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Role of Intravenous Immunoglobulin (IVIG) in Patients with Guillain Barre Syndrome with Severe Community Pneumonia in The Intensive Care Unit (ICU)

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ABSTRACT

Guillain-Barré syndrome (GBS) is an acute flaccid polyneuropathic disease that occurs after infection and is caused by an immune system response. GBS patients often experience acute respiratory distress that requires mechanical ventilation. Nerve impairment in GBS can lead to various problems such as difficulty breathing, ineffective coughing, and difficulty swallowing, increasing the risk of lung infection. Community acquired pneumonia (CAP) is a lung infection acquired outside the hospital. The severity of CAP is directly proportional to the mortality rate. Appropriate antibiotic therapy can reduce the duration of treatment and mortality in CAP. The case report involves a 50-year-old man with GBS and CAP who required treatment in the Intensive Care Unit (ICU). The management of GBS included the use of mechanical ventilation, antibiotics, and intravenous immunoglobulin (IVIG), resulting in improvement after 19 days, with the patient eventually being discharged from mechanical ventilation. It is necessary to describe the management of GBS and CAP cases so that further management can be better and in accordance with existing literature.

INTRODUCTION

Guillain-Barré syndrome (GBS) is an acute polyneuropathy that causes phasic paralysis with or without sensory/autonomic disturbances. GBS generally occurs in about 1 in 100,000 people worldwide. GBS patients may experience acute respiratory distress due to respiratory muscle weakness, and about 30% of them require mechanical ventilation assistance. Two-thirds of GBS cases begin with symptoms of a respiratory or gastrointestinal infection.[1-3]

Community Acquired Pneumonia (CAP) is an acute illness caused by infection of the lungs acquired outside the hospital environment. Basic Health Research (Riskesdas) 2013 data showed that the prevalence of CAP in Indonesia was 0.63%. CAP mortality in hospital inpatients ranges from 5 to 15%, increasing to 20 to 50% for treatment in the Intensive Care Unit (ICU).[4,5]

Currently, two treatment options for GBS, such as intravenous immunoglobulin (IVIG) and plasma exchange (PE) have been used to minimize the symptoms and duration of the disease. IVIG is often used to shorten the course of GBS and considered to be safer than PE due to its reduced complication and risks, although its specific action mechanism is still unknown.[6] IVIG should be given within 2-4 weeks after onset of GBS symptoms. Some researches showed that IVIG was superior to PE in reducing the duration ICU stay and mechanical ventilation with fewer complication although both has similar 28-days mortality.[6-8] In this

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case a GBS patient with CAP required mechanical ventilation and IVIG therapy underwent treatment in the ICU for 19 days.

CASE REPORT

A 50-year-old man presented to the emergency department of RSHS in an intubated state, referred from another hospital with a chief complaint of weakness in all four limbs. The weakness started from both legs accompanied by numbness and tingling 1 week ago, then spread to both hands. The limbs can only be shifted, and the hands can be lifted but fall back. The patient has difficulty holding a bowel movement, while complaints of urination are denied. Shortness of breath, hoarse voice, difficulty swallowing, cough with phlegm, and fever have been felt since 2 weeks ago.

Prior to intubation, the patient had a blood pressure of 180/100 mmHg, pulse rate of 132 beats per minute, respiratory rate of 50 beats per minute and oxygen saturation of 58 per cent with a non-rebreathing mask of 15 litres per minute, fever of 38.3°C.

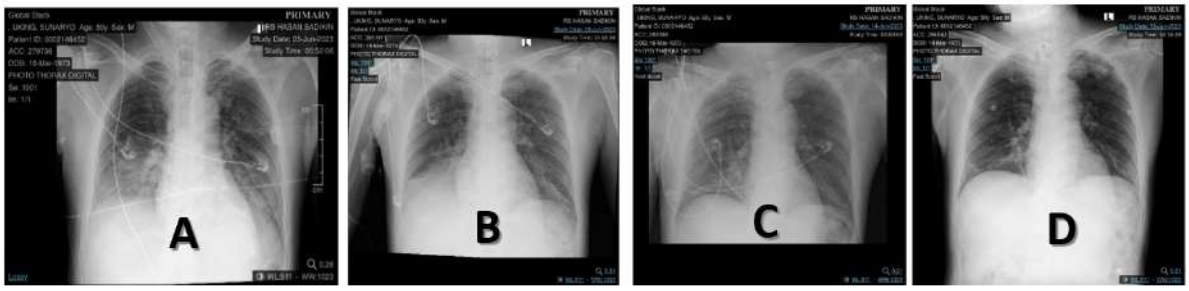

Figure 1. X-Ray Findings. (A) Chest X-Ray shows bilateral consolidation in both lungs (day 1).(B and C) Pneumonia improves (day 5 and day 10).(D) Complete resolution of both lungs (day 18)

The patient was previously diagnosed with respiratory failure due to Guillain-Barre Syndrome (GBS) and CAP. The patient received medications such as citicholin, mecobalamin, ceftriaxone, and levofloxacin previously. After ICU admission, the patient received mechanical ventilation support, antibiotics and was planned for Intravenous Immunoglobulin (IVIG). On day 7, the patient received IVIG therapy for 5 days, and on day 9, improvement in breathing was seen, although motor skills were not fully recovered (muscle strength 3/5 for upper limb and 3/5 for lower limb). Tracheostomy was performed on day 14, and on day 19, the patient was transferred to the High Care Unit (HCU).

