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The impact of quantitative and semi-quantitative culture of respiratory tract secretions on clinical decisions in a patient with suspected pneumonia – case study

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ABSTRACT

Pneumonia is one of the most common disease entities treated in the Intensive Care Unit. The standard diagnostic procedure for patients with suspected pneumonia is to evaluate the presence of symptoms of infection, physical examination, imaging, laboratory and microbiological tests, arterial blood gasometry and culture of respiratory tract secretions. In many Intensive Care Units, the preferred method of collecting material from the lower respiratory tract is an endotracheal aspirate. However, its semi-quantitative culture does not distinguish respiratory tract colonization from infection. Samples obtained by bronchoscopy are believed to be more representative of the presence of true pathogens in the lungs.

An 87-year-old patient with myasthenia gravis was admitted to the Intensive Care Unit for suspected pneumonia. Laboratory tests showed elevated inflammatory markers and a chest X-ray showed interstitial densities in the left lower lobe. The result of semi-quantitative culture of tracheal aspirate (TA) was heavy growth of *Staphylococcus aureus* and heavy growth of *Pseudomonas aeruginosa*. The result of the quantitative bronchoalveolar lavage (BAL) culture was *S.aureus* MSSA 10^5 colony-forming unit (CFU) per ml, *Pseudomonas aeruginosa* 10^2 CFU/ml. To consider a microorganism responsible for infection, the number of bacteria cells must exceed a designated threshold. For BAL it is $\geq 10^4$ CFU/ml, for TA it is $\geq 10^6$ CFU/ml, for PSB it is $\geq 10^3$ CFU/ml. In this case, the cutoff point for identifying the pathogen responsible for the infection was reached only by *Staphylococcus aureus* (10^5 CFU/ml), not by *Pseudomonas aeruginosa* (10^2 CFU/ml).

The final diagnosis was left-sided PN1 pneumonia of *S.aureus* etiology. A cloxacillin was used for the treatment. Clinical improvement was achieved.

The described case proves the advantage of quantitative culture over semi-quantitative culture of respiratory tract secretions. The advantage of BAL over tracheal aspirate is also noticeable.

Keywords: Quantitative culture; Semi-quantitative culture; Endotracheal aspirate; Bronchoalveolar lavage; Lower respiratory tract infections; Pneumonia.

INTRODUCTION

In Intensive Care Units (ICUs) the standard diagnostic procedure for patients with suspected pneumonia is to evaluate the presence of symptoms of lower respiratory tract infection, physical examination, imaging tests, laboratory tests, arterial blood gasometry and culture of material collected from the lower respiratory tract. Each sample of secretions can be cultured semi-quantitatively and quantitatively. In the second method, the result is the number of colony-forming units (CFU) per ml. To distinguish bacterial colonization from respiratory tract infection, designated threshold levels have been defined for samples cultured by the quantitative method, depending on the method of obtaining the material (1).

The infection indicator is the threshold level of 10^6 CFU/ml for tracheal aspirate (TA) cultures, 10^4 CFU/ml for bronchoalveolar lavage (BAL) cultures, 10^3 CFU/ml for protected specimen brush (PSB) cultures (2).

It is also worth mentioning that the PN classification allows to assign pneumonia to one of five categories, depending on the method used to obtain the secretion (2).

The article describes a case of a patient with pneumonia treated in the Intensive Care Unit, that proves the advantage of quantitative over semi-quantitative culture of respiratory tract secretions, as well as the advantage of collecting BAL over collecting tracheal aspirate. This enabled the differentiation of airway colonization from infection, thereby clarifying the etiology of pneumonia and contributing not only to the selection of the most effective antibiotic against identified microorganism, but also to the narrowing antibiotic therapy.

CASE REPORT

A 87-year-old male patient was admitted to the Intensive Care Unit with an exacerbation of chronic respiratory failure. The patient was chronically treated for myasthenia gravis, ischemic heart disease, diabetes mellitus type II, hypertension, with a history of NSTEMI myocardial infarction, status post coronary artery bypass grafting and aortic valve replacement, status post stroke. Patient with a percutaneous endoscopic gastrostomy (PEG), on industrial diet, on home mechanical ventilation program.

