Ventilator-Associated Pneumonia (VAP) in a Patient with Guillain-Barre Syndrome

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ABSTRAK

Seorang pria usia 46 tahun, dari ICU dengan diagnosis saat masuk Guillain-Barre syndrome (GBS) + sepsis ec suspek ventilator associated pneumoniae (VAP), dimintakan bahan pemeriksaan laboratorium: darah lengkap, kultur, resistensi ujung selang suction, urinalisis dan kultur urin, kultur darah dan resistensi, procalcitonin dan laktat. Didapatkan neutrofilia, peningkatan procalcitonin dan laktat sesuai diagnosis sepsis, dan pada hasil kultur selang suction didapatkan kuman Pseudomonas luteola MDRO yang kemungkinan berasal dari kolonisasi pada oropharynx pasien, akibat higiene oral pasien yang buruk dan tindakan perawatan higiene oral oleh perawat yang kurang efektif, sehingga kuman yang berkolonisasi tersebut terbawa saat pengambilan sampel. Perawatan higiene oral yang tidak efektif potensial untuk terjadinya VAP dan VAP berulang.

Kata kunci: *ventilator associated pneumonia (VAP), Guillain-Barre syndrome (GBS), alur gyssen, higiene oral.*

ABSTRACT

A 46-year-old man was admitted to ICU with a diagnosis at the time of admission of Guillain Barre Syndrome (GBS) and sepsis due to suspected Ventilator-Associated Pneumoniae (VAP). Specimens for the following laboratory workup were inquired, i.e. complete blood count, culture and resistance workup using specimens obtained from the tip of suction pipe, urinalysis and urine culture, blood culture and resistance, procalcitonin and lactate levels. Neutrophilia was found along with increased procalcitonin and lactate levels, which supported the sepsis diagnosis. Moreover, the result of culture from suction pipe demonstrated colonies of Pseudomonas luteola MDRO, which might be originated from the oropharyngeal colonization of the patients due to poor oral hygiene and ineffective oral hygiene nursing; therefore, the colonies of the microorganism were swabbed away when obtaining the specimens. Ineffective oral hygiene nursing may have a potency to cause VAP and recurrent VAP.

Keywords: *ventilator associated pneumonia (VAP), Guillain-Barre syndrome (GBS), Gyssen algorithm, oral hygiene.*

INTRODUCTION

Ventilator-associated pneumonia (VAP) is a pneumonia that occurs 48 hours or longer after mechanical ventilation or following endotracheal intubation.[1,2] It is the most common Healthcare Associated Infections (HAIs) in the Intensive Care Unit (ICU).[3,4] Risk factors for VAP include chronic obstructive pulmonary disease, abnormal cough reflex, neuromuscular diseases that may put the patients at risk of respiratory failure and may require mechanical ventilation using ventilator.[1,2,5] Healthcare personnel may have a role in VAP due to ineffective hand washing, poor oral hygiene, letting patients in supine position that may facilitate the occurrence of aspiration and invasive procedures such as installation of nasogastric tube (NGT) and ventilator.[5] The duration of installed intubation should be no more than 7 days and if the intubation is still necessary, it should be replaced with a new one.[6-8]

CASE ILLUSTRATION

Mr. M, a 46-year-old man came to the Emergency Department with a complaint of hands and feet paralysis and breathing difficulty. Since the last 2 weeks, he felt weakness of both legs so that he could not walk and along with time, he also experienced weakness of his both arms, which caused him unable to raise his hand and subsequently, he felt difficulty in breathing. He was admitted for further care. He had an intravenous line and had received neurological medications, but had no improvement, the patient asked for a referral.

