



## **CASE REPORT : SUCCESSFUL MANAGEMENT OF ISCHEMIC STROKE PATIENTS WITH PNEUMONIA, DIABETES MELLITUS, AND HYPERTENSION IN THE ICU**

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### **ABSTRACT**

**Background:** Stroke is one of the main causes of death worldwide. Although neurological complications are the leading cause of death, half of acute stroke patients may die from other medical complications, including pulmonary infections.

**Case Presentation:** It has been reported that a patient aged 65 years with ischemic stroke was treated in the ICU accompanied by diabetes mellitus, acute kidney injury, and hypertension. During treatment in the ICU, the patient experienced complications of pneumonia. The patient underwent endotracheal intubation and ventilator installation as well as a percutaneous dilatational tracheostomy (PDT). During treatment, the patient received antibiotic therapy, blood sugar regulation with insulin, and administration of antihypertensive drugs. The patient experienced clinical improvement and was discharged from the ICU after 18 days of treatment and was subsequently treated in the HCU. **Conclusion:** The length of stay of stroke patients in the ICU requires attention, especially the problem of nosocomial infections that may accompany the patient during the treatment. If there is an infection or other complications, an appropriate selection of antibiotics and supportive therapy is necessary during treatment.

**Keywords:** *Ischemic stroke, Pneumonia, Diabetes Mellitus and Hypertension*

### **BACKGROUND**

Stroke is one of the main causes of death worldwide. Although neurological complications are the leading cause of death, half of acute stroke patients can die from other medical complications, including lung infections. Among the non-neurological complications of acute stroke, pneumonia is a common infectious complication with a reported frequency of 10-20%.<sup>1</sup>

In patients with stroke, around 30% of sufferers experience permanent disability and become dependent on other people. A person's risk of stroke increases with age and the risk doubles every 10 years after a person is over 55.1 years old and stroke is often accompanied by morbidity related to the patient's age. In the past, this has led to less aggressive stroke management so the prognosis is difficult to predict and is thought to be self-limiting. The challenge for intensivists is to be able to identify patients most likely to survive, and not to offer aggressive therapy to those who are unlikely to survive. The stroke should be considered a medical emergency. Patients who come should be treated in an intensive unit or stroke unit because there is evidence of reduced mortality and dependency rates compared to those treated in regular wards.<sup>2</sup>

When stroke-related pneumonia occurs, patients will have a poor clinical prognosis including

increased long-term morbidity and mortality. One large cohort study reported that stroke patients complicated by pneumonia had a threefold greater risk of death within 30 days compared with those without pneumonia.<sup>1</sup> Appropriate patient management is needed as a reference for reducing mortality. In this case report, we report a successful patient management in the ICU of a 65-year-old female patient with ischemic stroke and accompanied by acute kidney injury, pneumonia, hyperglycemia, diabetes mellitus and hypertension.

### **CASE PRESENTATION**

The patient, a 65-year-old woman, weighing 60 kg, came to the ER with complaints of shortness of breath and decreased consciousness. The patient experienced decreased consciousness 1 day ago but was not immediately taken to the hospital. The patient has a history of diabetes and hypertension. The patient has no history of asthma, allergies, or heart disease.

From the primary survey examination, it was found that (A) there was gasping for breath, (B) respiratory rate 45 x/minute, SpO<sub>2</sub> 75% with room air, and 81% with NRM 15 lpm, (C) blood pressure 179/89, pulse rate 140 x / minute, (D) GCS E1M3V1, (E) temperature 36.5° C.

Patients diagnosed with decreased consciousness with DD, non-hemorrhagic stroke (SNH), respiratory



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distress, sepsis, diabetes and acute kidney injury (AKI) underwent initial treatment in the form of endotracheal intubation. After intubation, purulent discharge was obtained, and blood and sputum cultures were performed.

Laboratory examination showed Hb 12, leukocytosis 18,000, platelets 344,000, BUN 125, Cr 3.3 mg/dl. BGA examination showed PH 7.27, pO<sub>2</sub> 45, pCO<sub>2</sub> 43, SaO<sub>2</sub> 74%, Be -7, Lactate 1.5, Procalcitonin 44. Calculation of the patient's creatinine clearance value showed a value of 16.1

A CT scan of the head revealed a large acute infarction in the frontotemporal lobe, consistent with vascularization of the left MCA (ASPECT score 4) and sphenoid sinusitis. From chest X-ray examination, it was found that ET was attached to the tracheal projection with the distal end 4.17 cm above the carina, cast and the lung within normal limits.

