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Beyond Survival: Multisystem Life-Threatening Illness in an Infant with Congenital Heart Disease and Sepsis

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ABSTRACT

Introduction: Congenital malformations are a leading cause of infant disability and mortality. Congenital infections, particularly cytomegalovirus (CMV) and Toxoplasma gondii, are associated with structural abnormalities of multiple organ systems, including congenital heart disease (CHD). In utero infection may disrupt cardiac organogenesis, increasing the risk of heart failure. Infants with CHD are also highly susceptible to sepsis, frequently requiring pediatric intensive care. Managing life-threatening conditions in infants presents significant clinical challenges, including complex therapeutic decisions, drug dosing, and multidisciplinary care. Case Report: A 1-month-old male infant presented with poor feeding and lethargy. He had been previously diagnosed with failure to thrive and CHD consisting of atrial septal defect (ASD) and ventricular septal defect (VSD). Further evaluation revealed heart failure (Ross III), congenital CMV and toxoplasmosis infections, sepsis, bronchopneumonia, prolonged jaundice, and hydrocele dextra. The patient required PICU admission for 6 days followed by 7 days of inpatient care. Clinical improvement was achieved following comprehensive medical management, and the patient was discharged in stable condition. Conclusion: Congenital infections may play a critical role in the development and clinical severity of CHD, contributing to heart failure and increased susceptibility to sepsis. Early recognition and integrated multidisciplinary management are essential to improve outcomes in infants with multiple life-threatening conditions, emphasizing care that extends beyond survival toward functional recovery..

1. INTRODUCTION

Congenital malformations are defined as structural or functional anomalies that arise from abnormal development during embryonic or fetal life and remain a major contributor to infant morbidity and mortality worldwide (Ardi et al., 2024). These conditions represent the leading cause of long-term disability and the second most common cause of death during the first year of life. Among the etiological factors, congenital infections play a critical role, particularly cytomegalovirus (CMV) and Toxoplasma gondii, which have been strongly associated with abnormalities of the central nervous system, cardiovascular system, gastrointestinal tract, hepatobiliary system, and bronchopulmonary structures (Barycheva et al., 2019).

Congenital heart disease (CHD) is defined as a macroscopic structural abnormality of the heart or intrathoracic great vessels with functional significance (Hariyanto, 2012). It is the most common form of congenital malformation, with an estimated incidence of approximately 0.8% of all live births. CHD results from disruption of cardiac organogenesis and contributes significantly to neonatal morbidity, functional limitation, and mortality, accounting for approximately 4% of neonatal deaths (Ascher et al., 2013). Importantly, increasing evidence demonstrates a causative association between congenital CMV and Toxoplasma infections and structural cardiac defects, whereby in utero infection interferes with cardiac morphogenesis, predisposing infants to atrial septal defects (ASD), ventricular septal defects (VSD), and subsequent cardiac dysfunction (Barycheva et al., 2019).

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Pediatric heart failure (HF) frequently coexists with CHD and represents one of the most severe complications in affected infants. Heart failure in children is a progressive clinical and pathophysiological syndrome characterized by respiratory distress, edema, growth failure, and exercise intolerance, accompanied by complex circulatory, neurohormonal, and molecular disturbances (PNPK Management of Heart Failure in Children, 2023). Epidemiological data indicate that up to 40% of children with CHD develop HF, and CHD remains the leading cause of heart failure–related hospitalization and intensive care admission in pediatric populations, with a substantial risk of mortality (Ascher et al., 2013).

Beyond cardiovascular complications, sepsis remains a major cause of pediatric intensive care unit (PICU) admission and mortality, particularly in infants. Sepsis is defined as life-threatening organ dysfunction resulting from dysregulated host responses to infection (PNPK Management of Sepsis in Children, 2021). Infants under one year of age are up to ten times more susceptible to sepsis than older children. This vulnerability is further amplified in infants with CHD due to compromised hemodynamics, impaired immune responses, frequent exposure to invasive procedures, prolonged hospitalization, cardiopulmonary bypass, extracorporeal membrane oxygenation, and the presence of intravascular devices (Ascher et al., 2013).

The coexistence of CHD, heart failure, sepsis, congenital infections, prolonged jaundice, and bronchopneumonia creates a complex and potentially fatal clinical scenario characterized by a vicious cycle of multi-organ dysfunction. Hemodynamic instability caused by CHD and HF leads to impaired organ perfusion, increasing susceptibility to infection. Sepsis further exacerbates myocardial dysfunction, while congenital CMV and Toxoplasma infections contribute to hepatic involvement, manifesting as prolonged jaundice. Concurrent bronchopneumonia increases oxygen demand and cardiac workload, further worsening heart failure and hypoxia. This multifactorial interaction places infants at exceptionally high risk for adverse outcomes and presents a substantial challenge in critical care management.

