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■증 례■

Successful Transplantation of Organs from a Donor with Bacterial Meningitis Caused by *Streptococcus pneumonia*

− A Case Report −

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The number of organs transplanted worldwide is increasing annually. As a result, there is a shortage of available donor organs. This scarcity has led to the progressive broadening of donor organ criteria. The expanded criteria include infections such as bacterial meningitis. A 55-year old male visited our emergency room with cardiac arrest and recovered after cardiopulmonary resuscitation. The cause of the cardiac arrest was bacterial meningitis caused by *Streptococcus pneumoniae*. While proper antibiotics were applied, the patient met the clinical criteria for brain death. Prophylactic antibiotics were administered to the recipients, and liver and kidney transplantations were done successfully.

Key Words: donor selection, meningitis, organ transplantation.

The number of organs transplanted worldwide is increasing each year, creating the need for increased organ procurement.[1] The number of organ transplantations has been increasing in South Korea.[2,3] The availability of cadaveric organs continues to be the most important factor limiting the number of transplantations performed.[4] Compared to other developed countries, the organ donation rate from brain dead donors in South Korea very low.[2] The scarcity of organs available for transplantation has led to the progressive broadening of criteria for accepting organs from donors who have died due to infections such as endocarditis and bacterial meningitis.[2] We report a case of a patient with bacterial meningitis caused by *Streptococcus pneumoniae*, who met clinical criteria for brain death and whose liver and kidney were transplanted successfully.

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CASE REPORT

A 55-year old man visited the emergency room with loss of consciousness. He had complained of back pain for 10 days, which prompted visits to an orthopedic clinic and pain clinic. During the previous admission, he had received several intravenous injections of ketorolac, acupuncture, and intrathecal injection of opioid. Without any aura, he suddenly lost consciousness and breathing. At the time of the emergency room visit, carotid pulse was not palpated and cardiopulmonary resuscitation (CPR) was started. The initial rhythm was pulseless electrical activity. During CPR, chest compression was continued with minimal interruption. Simultaneous artificial ventilation following the insertion of an endotracheal tube and epinephrine injection following the introduction of an intravenous line was performed. After CPR for 4 minutes, return of spontaneous circulation was detected. Initial vital signs were blood pressure 90/54 mmHg, pulse rate 112 bpm, respiratory rate 18 bpm, and body temperature 36.4°C. His mental status was comatose. Fluid resuscitation and norepinephrine was infused and titrated to optimize blood pressure. Post cardiac arrest care including mechanical ventilation and therapeutic hypothermia was continued. The patient was admitted to the emergency intensive care unit. Initial laboratory results were white blood

cell (WBC) count 33,800/㎕, hemoglobin 11.1 g/dl, hematocrit 33.6%, platelet count 325,000/㎕, blood urine nitrogen 22.8 mg/㎕, creatinine 1.0 mg/㎕, sodium 144 mmol/L, potassium 3.5 mmol/L, total bilirubin 1.2 mg/dl, alanine aminotransferase 107 U/L, aspartate aminotransferase 60 U/L, creatine kinase 268 U/L, creatine kinase MB fraction 4.3 ㎍/L, troponine I <0.006 ng/ml, and S100 0.214 ㎍/L. Arterial blood gas analysis results were pH 6.955, pCO_2 92.2 mmHg, pO_2 122.9 mmHg, and base excess −14.0 mmol/L. Electrical cardiogram showed normal sinus rhythm without any ST segment or T wave abnormality. To search for the reason of cardiac arrest, brain computed tomography angiogram (CTA), transthoracic echocardiography (TTE), and coronary angiography were performed. TTE showed hypokinesia of mid-left-ventricle without concordance with coronary territories and coronary angiography showed normal coronary artery. Brain CTA showed the effacement of cortical sulci with severe ventricular enlargement that was consistent with meningoencephalitis (Fig. 1). To reduce intracranial pressure, an external ventricular drain was inserted. Cerebrospinal fluid (CSF) analyses revealed protein 447 mg/dl, glucose ＜10.0 mg/dl, WBC 100/㎕ (neutrophils 86%, lymphocytes 5%, monocytes 9%), and red blood cell count 490/㎕. To manage the meningoencephalitis, ceftriaxone, vancomycin, and ampicillin were administered. A CSF culture was positive for *S. pneumoniae* while two blood cultures, a urine culture, and sputum culture were negative for any pathogen. On the second hospital day, the mental status was comatose. Post cardiac arrest care of mechanical ventilation, norepinephrine infusion, and therapeutic hypothermia with rewarming phase was continued. The neurological exams including pupil light reflex, corneal reflex, and motor response were lost. Polyuria, hypernatremia (sodium 172 mmol/L) and low urine sodium level showed the development of diabetes insipidus. To control diabetes insipidus, vasopressin was infused and titrated. A brain CT taken at the second hospital day showed diffuse brain swelling with decreased hydrocephalus. Electroencephalogram showed severe diffuse encephalopathy. At the eighth hospital day, brain magnetic resonance imaging showed aggravated meningoencephalitis with hypoxic brain injury (Fig. 2). CSF at the ninth hospital day showed pus and the cellular examination could not be taken due to cellular degeneration. CSF culture did not show any growth of pathogen. Electroencephalogram at the twelfth hospital day showed severe diffuse encephalopathy. At day 24 of hospitalization, he was pronounced brain dead. The family consented to organ donation. Donor's renal and liv-

