftazidime-Avibactam,a novel non-β-lactam, β-lactamase inhibitor(restores the activity of ceftazidime against the majority of β- lactamases,ESBLs and carbapenemases, including KPCs– Ambler Class A, AmpC —Class C and oxacillinase OXA-48—Class D).Patient state was improuved and discharged with suitable recommendations.

Conclusion: in the therapy of XDR Gram-negative bacteria, colistin was continued to be considered as a companion drug with novel agents es ceftazidim/avibactam for the treatment of carbapenem-resistant Enterobacteriaceae, also fosfomycin as part of combination treatment for CRE and XDR Pseudomonas aeruginosa infections.

Keywords: XDR infection. Multidrug resistant. Cavitation

Introduction
Infections due to multidrug resistance of the infected organism have become more common in clinical settings. The general/species are Escherichia, Proteus, Enterobacter, Klebsiella, Citrobacter, Yersinia, and Shigella. The non-fermenter, gram-negative bacilli cause severe hospital infections. In ICU patients who undergo invasive procedures they also cause opportunistic diseases.The main microorganisms are: Pseudomonas aeruginosa, Acinetobacterbaumannii, Stenotrophomonas. Alcaligenes, Moraxella. There are three main enzymes that inactivate antibiotics such as: β-lactamases, aminoglycoside-modifying enzymes, and chloramphenicol acetyltransferases (AACs). Bacteria that produce extended-spectrum β-lactamases, so called ESBL-producing bacteria, are resistant to penicillins, third-generation cephalosporins. Metallo-β-lactamases classes of enzymes are resistant to inactivation by clavulanate, sulbactam, aztreonam, and carbapenems. Cephalosporinases are produced by all Gram-negative bacteria with exception of Salmonella and Klebsiella. This class of enzymes is resistant to all β-lactams except carbapenems. The family of enzymes carbapenemase – KPC, NDM-1, IMP, VIM, OXA-48 – is one of the most significant health challenges. For microorganisms: Klebsiella pneumoniae, Acinetobacter baumanni, and Pseudomonas aeruginosa was launched the terms: extensively drug-resistant (XDR) and pan drug-resistant (PDR) Gram-negative microorganis

Two large groups, Enterobacteriaceae and the non-fermenters, are responsible for most clinical isolates; nevertheless, other clinically concerning gram-negative organisms exist, including Neisseria, Haemophilus spp., Helicobacter pylori, and Chlamydia trachomatis

The non-fermenter, gram-negative bacilli (BNF) have a lower frequency of isolation when compared to Enterobacteriaceae*;* however, they cause severe, fatal infections, especially in the hospital environment. They also cause opportunistic diseases in ICU patients who undergo invasive procedures. The main BNF microorganisms that cause disease in humans are Pseudomonas aeruginosa, Acinetobacter baumannii, Burkholderia cepacia, Stenotrophomonas., Alcaligenes, Moraxella.

Acinetobacter baumannii naturally produces AmpC cephalosporinase and also oxacillinase (OXA), leaving it spontaneously immune to many drugs. Colistin, one of the few antibiotics that still treat multiresistant infections, already has a mobile resistance gene, mcr-1, and Enterobacteriaceae has a crucial role in the spread of this gene.New antibiotics is targeting some of the current most problematic Gram-negative pathogens, namely Klebsiella pneumoniae carbapenemase (KPC)-producing Enterobacteriaceae and multi-drug-resistant (MDR) *P.* aeruginosa.

Patient 70 years old man,Caucasus,was admitted in hospital with respiratory failure, with agrevated state despite of treatment with antibiotics: ceftriaxone, azitromicine.

Chest X-ray and blood gas analysis confirmed diagnoses: bilateral pneumonia and adult respiratory distress syndrome. Sputum microbilogical analysis within admittion revealed staphylococcus haemolyticus.