DISCUSSION

Diagnosis of Guillain-Barré Syndrome (GBS)

Guillain-Barré Syndrome (GBS) is a rare but potentially fatal peripheral nerve disease. It was first reported in 1916 by Guillain, Barré, and Strohl.[1,9,10] GBS occurs after a respiratory or gastrointestinal infection, with the interval between infection and onset of symptoms usually 4 weeks. Infectious causes that trigger GBS include Campylobacter jejuni, cytomegalovirus, Mycoplasma pneumonia, Epstein-Barr virus, influenza virus, and JEV. Symptoms of GBS begin with distal paresthesias and limb weakness. The progressivity of GBS reaches a clinical nadir within 2 weeks, and after the progressive phase, the patient enters a plateau phase. GBS may relapse in 2-5% of patients. Pathophysiologically, a hyperactive immune response can lead to demyelination and/or axonal degeneration. GBS is divided into 2 demyelinating subtypes, namely acute inflammatory demyelinating polyneuropathy (AIDP) and axonal variations, such as acute motor axonal neuropathy (AMAN) and acute motor-sensory axonal neuropathy (AMSAN). AIDP due to acute inflammatory response and demyelination of peripheral nerves is the prototypical GBS. Axonal variations including AMAN and AMSAN occur most commonly in Asian countries.[1,10-13]

The diagnosis of GBS is based on clinical history, physical examination, and supporting examinations such as cerebrospinal fluid and electrodiagnostics. Laboratory tests such as complete blood count, blood sugar,

electrolytes, renal function, and liver enzymes are also performed on GBS suspects to rule out differential diagnosis. The results of these tests can exclude other causes of acute flaccid paralysis such as infection, metabolic or electrolyte disturbances.[10,11]

Respiratory distress of Guillain-Barré Syndrome (GBS)

Almost 50% of patients require treatment in the ICU, mainly due to respiratory and autonomic nervous system involvement. Mechanical ventilation should be considered in patients with respiratory muscle weakness.[14,15]

Some criteria for placement of GBS patients in the ICU include the development of respiratory muscle weakness, respiratory distress, dysotonomia or severe dysphagia, and Erasmus GBS respiratory insufficiency score (EGRIS) > 4. Mechanical ventilation should be considered if there is low vital capacity, hypercarbia, hypoxia, and intolerable respiratory distress.[1,10] Studies show that early insertion of mechanical ventilation does not reduce the incidence of pneumonia or hospitalisation time, and is not associated with the risk of serious adverse events.[2]