Fig. 1. Brain computed tomography angiogram taken at admission shows the effacement of cortical sulci with severe ventricular enlargement that was consistent with meningoencephalitis.

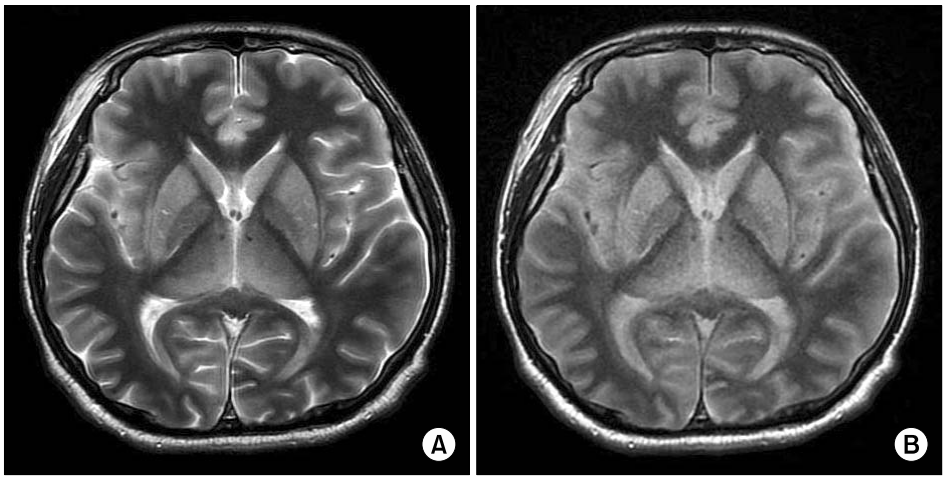

Fig. 2. Brain magnetic resonance imaging at the eighth hospital day shows aggravated meningoencephalitis with hypoxic brain injury. T2-weighted image (A) and fluid-attenuated inversion recovery sequence (B) shows hyperintense signals in the cortex of both cerebral hemispheres, basal ganglia and thalamus.

er functions were normal, and both liver and kidneys were normal on ultrasound examination. Six days from organ procurement, donor's urine culture and one blood culture examined at day 24 of hospitalization were positive for *Candida parapsilosis*, while the other blood culture and previous studies were negative.

Both of the liver and kidney recipients received injections of prophylactic antibiotics to control the infection from transplantation. They continued to receive antibiotics after the transplantation. Both recipients were not infected with *S. pneumonia* and have survived for 5 months since the organ transplantations.

DISCUSSION

To our knowledge, this is the first reported case of organ transplantation from a donor with bacterial meningitis caused by *S. pneumonia* in South Korea.