On physical examination, the patient was fully alert with blood pressure of 135/80 mmHg, pulse rate of 80 beats per minute, respiratory rate of 30 times per minute and a temperature of 36^0C. Poor oral hygiene, tetraparesis and motor strength grade 1 were found. There was no abnormality in sensory function. Pathological reflex was not found. Chest X-ray revealed that the heart and lung were within normal limit. A diagnosis of Guillain-Barre Syndrome (GBS) with a threat of respiratory failure was established. The patient received treatment of intravenous fluid drip (IVFD) of Ringer Lactate (RL) at the dose of 10 drips/minute and Gammaras (an intravenous immunoglobulin) at the dose of 0.5 ml/kgBW/day. At the Emergency Department, the patient had the following laboratory workup including complete blood count, urinalysis, blood chemistry test and blood gas analysis and then he was hospitalized in the ICU. Results of complete blood count revealed neutrophilia; while the urinalysis showed data of normal limit. The results of blood chemistry test demonstrated normal ALT, AST, total protein, albumin, globulin and blood glucose levels. Ureum and creatinine levels were within normal limits. The blood gas analysis showed an impression of acidosis with normal anion gap (**Table 1**).

Table 1. Results of laboratory workup

Variables	Value
Blood electrolytes	
- Sodium (mEq/L)	135
- Potassium (mEq/L)	3.8
- Chloride (mEq/L) (Normal anion gap)	106
Blood gas analysis	
- pH	7.350
- pCO_2 (mmHg)	55
- pO_2 (mmHg)	84.9
- HCO_3^- (mmol/L)	32
- O_2 Saturated (%)	95.9
- Base Excess (BE) (mmol/L)	-0.9
- Total CO_2 (mmol/L)	25.6

The results of complete blood count at the ICU showed that there was a neutrophilia with a count of 16,000uL (normal range: 5000–10,000/uL). Peripheral blood smear showed normocytic normochromic result and neutrophilia with toxic granulation and vacuolization. The reticulocyte count was 1.1% (normal range: 0.5–1.5%). Repeated chest X-ray showed a description of pneumonia on the left lung. The blood culture gave negative result. The resistance and culture test of the suction pipe tip showed results of Pseudomonas putida microorganism (**Table 2**).

The patient was then treated with ceftazidime at the dose of 3 x 1 gram/day dan Gammaras at the dose of 0.5 mL/kg BW/day. Five days later, the chest X-ray was repeated and a description of improved pneumonia was found; treatment using ceftazidime antibiotic was then stopped. Three days later, the patient seemed having short of

Table 2. Results of culture and resistance test of the suction pipe tip

Gram staining: negative-Gram rod, epithelial cells 5-6/ LPF, leukocytes 20-30/LPF			
Isolates: *Pseudomonas putida*			
Amoxycillin clavulanic acid	S	Amikacin	S
Ampicillin sulbactam	R	Gentamicin	S
Cefuroxime	R	Ciprofloxacin	S
Ceftazidime	S	Levofloxacin	S
Cefotaxime	R	Cotrimoxazole	S
Ceftriaxone	S	Chloramphenicol	S
Cefepime	S	Fosfomycin	S
Meropenem	S		

breath, leukocytosis and increasing neutrophila at 26,3 x103/uL (5.0–10.0) 10^3/uL. Results of blood gas analysis showed a combination of respiratory and metabolic acidosis along with increased anion gap (**Table 3**).

The microbiology culture test of the suction pipe tip was repeated and we found a result of Pseudomonas luteola MDRO; however, the possibility of contamination during obtaining the specimens due to colonization still could be excluded (**Table 4**).

DISCUSSION

A patient with a complaint of breathing difficulty and tetraparesis since approximately 2 weeks before hospitalized. He was diagnosed with Guillain Barre Syndrome with a threat of respiratory failure. Guillain-Barre syndrome

Table 3. Blood glass analysis and electrolyte

Variables	Value
pH	7.350
pCO2 (mmHg)	46.6
pO2 (mmHg)	85.9
HCO3- (mmol/L)	20.2
O2 Saturasi (%)	95.7
Base Excess (BE) (mmol/L)	-8.9
Total Co2 (mmol/L)	25.6
Sodium (mEq/L)	135
Potassium (mEq/L)	3.85
Klorida (mEq/L)	96
Anion Gap: 22.65 (increased); Impression: respiratory + metabolic acidosis	

