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Case Report

Japanese encephalitis in West Kalimantan

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Japanese encephalitis (JE) is an important, vaccine-preventable cause of viral encephalitis in Asia. This medical condition has a high morbidity and mortality rate, remains an under-recognized cause of encephalitis, with high rate of mortality and severe sequelae in children, especially in West Kalimantan. However, poor surveillance has made the burden difficult to quantify, hindering decisions about subsidized vaccine introduction.

In this serial case, the most common clinical presentations of JE were fever, altered mental status, seizures, vomiting, and positive meningeal irritation signs or pathologic reflexes. The JE mortality rate was as high as 40%. These highlight the need of disease surveillance, diagnostic kits supply, and health education to increase public disease awareness. **[Paediatr Indones. 2024;64:459-62; DOI: https://doi.org/10.14238/pi64.5.2024.459-62**].

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Japanese encephalitis (JE) is a mosquito-borne viral disease that attacks the central nervous system (CNS). First reported in the year 1871 in Japan, the disease was caused by the Japanese encephalitis virus (JEV) and primarily affected children. It remains the most important vaccine-preventable cause of viral encephalitis in Asia and the West Pacific, with an estimated 68,000 clinical cases every year. The JE has a high mortality rate, killing approximately 20-30% of patients who develop symptoms. Of those who survive, 30% have severe neurologic sequelae.[1,2] Japanese encephalitis virus is transmitted to humans mainly through infected Culex tritaeniorhynchus mosquitoes and is maintained in an enzootic cycle with pigs and wading birds as amplifying hosts. Hence, it is predominantly found in rural settings, where most people live in close proximity with hosts or near irrigated rice fields. In warm subtropical and tropical countries like Indonesia, the transmission can occur year-round, but is often higher during the rainy season.[3]

Despite the high burden of the disease, JE studies in Indonesia have been limited, and, as far as we know, no studies have been reported from West Kalimantan. In 2016, a total of 326 cases were reported in Indonesia, with the most in Bali (69.3%),[4] followed by West Kalimantan (20.7%).[5]

Japanese encephalitis is preventable through vaccination. The first vaccines licensed in 1954 had a 91-97.5% protective efficacy. Newer generation vaccines introduced in 2005 have a more advantageous safety profile.[6] Since 2006, the WHO has recommended that the JE vaccination be integrated into national immunization schedules. Countries with high burdens of JE, such as Japan, Taiwan, and South Korea, have had reductions to almost zero cases,

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mainly through high vaccination coverage.[7] Indonesia started to integrate JE vaccination into the national immunization program in 2017, but subsidized the JE vaccine only for Bali, as it was the most endemic province in Indonesia.[8] Given the high number of cases in West Kalimantan, providing subsidized JE vaccination to children in West Kalimantan remains a top priority, as JE has a high mortality rate and often resulting in severe sequelae.

We reported clinical manifestations and outcomes of 5 children with JE admitted in our hospital.

The cases

This was a serial case of five children who presented with acute encephalitis syndrome (AES) in St. Antonius General Hospital Pontianak, West Kalimantan, between November 2019 - January 2020. Demographic data, clinical presentation, JE vaccination status, and disease outcomes were recorded. Diagnosis of JE was confirmed by JE IgM antibody testing.

Patients suspected of having acute encephalitis syndrome (AES), characterized by acute onset of high fever, new onset of seizure and altered mental status. Serum and/or cerebrospinal fluid (CSF) of suspected JE cases who agreed to testing were examined by JEV specific IgM-capture ELISA test in *Balai Besar Teknik Kesehatan Lingkungan dan Pengendalian Penyakit* (Center for Environmental Health Engineering and Disease Control), Jakarta. Here we describe the initial presentation, physical examination and laboratory results, as well as outcomes of the disease in our subjects.

A total of 70 patients were diagnosed with AES. All patients were treated for bacterial meningitis until proven otherwise, and were given broad spectrum antibiotics. Of the 11 patients who agreed to be tested for JE virus infection, 5 patients tested positive. All positive patients were under 15 years of age, with median age of 7 (range 2-12) years, male to female ratio of 4:1; they also all lived in rural areas and none had been vaccinated for JE. Their mean duration of symptom onset to hospital admission was 4 days and the average initial *Glasgow Coma Scale* (GCS) score was 10 (range 9-14). Manifestations of JE patients on admission in descending order were high fever (n=5), altered mental status (n=5), vomiting (n=3), and headache (n=2). Status epilepticus was observed in 4 patients with an average occurrence time of 5 days after onset. Physical examination revealed 3 cases with positive meningeal irritation signs and 3 cases with positive pathologic reflex (**Table 1**).