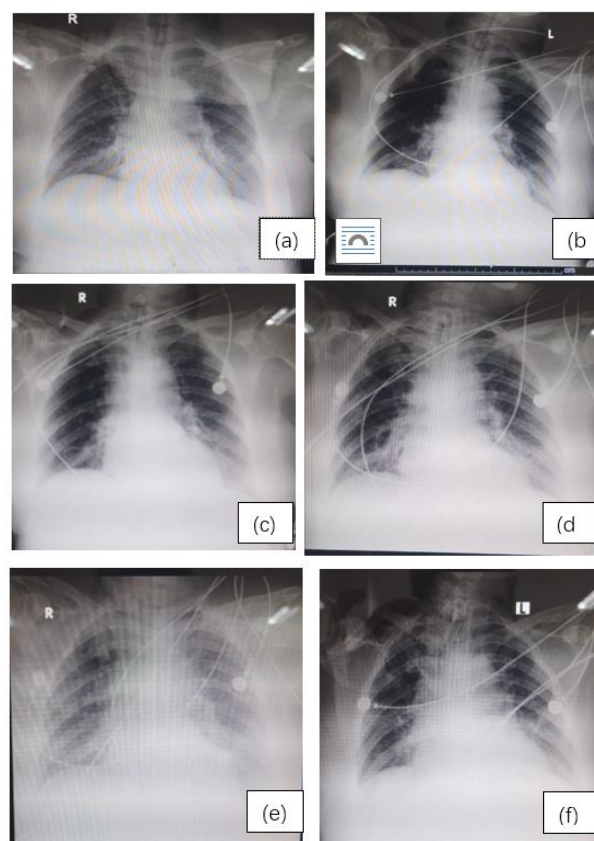
The patient was admitted to the ICU with a diagnosis of non-hemorrhagic stroke (SNH), respiratory distress, sepsis, diabetes and acute kidney injury (AKI). The patient received mechanical ventilation therapy with a ventilator, antibiotics ceftazidime 1 g/24 hours and levofloxacin 250 mg/48 hours, analgesics with fentanyl 50 mcg/hour, blood sugar management with insulin algorithm 1, vasopressor support with norepinephrine 0.1 mcg/kg/minutes with titration, mucolytic n-acetyl cysteine 200 mg/8 hours, combivent 1 res/ 8 hours, antiulcer omeprazole 40 mg/24 hours.

On day 2 the patient experienced improvement in hemodynamics so norepinephrine administration was stopped. The patient also received additional metoclopramide therapy at 10 mg/ 8 hours. On the 3rd day, a chest radiograph was performed and the results showed bilateral pneumonia. The patient had a fever with a temperature of 39.3oC and received additional paracetamol therapy at 1 g/8 hours. On day 4, the levofloxacin dose was increased to 750 mg/48 hours. The patient also received additional hypertension therapy of amlodipine 10 mg/24 hours. On the 6th day, the patient received additional antihypertensives in the form of nicardipine 2 mg/hour with titration. The CPIS score shows a value of 9, which means there is a tendency for pneumonia infections.<sup>3</sup>

**Table 1.** Patient CPIS score

CPIS score -4 d	Value	Score
Temperature	39,3	2
Leucocyte, mm3	18	1
Tracheal secretion	+ purulent	2
Oxygenation	<250	2
PaO <sub>2</sub> /FiO <sub>2</sub> , mmHg		
Thorax x-ray		
Tracheal culture	Bilateral pneumonia	1
	S. anginosus	1
<b>Total score</b>		<b>9</b>

On the 4th day, sputum culture results were obtained in the form of Streptococcus anginosus bacteria which were sensitive to erythromycin, oxacillin, gentamycin, cefoxitin, ciprofloxacin, imipenem, chloramphenicol, ofloxacin and intermediate to cefepime and ceftazidime. Blood culture and urine culture examinations showed sterile results.