On admission, the patient was conscious with resting dyspnea, purulent respiratory secretions, a fever of 39°C and sweats. In addition, redness of the skin around the tracheostomy and

gastrostomy was visible. Sedation with propofol and dexmedetomidine was administered and volume-support ventilation (VSV) was started with fraction of inspired oxygen (FiO₂) 0.4, positive end-expiratory pressure (PEEP) 5. The tracheostomy tube was replaced, tracheal aspirate was collected for microbiological diagnostics. Circulation was stable with a tendency to hypotension, diuresis was present. Crystalloid fluid therapy was implemented. Laboratory tests, arterial blood gasometry, chest X-ray were ordered. An arterial cannula and urinary catheter were placed. The ultrasound imaging showed no features of venous thrombosis of the lower extremities. Lung ultrasound (LUS) showed consolidation over the base of the left lung. A chest X-ray revealed an inflammatory infiltrate in the lower lobe of the left lung. Laboratory tests showed elevated inflammatory markers (table 1.).

Table 1. Laboratory results

Indicator name	Results – first day of hospitalization	Results – last day of hospitalization
RBC [x10 ⁶ /μl]	4.04	3.94
HCT [%]	35.9	35.9
MCV [fl]	88.9	91.1
HGB [g/dl]	12.0	11.5
WBC [x10 ³ /μl]	15.38	8.61
PLT [x10 ³ /μl]	175	303
MONO [x10 ³ /μl]	1.10	0.59
NEUT [x10 ³ /μl]	12.33	4.31
CRP [mg/l]	152.2	55.1
IL-6 [pg/ml]	594.3	65.91
PCT [ng/ml]	0.134	
Urea [mmol/l]	11.5	10.9
Cr [μmol/l]	103	81
AST [U/l]	19	
ALT [U/l]	13	
Kalium [mmol/L]	4.0	3.7
Natrium [mmol/L]	136	140

On the following day, the diagnostics was expanded, including bronchoscopy - the bronchi were obstructed, mucosa was reddened and swollen, and the bronchial lumen easily collapsed under negative pressure. After intubation of the eighth segmental bronchus of the left lung (localization based on the area of inflammatory infiltration in the lower lobe of the left lung on chest X-ray), BAL was collected. Empirical antibiotic therapy with piperacillin and tazobactam was initiated (9.0 g intravenously, 3 x 3.375 g after 4 hours in a 4-hour intravenous infusion). The result of semi-quantitative culture of tracheal aspirate was heavy growth of *Staphylococcus aureus* and heavy growth of *Pseudomonas aeruginosa*. The result of quantitative BAL culture was *S. aureus* MSSA 10^5 CFU/ml, *Pseudomonas aeruginosa* 10^2 CFU/ml. *Pseudomonas aeruginosa* was only susceptible to carbapenems and aminoglycosides, resistant to piperacillin/tazobactam, susceptible with increased exposure to fluoroquinolones. Clinical symptoms, laboratory, imaging and microbiological tests allowed to make a diagnosis of left-sided PN1 pneumonia of *S. aureus* etiology. Antibiotic therapy was de-escalated - targeted treatment with cloxacillin (6 x 2.0 g iv) was started and continued for 5 days. Clinical improvement and reduction of inflammatory markers were achieved. The patient was discharged from the hospital with the recommendation of sequential therapy with first-generation cephalosporin (cefadroxil 2 x 1.0 g per os for 10 days).

DISCUSSION

In the Intensive Care Unit, the diagnosis of lower respiratory tract infection (LRTI) includes the presence of clinical symptoms, abnormal radiological and laboratory findings and positive microbiological tests (3) . In described case, the patient met the classic criteria for the diagnosis of pneumonia. Symptoms were present both from the lower respiratory tract (purulent discharge) and systemically (fever, sweats). A chest X-ray showed inflammatory infiltrates in the lower lobe of the left lung. Laboratory results showed high inflammatory parameters - leukocytosis, elevated interleukin-6 (Il-6) and C-reactive protein (CRP) levels. The result of semi-quantitative culture of tracheal aspirate was heavy growth of *Pseudomonas aeruginosa* and heavy growth of *Staphylococcus aureus* MSSA. Considering the fact that the patient had been on home mechanical ventilation for many years, which is associated with a high risk of colonization of his airways by pathogens, the decision was made to perform bronchoscopy. A tracheobronchial toilet was performed and BAL was collected. The BAL was cultured quantitatively. The cut-off point for identifying the pathogen responsible for the infection was reached only by *Staphylococcus aureus* (10^5 CFU/ml), not by *Pseudomonas*

aeruginosa (10^2 CFU/ml). All this allowed to make the diagnosis of pneumonia of *Staphylococcus aureus* etiology.

In patients with artificial airways, tracheal aspirate (TA), bronchoalveolar lavage (BAL) and protected specimen brush (PSB) can be used for culture (4). In many Intensive Care Units, direct tracheal aspirate is the most common method of obtaining material (5).