Staphylococcus haemolyticus	MB19(F-SOP_028B-001-03)
Oxacillin,cefoxitin., ampicillin/sulbactam, Amoxicillin/sulbactam, pipearacillin/tazobactam,cefuroxime,**ceftazidim,** ceftriaxone,cefepime, meropenem,erythromycin,clindamycin,cipriflixacxin, moxifloxacin,levofloxacin, ofloxacin,	R
Teicoplanin,vancomycin,fosfomycin	S

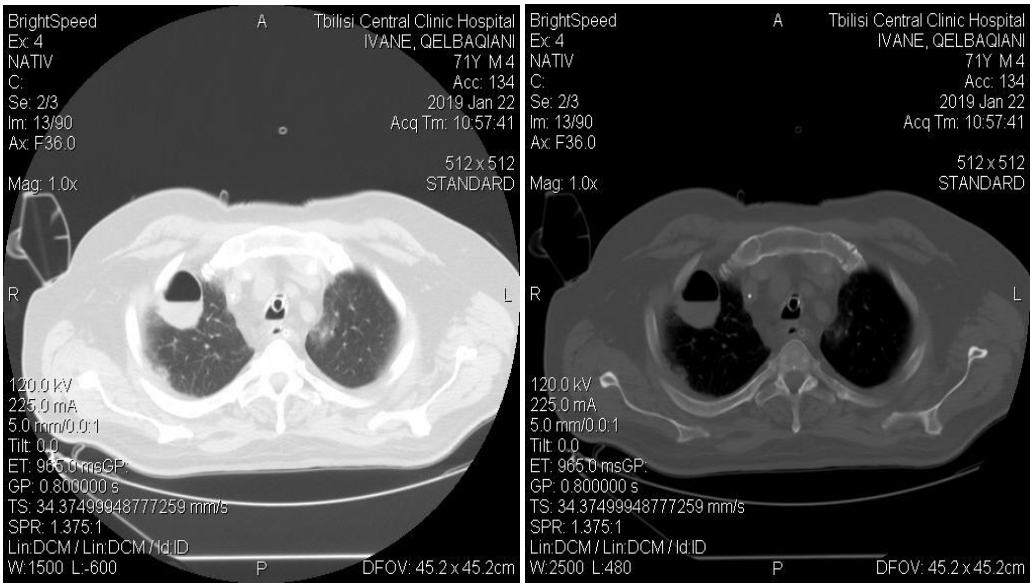
Patient started mechanical ventilation and was changed antibacterial treatment with piperacillin/tazobactam, moxyfloxacin and vancomycin. After 4 day treatment sputum culture revealed new microbs: Acinetobacter baumannii and klebsiella pneumonia.

Acinetobacter baumani complex 10^6/ml	AG3MB.19(F-SOP-028B-001-03
Ticarcilin,ticarcilin/clavulatic acid,piperacillin/tazobactam.Ceftazidime, cefepime, Aztreonam,Imipenem,Meropenem, Amikacin, Gentamicin,Tobramicin, Ciprofloxacin,Pefloxacin, Levofloxacin,ofloxacin, Cefoperazone.Sulbactam	R
Minocycline,Colistin	S
Rifampicin	I

Klebsiella pneumonia 10^6/ml	MB19(F-SOP_028B-001-03)
Ticarcilin,tTicarcilin/clavulatic acid, Piperacillin/tazobactam.Ceftazidime, Cefepime, Gentamicin, Ciprofloxacin, Levofloxacin, Ofloxacin,, Imipenem,Meropenem	R
Colistin	S

Antibacterial treatment regimen was changed with meropenem, colomycin. Chest computer tomography revealed bilateral diffuse infiltrates in lung parenchyma, alveolitis in upper part of lung,cavitation with horizontal level of air and liquid, size -1.3cm x 4.6cm, in upper,lateral part of right lung,near II riber. GeneXpert MTB diagnostic test for identification of Mycobacterium tuberculosis in bronchoalveolar liquid by PCR method was negative.