**Figure 1.** Torax xray t (a) 1st day (b) 3rd day (c) 7th day (d) 10th day (e) 14th day (f) 17th day



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On the 7th day, chest radiographs still showed bilateral (persistent) pneumonia. On the 8th day, the patient underwent percutaneous dilatational tracheotomy (PDT). The levofloxacin dose was increased to 1000 mg/48 hours. On the 10th day the patient received additional therapy with UDCA 250 mg/12 hours, clopidogrel 75 mg/24 hours, aspirin 80 mg/24 hours, simvastatin 20 mg/24 hours, nicardipine was replaced with bisoprolol 2.5 mg/24 hours and candesartan 16 mg/ 24 hours.

On the 14th day, the sputum culture results showed that *Serratia marcescens* bacteria were sensitive to the antibiotics amikacin, meropenem, trimethoprim sulfamethoxazole and resistant to ampicillin, cefazolin, gentamicin, ampicillin-sulbactam, cefepime, ceftriaxone, ciprofloxacin, levofloxacin, aztreonam, ceftazidime and piperacillin-tazobactam. The antibiotic administration was changed from levofloxacin to meropenem 1 g/8 hours.

On the 17th day the patient had no fever so the administration of paracetamol was stopped. Chest radiographs showed improvement in pneumonia. On the 19th day the patient was discharged from the ICU to the high care unit (HCU). The patient was treated in the HCU for 4 days, then transferred to the regular care ward with the tracheostomy cannule still in place.

## DISCUSSION

In stroke patients with airway disorders, due to a decrease in the level of consciousness, it can be life-threatening and cause cardiorespiratory disorders so they will require treatment in the intensive care unit (ICU). This treatment requires special attention to basic resuscitation, airway stabilization, breathing and circulation.<sup>2</sup>

Patients with a Glasgow Coma Scale (GCS) score of 8 or less, or patients who are unable to vomit and have difficulty swallowing (both of these things can occur in patients with a higher GCS), will require intubation to maintain the airway and prevent aspiration. If this condition is likely to persist for a long time, an early tracheostomy may also be considered. Adequate oxygenation and ventilation can be determined by arterial blood gas analysis, and additional oxygen support can be given if the patient is still hypoxic. If hypercarbia occurs, ventilation is necessary to achieve normocarbica so that it can

prevent exacerbation of cerebral edema that occurs in stroke patients.<sup>2</sup>

In a multicenter study, it was shown that the ICU mortality rate for hospitalized stroke patients was 37%. In stroke patients who use ventilators, the death rate reaches 45%. This study also shows that stroke patients require longer ventilation assistance and the need for tracheostomy is higher than other non-neurological ICU patients.<sup>4</sup>

Most stroke patients usually have elevated blood pressure on admission, perhaps as a compensatory effort by the vasomotor center to increase cerebral perfusion. In patients with hypertension, who have impaired cerebral autoregulation and perfusion, their oxygenation requirements may be highly dependent on blood pressure. The patient's clinical condition and the patient's neurological status determine the next therapy plan, and do not just look at the patient's blood pressure alone. Current recommendations are that immediate administration of antihypertensive drugs be delayed unless the systolic pressure is >220 mm Hg or the diastolic pressure is >120 mmHg. Aggressively lowering blood pressure is not without risk and may result in the worsening of ischemic stroke, so reductions should be closely monitored (not exceeding 15% of normal BP). So, in stroke patients, efforts are made to avoid drugs that cause cerebral vasodilation because they can worsen cerebral edema, although there is no strong evidence regarding this. Cardiac output should be maintained and any underlying cardiac pathology, such as heart failure, infarction and atrial fibrillation can be managed properly.<sup>5,6</sup>

Blood glucose checks must be carried out to determine the presence of diabetes and rule out hypoglycemia as a cause of symptoms of decreased consciousness in the patient. Both hypo- and hyperglycemia have been shown to worsen the prognosis after acute stroke; therefore blood sugar levels must be maintained within the normal range. (<8.6 mmol/L).<sup>2,7</sup>

Routine use of prophylactic heparin in immobile stroke patients is avoided because the risk of intracerebral hemorrhage is quite high. Anticoagulation may be recommended in patients who have a high risk of recurrence, such as in patients with artificial heart valves, atrial fibrillation with thrombus or patients with coagulation disorders. A CT scan is performed before starting anticoagulant