Table 4. Results of culture and resistance test of the suction pipe tip

Gram staining: negative-Gram rod, epithelial cells 5-6/LPF, leukocytes 20-30/LPF			
Isolates: *Pseudomonas luteola*			
Amoxycillin clavulanic acid	R	Amikacin	R
Ampicillin sulbactam	R	Gentamicin	R
Cefuroxime	R	Ciprofloxacin	R
Ceftazidime	R	Levofloxacin	R
Cefotaxime	R	Cotrimoxazole	S
Ceftriaxone	R	Chloramphenicol	R
Cefepime	R	Fosfomycin	R
Meropenem	S		
Procalcitonin level (semiquantitative test): ≥0.5 - <2 ng/ mL; lactate level of 6.2 mmol/L			

is a rare autoimmune disease in the form of polyneuropathy due to demyelination of nerve fibers with characteristics of symmetrical and progressive ascending muscle weakness, paralysis and hyporeflexia, with or without sensory or autonomic symptoms. The muscle weakness causes respiratory failure and medical emergency that requires immediate care. The blood gas analysis results indicated a respiratory acidosis due to neuromuscular disease (GBS) causing abnormal chest wall motion and respiratory depression since there was abnormal CO_2 expiration, CO_2 accumulation and those resulting in respiratory acidosis and a threat of respiratory failure.[9,10]

The patient was then admitted to the ICU and a ventilator was installed. Two days following the ventilator installation in the ICU, the patient had a fever (37.8^0C), severe leukocytosis and his chest X-ray revealed a description of pneumonia in his lower left lung and a diagnosis of sepsis due to VAP (early onset VAP) was established since it was developed during the first 4 days following an intubation or a ventilator installation. Based on the onset of infection, VAP is categorized into 2 groups, i.e. the early-onset VAP, which the VAP occurs within the first 4 days following an intubation and a ventilator installation; while the late-onset VAP is VAP that occurs more than 5 days after a ventilator installation. About 50% of VAP cases occur in the first 4 days following a ventilator installation (early-onset VAP), which

usually has a good prognosis and caused by bacteria that are still sensitive to many antibiotic treatment. On the contrary, late-onset VAP is caused by multidrug-resistant organism (MDRO) to antibiotics, which is usually due to excessive exposure to antibiotics or irrational antibiotic treatment and it has been associated with higher morbidity and mortality rate compared to the early-onset VAP.[1,5,6]

Furthermore, urinalysis, urine culture, blood culture and culture of the suction pipe tip were estimated. Results of urinalysis showed no abnormality and urine culture demonstrated no growth and blood culture also gave negative results, but the results of suction pipe tip culture revealed Pseudomonas putida, which was only resistant to ampicillin sulbactam, cefotaxime and cefuroxime.

Ventilator-associated pneumonia is usually caused by negative-Gram bacteria, either single or polymicrobial infection or by positive-Gram bacteria as well. In immunocompromised patients, although it is a rare occasion, VAP may be caused by fungi such as Candida sp or Aspergillus sp. The negative-Gram bacteria that commonly serve as the etiology are *Escherichia coli, Klebsiella pneumoniae, Pseudomonas sp* (mostly *P aeruginosa*) and *Acinetobacter sp*; while the positive-Gram bacteria such as Staphylococcus aureus or Streptococcus sp may also be the cause of VAP.[1,2,6] El Sohl[1] as quoted from the American Thoracic Society, has found data that the causal bacteria of late-onset VAP are *S. aureus* (29%), negative-Gram rod (15%), *S. pneumoniae* (9%) and Pseudomonas sp (4%). MDRO pathogens are mostly found in patients with late-onset VAP or those with immunocompromised condition.[1] Other *Pseudomonas sp.* such as *P putida and P luteola* are microorganisms that very much live in moist environment and places. They rarely infect humans, but may contaminate water and cause HAIs; however, they are not the causal microorganism of VAP.[2] Considering the less common type of microorganism found in the cases, the possibility of contamination during obtaining specimens due to colonization still cannot be ruled out and good oral hygiene care is recommended for the patient to prevent microorganism colonization along with providing education for the ICU nurses on how to obtain correct and appropriate specimens as well as repeated specimen collection.