Next microbiological analysis of sputem revealed MDR klebsiella pneumonia with intermadiate sensitivity on colomycin. Antibacterial treatment was continiued with colistin - zavicefta (ceftazidim /avibactam) combination. Zavicefta dose was 2/0, 5 mg. in every 8 h.



Pict. 1

GeneXpert MTB diagnostic test for identification of Mycobacterium tuberculosis (MTB) in bronchoalveolar liquid by PCR method was negative.

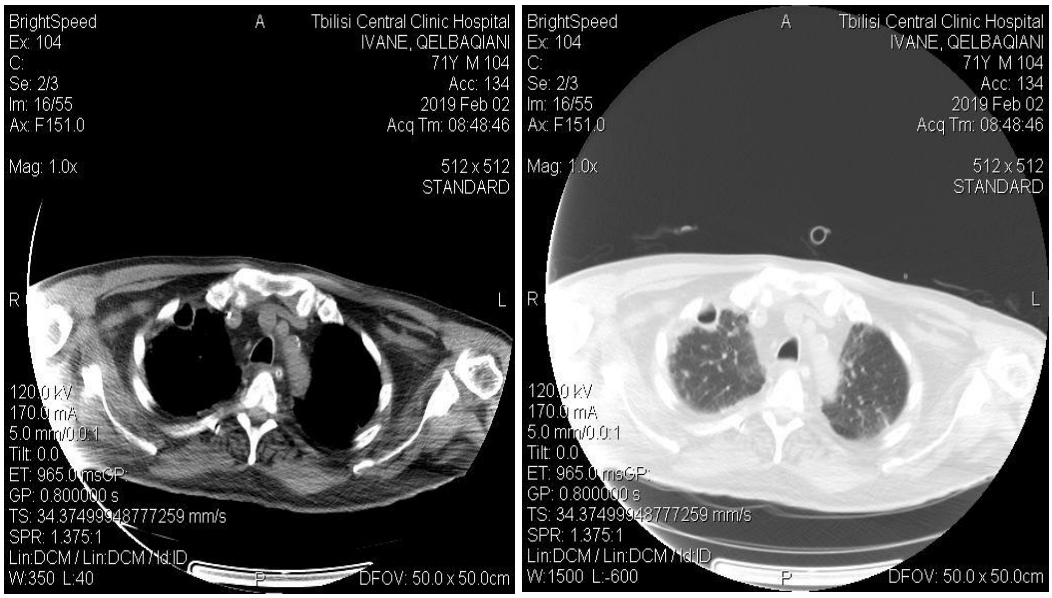
Next microbiological analysis of sputem revealed MDR Acinetobacter baumani with intermadiate sensitivity on colomycin. Antibacterial treatment was continiued with colistin and zavicefta (ceftazidim /avibactam).Zavicefta dose was 2/0, 5 mg. every 8 hours.

After one weak of treatment chest computer tomography revealed increased intensity of bilateral diffuse infiltrates in parenchyma in lower part of lung. In upper,lateral part of right lung,near II riber, increased size of cavitation 4.3X 4.6cm, with horizontal level of air and liquid.

Antibacterioal treatment was defined as follows: zavicefta,colomycin, vancomycin, in next period was continued with zavicefta,fosfomycin and in last decade with zavicefta, clindamycin(1.8g/per day).

Ct scan shows a decrease in size of cavitation and intensity of infiltration.