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therapy to rule out bleeding. Patients with extensive infarctions have a risk of bleeding (hemorrhage) at the infarction site so early heparinization should be avoided. Aspirin 160-300 mg may be given within 48 hours of thrombolysis and continued for 2 weeks while antithrombotic therapy is initiated. If the patient is intolerant to aspirin, an alternative can be given in the form of clopidogrel.<sup>8</sup>

Aspirin can reduce the risk of stroke recurrence and is widely used for this indication. Use of HMG CoA reductase inhibitors (statins) reduces the risk of ischemic stroke by 16% to 30% for patients with or without comorbid ischemic heart disease.<sup>9</sup>

Local complications of stroke include cerebral edema, infarction site bleeding or secondary hydrocephalus. Common complications include bronchopneumonia, aspiration pneumonia, deep vein thrombosis, urinary tract infections, pressure ulcers, contractures and depression. Stroke patients who use ventilators are very susceptible to pneumonia.<sup>10</sup>

Streptococcus anginosus group (SAG) is a group of gram-positive Streptococcus bacteria that usually colonize the upper respiratory tract, digestive and reproductive tracts and consists of three different species, *S. anginosus*, *S. constellatus* and *S. intermedius*. SAG is not a pathogen that causes infection. However, under certain conditions, colonized SAGs directly induce noninvasive infections and cause invasive infections after entering the sterile environment of the body, including the blood and serous cavities, ultimately affecting the tissues and organs of various body systems. The number of patients infected with SAG is known to be increasing over time. However, there is still little information about this bacterium as an opportunistic pathogen that can cause invasive infections.<sup>11</sup>

Infections caused by SAG should be considered in the clinical diagnosis and treatment of associated infections.<sup>11</sup> Systemic risk factors for SAG include inflammation and ulceration of gingival tissue, periodontal disease (periodontitis, gingivitis), solid tumors, hematological malignancies, diabetes mellitus type 2, central nervous system diseases (cerebral infarction, cerebral hemorrhage, brain trauma, myasthenia gravis, and Parkinson's disease), chronic kidney failure, chronic respiratory disease, heart failure, liver disease, dementia, viral hepatitis and peptic ulcer disease.<sup>12</sup>

*Serratia marcescens* is a gram-negative bacillus, which has been classified as a member of the Enterobacteriaceae family. This germ is widespread in the environment, but rarely causes disease in humans. *Serratia* species are sometimes known to cause hospital-acquired infections that can cause a wide spectrum of clinical illnesses such as urinary tract infections, respiratory tract infections, and wound infections. The main factors involved in the development of *Serratia* infections include contamination of respiratory equipment and catheterization procedures. *S. marcescens* is now known to be a clinical pathogen, and this bacterium is known to be resistant to various antibiotics. (Mahlen, 2011) The mortality rate for nosocomial bloodstream infections caused by *Serratia* is 26%, but in the case of urinary tract infections, the mortality rate is very low. In addition, more than 90% of cases of urinary tract infections are caused by device insertion. Patients can become infected during hospitalization after the installation of medical instrumentation (because in this infection, the patient usually has a history of medical instrumentation, either urinary catheterization or installation of an endotracheal tube for ventilation).<sup>13</sup>

Levofloxacin is a broad-spectrum, third-generation fluoroquinolone antibiotic used to treat bacterial infections. Levofloxacin is a bactericidal antibiotic from the fluoroquinolone group which directly inhibits bacterial DNA synthesis. Among the fluoroquinolone group, levofloxacin has the highest activity against penicillin-resistant gram-positive organisms, especially *Streptococcus pneumoniae* and is bacteriostatic against gram-negative bacilli, especially *Pseudomonas aeruginosa*, compared to ciprofloxacin. Levofloxacin is a drug that is concentration dependent and has effectiveness against other common respiratory organisms, especially *Haemophilus influenzae*, *Moraxella catarrhalis*, *Legionella* spp, *Mycoplasma* spp, and *Chlamydia pneumoniae*.<sup>14-16</sup>

In patients who experience AKI, the dose of antibiotic medication needs to be adjusted due to interference with renal clearance of the drug. After administering the loading dose, the antibiotic dose of levofloxacin was adjusted to 250 mg/48 hours when known and to 500 mg/48 hours. A 50% reduction in the total daily dose of levofloxacin is recommended in patients with renal impairment (glomerular