In the Guillain-Barre syndrome, abnormal cough reflex may occur[4,5] and patients may have difficulties in expectorating sputum; moreover, the oral hygiene of the patient is also poorly maintained. Pseudomonas putida, which was found in the culture is probably an environmental microorganism that had been colonized in the oral cavity and oropharynx of the patient and it was taken during collecting the sample from the suction pipe in the ICU. Collecting specimen from difficult sputum expectoration and considering that the specimen could be presented by a piece cut of suction pipe is actually not recommended as there is a huge possibility of contamination of colonization due to sample collection. However, when we look at the pathogenesis of VAP, P. putida may still be considered as the cause of VAP, which initially formed a colonization in the oropharynx and then it was inhaled during ventilator installation and it is assumed causing lung infection (VAP) although it is a less common microorganism for causing VAP and rarely cause infection in human. Moreover, until now, there is no literature that suggests P. putida as the cause of VAP. To confirm it, repeated sampling should be done at that time using the correct and appropriate technique of collecting specimens.

Without waiting for culture results, the patient was given empiric treatment, i.e. 5-day course of ceftazidime and he had improvement with normal description of chest X-ray. An evaluation using Gyssen algorithm for ceftazidime treatment without waiting for the results of culture in the patient (empiric treatment) was found in his complete medical record, which also include appropriate indication, narrow-spectrum antibiotic, non-expensive, safe and most effective treatment as well as appropriate duration, dose, interval and route of administration; therefore, the evaluation using Gyssen algorithm for empiric treatment of ceftazidime was seized at the number of zero, i.e. it was included as correct and appropriate category (**Figure 1**).

Three days later, the patient had another

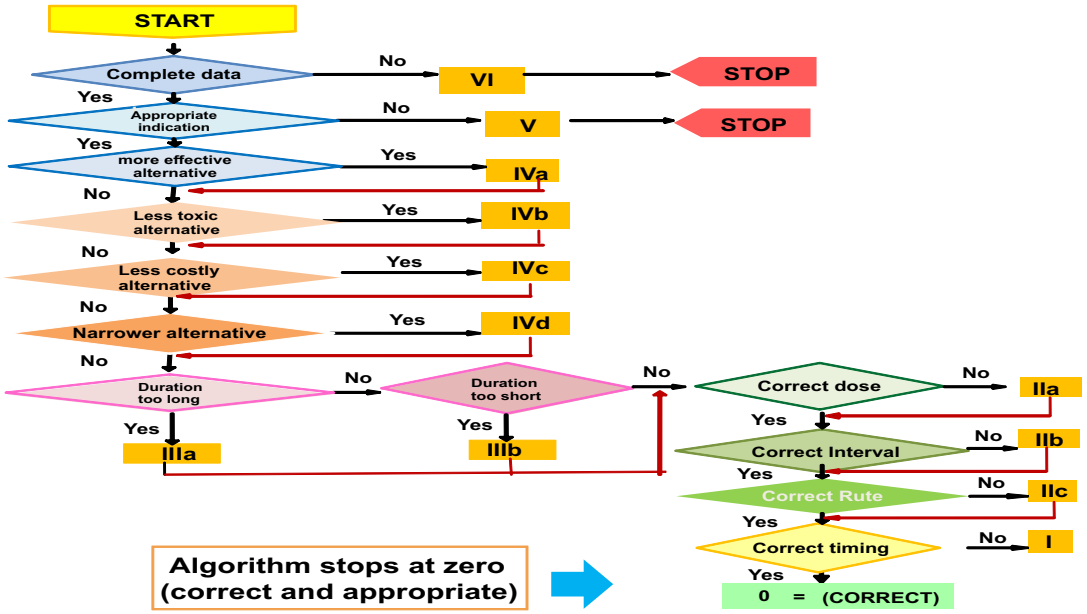

Figure 1. Gyssen algorithm for evaluating ceftazidime (empiric treatment)

fever (38^{0}C), neutrophilia and his chest X-ray revealed pneumonia on his upper right lung, he had purulent sputum, elevated procalcitonin and lactate levels and the blood glass analysis showed a description of respiratory and metabolic acidosis with increased anion gap. Increased anion gap in this case occurred due to increased lactate levels. Elevated HCO_3- that may occur to compensate respiratory acidosis resulting from increased CO_2 levels in the blood (due to respiratory failure), had actually never been achieved.