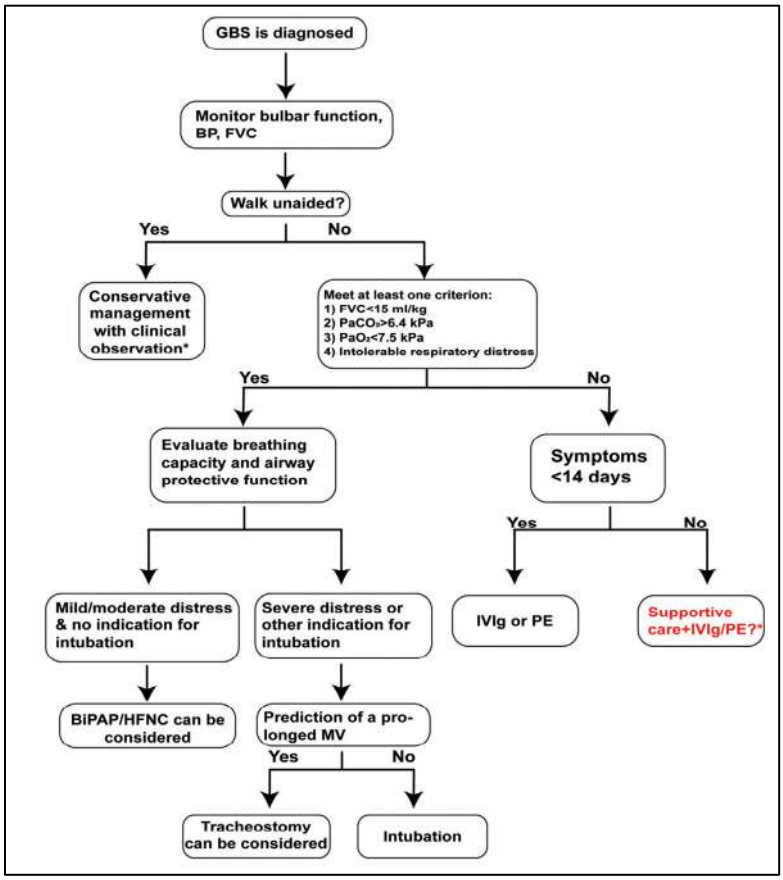

Figure 2. Treatment Algorithm of Guillain-Barre Syndrome in ICU.[1]

The patient in this case was diagnosed with GBS because the patient experienced limb weakness starting with limb weakness, followed by upper limb weakness, accompanied by difficulty swallowing, and shortness of breath and there was a history of previous respiratory infections. The patient was also intubated and admitted to the ICU because there were signs of respiratory failure and EGRIS more than 4, namely 6.

Tracheostomy in GBS patients should be considered if mechanical ventilation is expected for more than 3 weeks in the ICU. Early tracheostomy may provide advantages such as comfort, early enteral nutrition, adequate oral hygiene, easier oral communication, and easier mobilisation. In this patient's case, tracheostomy was performed on day 14, a few days after which the patient could be taken off the ventilator and transferred

to the High Care Unit (HCU). However, the decision to perform tracheostomy was considered too late, and earlier implementation may have accelerated the weaning process and reduced ICU stay.[1,9]

GBS therapy involves Therapeutic Plasma Exchange (TPE) and intravenous immunoglobulin (IVIG). TPE helps remove pathological antibodies and immune complexes, while IVIG contains antibodies that can dampen the immune response.[6-8,16] IVIg is a plasma product that contains a wide range of diverse antibodies. It possesses various immunomodulatory effects, such as inhibiting the activation of macrophages through Fc-mediated pathways, preventing the binding of antibodies to neural targets, and blocking complement activation that could lead to further nerve damage. The dimerization of antiganglioside IgG antibodies induced by IVIg has been found to alleviate their immunoreactivity in patients with GBS. The administration of high-dose IVIG, typically ranging from 1000 to 3000 mg/kg body weight (BW) exhibits immunosuppressive and anti-inflammatory properties, making it a widely used treatment for autoimmune diseases like GBS.[1] In this patient, IVIG was administered 2000 mg/kgBW, divided into 5 day-dose with satisfactory result.

IVIg is commonly recommended for GBS because of its uncomplicated administration process and independence from specific machines. In addition to being easier to deliver, IVIg also accelerates recovery effectively.[1] A systematic review showed that IVIg and PE have similar efficacy in hastening recovery from GBS, but IVIG group has lower Risk Ratio (RR) of treatment discontinuation. This significant difference was anticipated due to the simplicity of administering IVIg compared to PE. PE necessitates access to two veins, with one vein needing to accommodate high flow volumes and often requiring the insertion of a central venous line. Additionally, PE requires a dedicated machine and specially trained personnel. On the other hand, IVIG only requires access to a single peripheral vein and does not necessitate any special equipment or specially trained staff.[6,7]

In 2023, a Meta-analysis has additionally revealed that GBS patients experience a relatively reduced duration of hospitalization when IVIG is administered as the treatment choice. Nevertheless, there is no significant statistical difference when compared to PE.[6]

IVIg may lead to various side effects such as fever, myalgia, headache, hypotension, meningism, urticaria, eczema, and, in rare cases, renal tubular necrosis, thromboembolic events, pancytopenia, alopecia, and anaphylaxis in less than 10% of cases. In all trials comparing IVIg with PE for which the information was available, there were more complications in the PE than the IVIg group.[7]

In patients with GBS (Guillain-Barré Syndrome), nutrition is an important aspect to consider. Enteral nutrition should be started as soon as possible, with the aim of preventing muscle mass loss and accelerating weaning. Continuous enteral feeding is more recommended than bolus feeding in GBS patients. Before providing nutrition, it is necessary to assess high or low nutritional risk using NRS or NUTRIC score.[17]

The patient's NUTRIC score can help assess nutritional requirements. In this patient, a NUTRIC score of 0 indicates that the patient can receive nutrition. Calorie and protein requirements can be calculated as 25-30 kcal/kgBB/day and 1.2-2 g/kg body weight.[17]

In the case of a patient with a height of 165 cm, predicted body weight of 57 kg, the nutritional requirement is 1,425 - 1,710 kcal/day with 72 - 120 grams of protein per day. During treatment in the ICU, the patient underwent test feeding on the first day, then received 1500 kcal/day from the second to 12th day, and 1800 kcal/day on the 13th to 19th day of treatment.