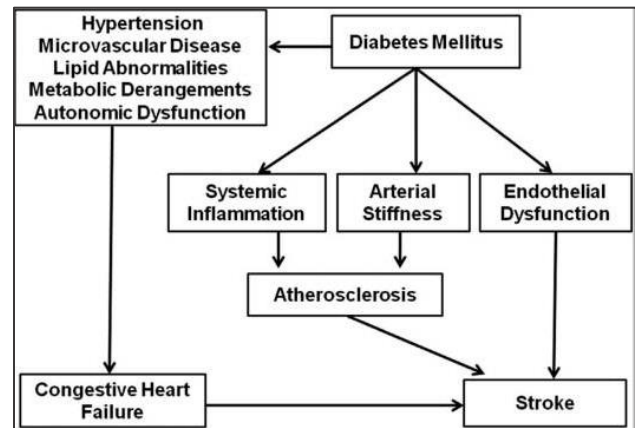
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filtration rate between 10 and 50 mL/minute) and the administration time may be extended to every 48 hours if the glomerular filtration rate falls less than 10 mL/minute).<sup>15</sup>

A diabetic is very susceptible to cerebral small vessel disease. Hyperglycemia provides a greater risk of stroke. This increased risk is frequently seen in individuals with diabetes and is associated with worse clinical outcomes (including higher mortality), especially after ischemic stroke. The main risk factors for stroke include hypertension, diabetes, smoking, and dyslipidemia. Diabetes is one of the known risk factors for stroke. This is because in patients with diabetes there are pathological changes in the blood vessels in various locations and can cause stroke if the brain vessels are directly affected. In addition to higher mortality rates, patient outcomes are worse in stroke patients with uncontrolled glucose levels. Controlling blood sugar and other related risk factors can be effective in preventing initial stroke as well as stroke recurrence.<sup>17,18</sup>

There are several possible mechanisms by which diabetes can cause stroke. These mechanisms include vascular endothelial dysfunction, increased early arterial stiffness, systemic inflammation and thickening of the capillary basement membrane. Abnormalities in early left ventricular diastolic filling are commonly seen in type II diabetes. Mechanisms of congestive heart failure that can occur in type II diabetes include microvascular disease, metabolic disorders, interstitial fibrosis, hypertension, and autonomic dysfunction (Figure b).<sup>17</sup>

Hyperglycemia is a common phenomenon that appears in the early phase of acute stroke. This may be related to the patient's non-fasting state and the patient's stress response to disturbances in glucose metabolism. Stroke triggers a general stress reaction involving activation of the hypothalamic-pituitary-adrenal axis, which in turn leads to increased serum glucocorticoid levels, activation of the sympathetic autonomic nervous system and increased release of catecholamines. Elevated stress hormone levels increase the rate of aerobic glycolysis, promote glucose release from gluconeogenesis and glycogenolysis, and inhibit insulin-mediated glycogenesis.<sup>17</sup>



**Figure 2.** Mechanism of stroke in diabetes patients<sup>17</sup>

Baseline plasma glucose levels are highly correlated with poor poststroke outcomes. Acute hyperglycemia increases cerebral lactate production, reducing penumbral tissue salvage and leading to larger final infarct size. Hyperglycemia further aggravates stroke through reperfusion injury coupled with increasing oxidative stress, stimulating systemic inflammation and increasing membrane permeability. Patients with acute ischemic stroke with diabetes and hyperglycemia have increased aggregation and adhesion of platelets to the endothelium. A study conducted in Glasgow showed that higher plasma glucose predicted a worse prognosis in patients even after correction for age, stroke severity, and stroke subtype.<sup>17,19</sup>

Because hyperglycemia is associated with poor outcomes, appropriate management of post-stroke hyperglycemia is critical to improving patient outcomes. The American Heart Association (AHA)/American Stroke Association, in its guidelines for the initial management of patients with acute ischemic stroke, recommends "to achieve a serum glucose concentration in the range of 140-180 mg/dL (7.8-10 mmol/L) within 24 hours first after acute ischemic stroke in all hospitalized patients. The European Stroke Initiative guidelines also recommend "blood glucose of 180 mg/dL (10 mmol/L) with prompt titration of insulin. Normalization of blood glucose within the first 48 hours of hospitalization appears to provide a recovery benefit in patients suffering from ischemic stroke. Intensive glucose control in patients with acute ischemic stroke can be achieved with titrated insulin