It may happen since there was metabolic acidosis due to increased lactate levels and therefore, the HCO_3- concentration was reduced with decreased base excess. Consequently, a condition of combined respiratory and metabolic acidosis took place. Based on results of physical examination and laboratory data, a diagnosis of sepsis caused by VAP was made, which was supported by the laboratory result of procalcitonin of >0.5-<2 ng/mL, which was in accordance with the sepsis category. Moreover, there was also increased lactate levels (6.2 mmol/L), which was appropriate to the tissue hypo-perfusion that may be found in sepsis. Based on those clinical and laboratory data, a diagnosis of Guillain Barre Syndrome (GBS) + sepsis due to suspected Ventilator Associated Pneumonia (VAP) was established. An evaluation of culture and resistance test of the suction pipe tip was repeated including blood culture and resistance as well as urinalysis and urine culture and procalcitonin and lactate levels. It revealed a normal result of urinalysis, negative result of urine culture and negative result of blood culture. The culture of suction pipe tip showed a result of MDRO Pseudomonas luteola, which was still sensitive to cotrimoxazole and meropenem. The microorganism may probably derive from colonization of the patient's oropharynx that was taken during sample collection from the suction pipe tip by nurse. However, it is also possible that P. luteola was the causal microorganism of VAP that had been originally colonized in the patient's oropharynx, which was then inhaled during ventilator installation and infected the lung. Subsequently, VAP may occur although until now *P. luteola* is rarely found cause direct infection in human and there is no data about *P. luteola* as the cause of VAP.

The intubation itself would suppress cough reflex that has a function as protection against incoming pathogens. It also suppressed reflex of the epiglottis and therefore disturbing secretion clearance surrounding endotracheal tube (ETT). Therefore, when the pathogens have successfully managed the entrance, they will easily form

colonization in the area. Aspiration of pathogens that have been colonized in oropharynx or the insertion of secretion containing microorganism from the surroundings of installed ETT, is the main entrance for microorganism into the trachea.[5]

Continuous aspiration of subglottis secretion will reduce the risk of microorganism invasion to the trachea.[8] DeRiso as quoted by the American Throacic Society[4] suggested that oropharyngeal colonization, particularly by negative-Gram bacteria such as Pseudomonas aeruginosa, which occurs before hospital admission or which is acquired during hospitalization in the ICU are factors that have important roles in the development of VAP. Moreover, VAP may also occur by colonization of pathogens in the ventilator circuit system such as humidifier and suction. Colonization in the ETT or in ventilator circuit may also have the potency as a reservoir which contribute to the development of VAP.[1,5] Supine position facilitates the occurrence of aspiration compared to semi-recumbent or half-sitting position (30-45^0); therefore, the patient should be maintained at semi-recumbent position to prevent aspiration.[1,2,11]

A closed suctioning system may also reduce the risk of VAP, but it is costly and has not been used widely.[6,8] An immunocompromised condition or underlying disease related to respiratory disorder, colonization on the intubation pathway (oropharynx) prior to intubation, installation of invasive contaminated equipment and the presence of secretion retention in the contaminated subglottis area have a great role on the risk of developing VAP. A procedure of continuous aspiration of subglottis secretion can reduce the risk for developing VAP.[1,2,5] In the ICU, a close-system ventilator has been used and a 450-HOB position has been performed; however, a contamination when obtaining sample due to colonization may still occur considering the poor oral hygiene of the patient. Oral hygiene care was not effectively performed by the nurse. Moreover, one of ventilator bundles, i.e. continuous suction of subglottis secretion was actually and technically difficult for the healthcare personnel and the maximum attempts were not performed; therefore, there is a possibility of microorganism colonization in the secretion concentrating in the subglottis area. The colonization of microorganisms has the potency for developing recurrent VAP.