Bacterial meningitis remains an important infectious desease worldwide. The overall incidence of bacterial meningitis in developed countries is 3 per 100,000 population, with a variability depending on age, race, and geographical area.[5] Moon and colleagues reported the mortality rate of bacterial meningitis as 20% and the proportion of patients with neurological sequelae as 16% in South Korea.[6] As a consequence, bacterial meningitis is responsible for 3.4% to 8% of brain-dead adults patients and for 13% to 15% of brain-death pediatric patients.[5] Inclusion of these types of patients might increase the potential pool of organ donors by over 5%.[5]

According to the Korean Network for Organ Sharing (KONOS), the number of organ donors and number of recipients on the waiting list have been increasing in South Korea. The numbers of cadaveric donors has increased from 10 to 20% in 2,000 to 40% in 2008.[2] Moreover, all hearts, lungs, corneas were from cadevaric donors.[2] Despite the incremental increase in the number of donors, the supply to demand ratio of donors decreased from 24.4% in 2000 to 14.4% in 2011 according to a KONOS report. This phenomenon is also presented worldwide.[7-9] However, in South Korea, the organ donation rate following brain death if 3.1 per million population in 2007 was much lower than Spain (34.3), the United States (26.6), France (25.3), and the United Kingdom (13.2).[2]

One of the ways to tackle the shortage of donors might be to expand the donor pool by accepting "marginal donors."[7,10] Only 15 to 20% of individuals who satisfy criteria for becoming organ donors actually donate in the U.S.[9] The criteria of marginal donors include older donors, mildly elevated serum creatinine, and sepsis.[10-15] However, what constitutes a marginal donor is a matter of debate.[7] Moreover, meningitis has been frequently considered as a contraindications.[16-18] Regarding meningitis of a reversible cause of coma prevents a diagnosis of brain death.[18] The risk of bacterial transmission to the recipient also prevents transplantation of organs of patients with bacterial meningitis.[15] Especially bacterial organisms with a more significant hazard for blood vessel disruption like *Staphylococcus aureus*, *Bacteriodes species*, *Klebsiella enterobacter*, *Escherichia coli*, and *Pseudomonas aeruginosa* may be transmitted to recipients.[15]

The most common bacterial pathogens of bacterial meningitis are *Haemophilus influenza*, *S. pneumoniae*, and *Neisseria meningitidis*.[19] Under these circumstances, the administration of proper antibiotics to a potential donor makes transplantation possible.[15] Recently it was reported that organ transplantation from donors with bacterial meningitis caused by other organisms can be safely performed. Lopez-Navidad and colleagues reported five cases of susscessful transplantation with organs from donors with bacterial meningitis.[1] The organisms included *S. pneumoniae*, *N, meningitidis* and *E. coli*. The authors opined that the risk of transmission of infection does not increase provided antibiotics are administered to donors and recipients.[1] Successful transplantation with organs from bacterial meningitis patients with no transmission of infection was reported by Paig et al.[5] Bahrami et al. reported thier 20-year experience with 39 donors with bacterial meningitis.[7] There were no infectious complications caused by meningeal pathogens. These two studies also involved the appropriate administration of antibiotics to both donors and recipients before transplantation and to recepients after transplantation.[5,7] Moreover, the survival rate of recipients with organs from meningitis-negative donors and from meningitis-positive donors showed no significant difference at 1, 5, and 10 years.[7]

The present case is another report of a successful transplantation with organs from a patient with bacterial meningitis. Different management strategies from the general management strategy for organ donation were adopted; the general management strategy does not include the usage of empirical antibiotics.[20] However the donor in this case was injected with empirical antibiotics (ceftriaxone, vancomycin, and ampicillin), which were recommended in the guideline for the management of bacterial meningitis.[19] The recipients were also injected antibiotics for the prophylaxis of *S. pneumoniae* infection resulting in no transmission of *S. pneumoniae* infection. Curren-

tly published articles about the expanded criteria for organ donation in South Korea have not reported the criteria regarding an infected donor.[10] The present study introduces expanded criteria for a donor with meningitis. More studies of the cases of such donors will helpful to expand the number of organ donors.

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