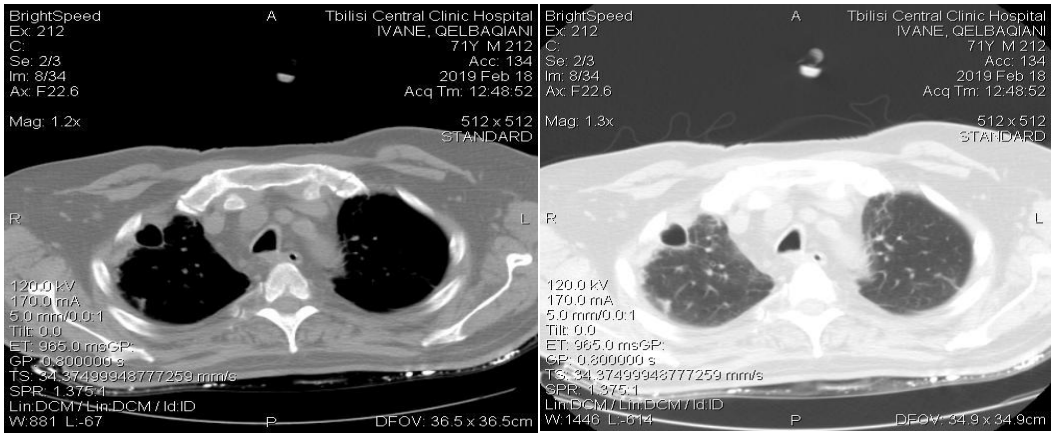
Patient was discharged with suitable recommendations.



Pict. 2

By sputum and blood microbiological analysis does not revealed any microb,antibacterial treatment continued with Zavicefta 7.5mg and fosfomycin 18 within one weak, and zavicefta –clindamicin combination within 2 weak. Patient state was improuved and was disconnected from mechanical ventilation.

On Ct scan revealed decreased intensity of bilateral infiltrates in lower part of lung, bilateral diffuse sclerosis, decreased size of cavitation to 1.7X1.8cm with air level**.** **(**pict.3)



Pict.3

Discution

There are three main enzymes that inactivate antibiotics such as: β-lactamases, aminoglycoside-modifying enzymes, and chloramphenicol acetyltransferases (AACs). Bacteria that produce extended-spectrum β-lactamases, so called ESBL-producing bacteria, are resistant to penicillins, third-generation cephalosporins. Metallo-β-lactamases classes of enzymes are resistant to inactivation by clavulanate, sulbactam, aztreonam, and carbapenems. Cephalosporinases are produced by all Gram-negative bacteria with exception of Salmonella and Klebsiella. This class of enzymes is resistant to all β-lactams except carbapenems. The family of enzymes carbapenemase – KPC, NDM-1, IMP, VIM, OXA-48 – is one of the most significant health challenges. For microorganisms : Klebsiella pneumoniae, Acinetobacter baumanni, and Pseudomonas aeruginosa was launched the terms : extensively drug-resistant (XDR) and pan drug-resistant (PDR) Gram-negative microorganisms.The non-fermenter, gram-negative bacilli (BNF) have a lower frequency of isolation when compared to Enterobacteriaceae*;* however, they cause severe, fatal infections, especially in the hospital environment. They also cause opportunistic diseases in ICU patients who undergo invasive procedures. The main BNF microorganisms that cause disease in humans are Pseudomonas aeruginosa, Acinetobacter baumannii,Burkholderiacepacia,
Stenotrophomona., Alcaligenes, Moraxella.
Enterobacteriaceae are a heterogeneous group, account for about 80% of gram-negative isolates. The general species that frequently affect humans areEscherichia, Proteus, Enterobacter,
Klebsiella,Citrobacter,Yersinia,Shigella,and Salmonella am ong others. Avibactam, a novel non-β-lactam, β-lactamase inhibitor, restores the activity of ceftazidime against the majority of β- lactamases (ESBLs and carbapenemases, including KPCs– Ambler Class A, AmpC —Class C and oxacillinase OXA-48—Class D). Avibactam is not able to inhibit strains producing metallo-β-lactamases (MBL—Class B)

Conclusion

In the therapy of XDR Gram-negative bacteria, colistin was continued to be considered as a companion drug with novel agents es ceftazidim/avibactam,also fosfomycin as part of combination treatment for CRE carbapenem-resistant enterobacteriaceae and XDR Pseudomonas aeruginosa infection.

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