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infusions. However, a recently published systematic review of 11 randomized controlled trials involving more than 1,500 participants with acute ischemic stroke showed no benefit from intensive glycemic control. There was no difference in terms of mortality or dependency between the intervention and control groups, and there was also no difference in late neurological deficits. In fact, the intervention group actually had a higher rate of symptomatic hypoglycemia.<sup>17</sup>

Although it is important to actively manage hyperglycemia, drug overdose and hypoglycemic events may increase the risk of death in patients and should be avoided. Severe or prolonged hypoglycemia can result in permanent brain damage, and is a concern with insulin therapy. Low blood glucose levels (<60 mg/dL) must be corrected immediately.<sup>17</sup>

Proper management of blood pressure is the cornerstone of acute stroke prevention and treatment. Hypertension is a common condition in stroke patients, carrying a high risk of stroke (25% -50%), and clinical trials and observational studies have shown a reduced risk of first and recurrent stroke with antihypertensive therapy. Intensive lowering of blood pressure is also associated with a reduced risk of dementia and mild cognitive impairment.<sup>20</sup>

In a large sample RCT study (N=4071) in China, which studied the effects of immediate antihypertensive administration after acute ischemic stroke within 24 hours, (with the active treatment group, who had a mean SBP 9.1 mm Hg lower compared with controls and SBP value of 137.3 mmHg on day 7) it was found that there was no difference between the treatment group and the control group in terms of death or major disability on day 14 or discharge from hospital (primary outcome) and three months. Similar results were also obtained in several smaller RCTs of acute ischemic stroke.<sup>20</sup>

Initial guidelines for managing acute ischemic stroke based on AHA 2019 include the following: (1) Hypotension and hypovolemia must be avoided to facilitate systemic perfusion (I/C-EO); (2) Before intravenous fibrinolytic therapy is administered, BP should be <185/110 mm Hg, and <180/105 mm Hg in the first 24 hours after such treatment; (3) If mechanical thrombectomy is planned and intravenous thrombolytic therapy has not been administered, BP should be reduced to <185/110

mm Hg before the procedure, and <180/105 mm Hg within the first 24 hours after the procedure; (4) In patients undergoing successful reperfusion with mechanical thrombectomy, BP is maintained to <180/105 mm Hg (I/B-R); (5) Early treatment of hypertension may be indicated in the presence of certain comorbid conditions (eg, heart failure, aortic dissection, acute myocardial infarction) (6) The utility of BP augmentation in acute ischemic stroke remains uncertain (IIb/B-R); (7) For patients not treated with intravenous fibrinolytic therapy or mechanical thrombectomy: (a) If BP is  $\geq 220/120$  mm Hg and there are no comorbid conditions requiring acute BP-lowering treatment, it is reasonable to lower the initial BP by 15% although the benefit of reducing or restarting BP therapy at 48-72 hours is uncertain (IIb/C-EO); (b) Lowering BP when <220/120 mm Hg in the first 48 to 72 hours appears to be a safe strategy but does not reduce mortality or improve functional outcomes (III: no benefit/A).<sup>6</sup>

### CONCLUSION

In stroke patients with decreased consciousness, airway problems can occur which can be life threatening, cardiorespiratory problems and require treatment in the intensive care unit (ICU). This treatment requires special attention to basic resuscitation, airway stabilization, breathing and circulation.<sup>2</sup>

Hyperglycemia and hypertension during the acute phase of stroke are associated with poor outcomes in stroke. This situation needs to be managed well. Controlling blood glucose and administering antihypertensive drugs during the treatment period can improve patient outcomes. (R. Chen et al., 2016)

The length of treatment for stroke patients in the ICU requires attention, especially in relation to the problem of nosocomial infections that can accompany the patient during the treatment. If there is infection or other complications, appropriate selection of antibiotics and supportive therapy is necessary during treatment.

### ETHICAL APPROVAL

There is no ethical approval.

### CONFLICTS OF INTEREST

The authors declare no conflict of interest.



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