Community Acquired Pneumonia in Guillain-Barré Syndrome (GBS)

Pneumonia is an acute respiratory infection that affects the alveoli and bronchi of the lungs. There are two types of pneumonia, community-acquired pneumonia (CAP) and hospital-acquired pneumonia (HAP, including ventilation-associated pneumonia (VAP)). Aspiration pneumonia is also a concern, occurring in 5-15% of CAP cases.[18]

Pneumonia can be classified as CAP if there are acute infiltrates on thoracic x-ray or physical signs of pneumonia after 48 hours of hospitalisation. Severe CAP or severe community pneumonia requires supportive

therapy in critical care and is associated with high mortality. CAP in GBS is often associated with aspiration and delayed intubation, which may increase the risk of respiratory failure.[18] The incidence of CAP varies, and approximately 40-60% require hospitalisation. Studies show a correlation between age, comorbidities, and mortality of CAP. The Pneumonia Severity Index (PSI) and CURB-65 are used to assess the severity of CAP, but SMART-COP can also provide an estimate of ICU requirements by predicting intensive respiratory and vasopressor support (IRVS).[19-22]

Pneumonia can occur when the lung defence mechanisms are unable to respond to inhaled or aspirated pathogens, especially in individuals with reduced immune function or in highly virulent pathogens. GBS patients are also at risk of pneumonia, mainly due to respiratory muscle weakness. Pneumonia can be a serious complication and requires rapid intervention Approximately 50% of patients are unable to detect a microbial cause in CAP. S. pneumoniae remains the main cause of CAP, while a small proportion is caused by MRSA and antibiotic- resistant gram-negative bacteria, such as P. aeruginosa and Klebsiella pneumoniae.[20]

Antibiotic resistance often hampers treatment, so clinicians need to identify risk factors for this pathogen to initiate appropriate empiric therapy. Risk factors include immunosuppression, previous antibiotic use, history of previous treatment, medications that lower gastric acid, tube feeding, and non-ambulatory status. PES score is used to assess the risk of MDR pathogen infection.[18]

Early diagnosis and aggressive intervention can prevent disease progression, especially in patients at high mortality risk. Early parenteral antibiotic administration can improve patient outcomes, with multiorgan failure being the leading cause of death in severe CAP. Research suggests that antibiotic administration according to IDSA/ATS protocols is associated with reduced mortality.[19,20]

Management of Guillain-Barré Syndrome (GBS) with CAP

In hospitalised CAP patients, antibiotic therapy involves a β-lactam-macrolide or quinolone combination. Studies show the addition of a macrolide can reduce mortality, especially in Legionella spp. infections. If there is a risk of P. aeruginosa or MRSA, additional therapy is required. The duration of antibiotics should be adjusted according to clinical stability, and antibiotics should be continued until the patient is stable, at least five days. Longer duration may be required for cases with complications or non-guideline pathogens.[18,20,22]

In this patient, the administration of Ceftriaxone and Levofloxacin was in accordance with ATS/IDSA empiric standards for CAP therapy. The duration of antibiotics should be based on clinical stability parameters (return of vital sign abnormalities to normal, ability to eat, good consciousness) and antibiotics should be continued until the patient is stable and not less than five days in total. All clinicians should use clinical stability assessment to treat CAP patients. Longer duration of antibiotic therapy may be given in patients with 1) pneumonia complicated by meningitis, endocarditis, and deep-seated infection; or 2) infection with pathogens not included in the guideline (Burkholderia pseudomallei, Mycobacterium tuberculosis or endemic fungi).[21]

Overall, GBS management involves a multidisciplinary approach with a focus on supportive care, immunomodulatory therapy, and prevention of complications such as pneumonia.

CONCLUSION

Guillain-Barré Syndrome (GBS) is a peripheral polyneuropathic disease that causes acute muscle weakness following infection. GBS can result in decreased respiratory muscle function, risk of airway obstruction, ineffective coughing, and increased chance of pneumonia. Pneumonia, which can be acquired from the community, is known as CAP (Community Acquired Pneumonia). GBS patients with CAP have a higher mortality rate, requiring appropriate management, including the mechanical ventilation support, empiric antibiotics to prevent CAP progression, and definitive antibiotic therapy. Administration of Intravenous Immunoglobulin (IVIG) at 2 weeks after onset of GBS shows satisfying result. IVIG can reduce duration of mechanical ventilation and GBS course, with minimal complication.

DECLARATIONS

The research has received approval from Faculty of Medicine, Padjadjaran University / Hasan Sadikin Hospital Research and Ethics Committee. Participants were informed about this report.

CONSENT FOR PUBLICATION

The Authors agree to publication in Journal of Society Medicine.

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COMPETING INTERESTS

The authors declare that there is no conflict of interest in this report.

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