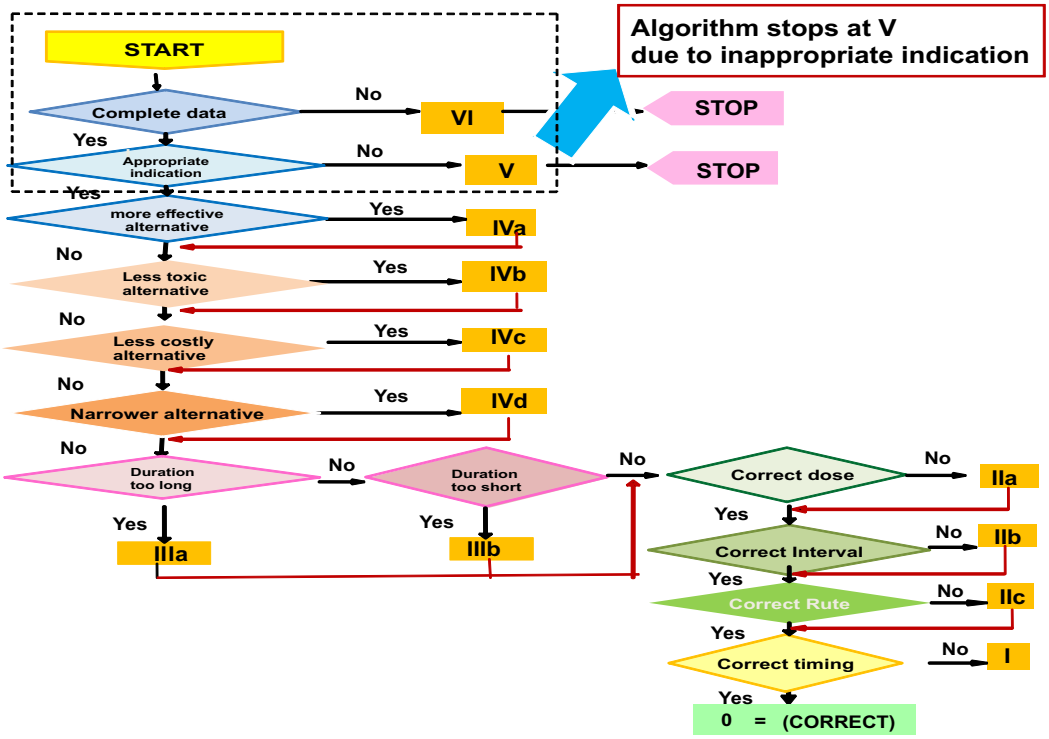

Figure 2. Gyssen algorithm for evaluating meropenem (definitive) based on results of culture test

The patient was then treated in accordance with the results of culture and resistance test, i.e. receiving meropenem and had an improvement. The evaluation using the Gyssen algorithm can be considered from 2 points of view, which is when the treatment of meropenem as a definitive therapy based on the issued results of culture and resistance, then the definitive therapy of meropenem in this case is not appropriate to the indication, which was therapy against colonization; therefore, on the evaluation using Gyssen algorithm, the meropenem therapy stops at the number V (**Figure 2**). Nevertheless, if *P. luteola* is actually considered as the cause of VAP, then the evaluation of meropenem as the definitive treatment, we found a complete data of medical records, an appropriate indication, narrow-spectrum, less expensive, safe and most effective antibiotic with appropriate duration, dose, interval, route of administration and timing and the evaluation using Gyssen algorithm for meropenem therapy stops at the number zero, i.e. it is included in the correct and appropriate category. To confirm this issue, repeated culture specimen collection before antibiotic treatment should be performed along with a correct and appropriate procedure, which in this case had not been done.

CONCLUSION

Ineffective oral hygiene care has the potency of developing VAP and recurrent VAP. Obtaining samples must be performed using an appropriate procedure and if necessary, it must be repeated to have an accurate result. The interpretation of culture results must also be meticulously evaluated in order to provide useful information and effective for its management and treatment.

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