The benefits of TA collection may apply to resource-limited cases (4). However, it should be noted that non-quantitative TA cultures cannot distinguish colonization from infection (6).

Bronchoalveolar lavage is a minimally invasive procedure that contributes to the diagnosis of various lung diseases, such as lower respiratory tract infections, unexplained pulmonary infiltrates or hypoxemia (7,8). It involves injecting saline into a lung subsegment, aspirating it and collecting it for analysis (7). This material provides many important microbiological clues indicating the etiology of LRTI, which determine further treatment (9,10). It is believed that samples obtained during bronchoscopy are more representative of the presence of true pathogens in the lungs (11, 12). Using a protected specimen brush in the diagnosis of pneumonia has a great advantage. Namely, it protects the sample from contamination by proximal secretions, thereby reducing the risk of false-positive results (13).

The method of microbiological diagnostics should always be considered individually. Early assignment of patients to a group at risk for severe pneumonia is valuable, because it determines who will benefit from invasive procedures (14). However, if pneumonia is suspected in a critically ill patient and invasive procedures such as BAL or PSB are not possible, quantitative TA cultures are useful (15).

It is important to always be aware of the phenomenon of colonization, especially since the endotracheal tube and airway are colonized quickly after intubation (12). By definition, colonization is the presence of a microorganism on a body surface that does not cause disease in an organism (16, 17). Distinguishing colonization from infection is an important factor in making a correct diagnosis, so the use of a quantitative cut-off for the number of CFU is recommended (12, 18). Qualitative and semi-quantitative cultures are considered to have poorer diagnostic value than quantitative cultures (10,12,16).

To consider a microorganism as an etiological agent of infection, the number of bacteria cells in a quantitative culture should exceed a designated threshold. There are different cut-off

points depending on the lower respiratory tract material. For BAL it is $\geq 10^4$ CFU/ml, for TA it is $\geq 10^6$ CFU/ml, for PSB it is $\geq 10^3$ CFU/ml (2).

Depending on microbiological findings, pneumonia can be assigned to 1 of 5 subcategories in the PN classification. PN 1 includes BAL with a threshold level of $\geq 10^4$ CFU/ml or PSB with a threshold level of $\geq 10^3$ CFU/ml, PN 2 includes TA with a threshold level of $\geq 10^6$ CFU/ml, PN 3 includes alternative microbiological methods such as positive blood culture, positive growth in pleural fluid or lung abscess culture, etc. (2). PN 4 includes positive sputum culture or non-quantitative LRT sample culture (2). Finally, PN 5 without a positive microbiological test (2).

Reduced diversity of the lung microbiome and increased numbers of potential pathogens such as Staphylococci and Pseudomonas spp. have been reported in mechanically ventilated patients (20). Prolonged hospital stay, antibiotic use and severity of illness are thought to increase the risk of Pseudomonas aeruginosa colonization (21). P. aeruginosa is an opportunistic pathogen that has the ability to acquire antibiotic resistance and form antibiotic-resistant biofilms, which can cause many therapeutic problems (22). A biofilm is a structure that surrounds bacteria and protects them from environmental stress - allowing them to colonize and survive for a long time (23). It can be found on medical devices such as catheters, nebulizers and humidifiers (22). Pseudomonas aeruginosa usually causes respiratory and urinary tract infections, burn wound infections, meningitis and sepsis (17). It is also worth mentioning that tracheal colonization by P. aeruginosa increases the risk of VAP eight times (21).

The adequacy of initial antimicrobial treatment plays a crucial role in the prognosis of pneumonia. The etiologic agent of the infection must be diagnosed in order to manage and appropriately guide antimicrobial therapy (19). Antimicrobial resistance is noticeable, so targeted antibiotic therapy must be implemented (1). In addition, limiting the use of antibiotics reduces mortality in critically ill patients (20).

CONCLUSIONS

In summary, the etiology of pneumonia must be identified to initiate optimal therapy. The method of microbiological diagnostics should always be considered individually. Samples

obtained during bronchoscopy are recommended due to the greater representativeness of the presence of the true pathogen in the lungs. In addition, all samples should be cultured quantitatively, as this allows to distinguish colonization from infection.

In this case, BAL and its quantitative culture allowed to avoid misdiagnosis, i.e. pneumonia of dual etiology. Then the included antibiotic therapy would cover both *Pseudomonas aeruginosa* and *Staphylococcus aureus* in the spectrum, which would not be appropriate and would contribute to the unfavorable phenomenon of massive use of antibiotics.

DISCLOSURES

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