Routine blood test results on the first day of admission showed increases in white blood cell/WBC (n=2) and neutrophils (n=5) in their peripheral blood; other results were within normal limits (**Table 2**). Cerebrospinal fluid (CSF) taken from 4 patients on the second day of hospitalization had a clear and colorless appearance, with increased WBC in 2 cases with predominant lymphocytes; glucose level was within normal limits.

Of the 5 cases, two died and one patient developed severe sequelae (motoric and behavioral disability) that required constant nursing care and attention, while 2 cases were discharged with mild sequelae.

Discussion

In this case series, the JE positivity rate was 5/11 in children up to 12 years, which was higher than reported

Table 1. Symptoms and physical examination results of the JE-positive patients

Symptoms	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
High fever	+	+	+	+	+
Altered mental status	+	+	+	+	+
Status epilepticus	+	+		+	+
Vomiting		+	+		+
Headache		+	+		
Meningeal sign		+	+	+	
Pathologic reflex		+	+		+

Table 2. Laboratory test results and outcomes of JE-positive patients

Variables	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Blood					
WBC, /mm^3	9.1	19.7	10.5	6.8	17.7
Hemoglobin, g/dL	10.2	13.1	13.9	6.9	11.4
Hematocrit, %	29.9	40.2	20.9	24.2	31.5
Platelets, /mm^3	167	264	372	395	388
Basophils, %	0	0	0	0	0
Eosinophils, %	0	0	0	0	0
Neutrophils, %	70	82	84	80	81
Lymphocytes, %	25	10	7	26	12
Monocytes, %	4	8	8	15	6
Serum glucose, mg/dL	154	142		133	190
CSF					
WBC, /mm^3	10	40	*	10	90
Lymphocytes, %	69	66		73	86
Monocytes, %	31	32		25	10
Neutrophils, %	0	2		2	4
Glucose, mg/dL	80	82		77	102
Outcomes	Mild sequelae	Severe sequelae	Mild sequelae	Died	Died

by other studies in India (14.18% and 14.4%).[9,10] The high rate of JE cases in our study may have been due to the small sample size of patients who underwent JE testing. Furthermore, lack of awareness and lack of vaccination subsidies may have contributed to the high percentage of cases. The JE-positive patients were children ranging in age from 2 to 12 years. This result was similar to other Indian studies, in which the incidence of JE cases in children were particularly prevalent in older children (most cases aged 5-12 years).[10] All 5 of our patients were unvaccinated and lived in rural areas. This finding correlated well with earlier studies, in which most cases were children from rural areas where most people lived close to pig farms or irrigated rice fields which support the breeding of vector mosquitoes.[9,10]

Fever, altered mental status, seizures, and vomiting were the most common symptoms observed, and most patients presented with either a positive meningeal irritation sign or pathologic reflex. The average time to hospital admission after developing symptoms was 4 days, similar to findings in a Japanese study.[11]

It was not until 2017 that JE vaccination was included in the Indonesian government's subsidized vaccination program. Even so, the program was implemented only in selected areas, leaving areas with lower numbers of reported cases without access to free JE vaccinations. Currently, it is available only in Bali, where the incidence is the highest.[8] This may be the biggest reason for low coverage. Furthermore, even if the patient can afford the vaccine, its availability in rural areas is scarce. Low awareness and limited understanding of the disease and the importance of having children vaccinated are other important considerations.

Diagnostic testing for JE should be performed using JEV-specific IgM-capture ELISA on CSF and/or serum, as recommended by the WHO.[7] In most patients, the virus-specific IgM can be detected in CSF at 4 days and in serum at 9 days after onset of symptoms.[12] Recent JE can present as a 4-fold or more increase in JEV-specific IgM between the acute and convalescent phases.[13] To date, JE remains difficult to diagnose, especially in West Kalimantan where facilities cannot conduct the JE-specific tests. Specimens are sent to Jakarta and can take 1-2 months until results are confirmed. Testing of CSF specimens is preferred, in order to reduce false positivity rates from previous infection or vaccination. However, many patients were reluctant to undergo lumbar puncture.

In conclusion, Japanese encephalitis remains an under-recognized cause of encephalitis in children, especially in West Kalimantan. It is a vaccine-preventable disease. However, with the general public lacking knowledge of the disease and the high cost of vaccines, JE vaccine coverage in West Kalimantan

remains low. The most common clinical presentations in our cases are fever, altered mental status, seizures, vomiting, and positive meningeal irritation signs, or pathologic reflexes. The JE mortality rate is as high as 2 out of 5. However, poor surveillance in West Kalimantan has made the burden difficult to quantify, hindering decisions about subsidized vaccine introduction. Hence, the local government needs to accelerate surveillance so that West Kalimantan can be evaluated for eligibility into the subsidized vaccine program. JE-specific diagnostic kits should be available in health facilities in order to support disease surveillance and to help clinicians provide early management of JE. Furthermore, health education and promotion should be given to the public to increase disease awareness and JE vaccination coverage.

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