In this context, the concept of "Beyond survival" becomes essential. Successful management of infants with life-threatening critical illness should not be measured solely by survival outcomes, but also by hemodynamic stabilization, recovery of organ function, prevention of long-term complications, optimization of growth and neurodevelopment, and improvement in overall quality of life. Infants represent the most vulnerable population, where incomplete organ maturation, limited physiological reserve, and difficulties in clinical assessment complicate diagnosis, monitoring, and therapeutic decision-making.

Despite the high clinical relevance, reports describing infants with multiple concurrent life-threatening conditions—combining CHD (ASD and VSD), advanced heart failure (Ross III), sepsis, congenital CMV and Toxoplasma infections, prolonged jaundice, and bronchopneumonia—remain scarce. Most published case reports focus on a single diagnosis or organ system, with limited discussion of integrated, multidisciplinary critical care strategies and therapeutic responses in complex multimorbid infants. This represents a significant gap in the literature.

Managing such cases requires meticulous individualized therapy, precise drug dosing, careful monitoring of therapeutic response, and coordinated multidisciplinary collaboration involving pediatric cardiology, infectious disease specialists, intensive care teams, and family-centered psychosocial support. The absence of specific guidelines for such complex presentations further underscores the need for shared clinical experience. Therefore, this case report aims to describe the comprehensive management and clinical course of an infant with multiple life-threatening critical illnesses, highlighting diagnostic challenges, therapeutic strategies, multidisciplinary interventions, and clinical outcomes. By presenting this case, we seek to contribute meaningful clinical insights and practical lessons for the management of similarly complex pediatric patients, emphasizing that optimal care extends beyond survival toward holistic recovery and long-term well-being.

2. METHOD

Case Report

A 1 month 7 days old baby boy born to a P2A0 mother came to the Emergency Department (ED) of Margono Soekarjo Regional General Hospital (RSMS) on November 9, 2024 with his mother with complaints of weakness and unwillingness to breastfeed since 3 days before admission. Initially, in October 2024, the patient's mother complained that the patient often coughed, the sound of crying decreased and appeared to be shortness of breath which was characterized by deep breathing and increased breathing frequency. When the initial complaint arose, the patient's mother brought the patient to the emergency room of Hospital A to consult a pediatrician (DSA). On examination, the patient was diagnosed with failure to thrive and suspected of congenital heart disease so it was recommended to consult a DSA subspecializing in heart and blood vessels. At Hospital A, the patient was treated for 2 days. The patient was then brought to the emergency room of W Hospital with the same complaints as well as consulting regarding the patient's heart condition and then a series of examinations were carried out including an echocardiogram. The doctor said that the patient suffered from ASD (atrial septal defect) or atrial septal defect and VSD (ventricular septal defect). In addition, the patient was also diagnosed with bronchopneumonia which was confirmed by a plain chest examination. At W Hospital, the patient was admitted for 4 days.

Four days before entering the emergency room of RSMS, the patient was discharged and received discharge medications, namely Captopril 2x1mg and Furosemide 2x1 mg. After being discharged, the day after the patient's mother complained that the patient was lazy to breastfeed. Two days after the patient was discharged from W Hospital, the patient's mother found that the patient looked weak and did not want to breastfeed, so the patient's mother decided to take the patient to the Emergency Room of RSMS because she wanted to get further treatment. At the time of the history taking, the patient's mother said there were no things or activities that alleviated the symptoms. The patient tended to have to be woken up during breastfeeding hours. The patient's mother also said the patient suckled intermittently and breathed quickly after breastfeeding, besides that the mother said the patient sometimes coughed and choked. Other complaints such as the baby looking bluish, nausea, vomiting, were denied. Complaints related to defecation and urination were denied. The patient was admitted to RSMS for laboratory tests and clinical evaluation.

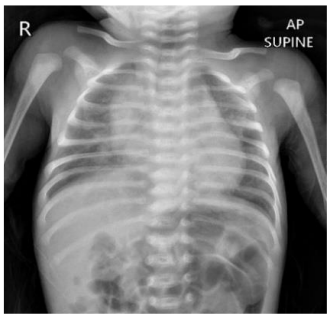

Figure 2. RSMS Thoracic Plain Photo Image (November 10, 2024)

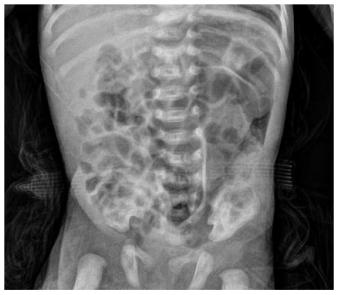

Figure 3. RSMS Abdominal Plain Photograph (November 10, 2024)

According to the patient's mother, after birth, the patient was said to be actively breastfeeding and no similar complaints were found before. But the patient's mother after about a week after birth the patient looked yellow, the patient was less active, coughing, and rarely crying which gradually until finally the patient was taken to DSA and received 14 hours of phototherapy.

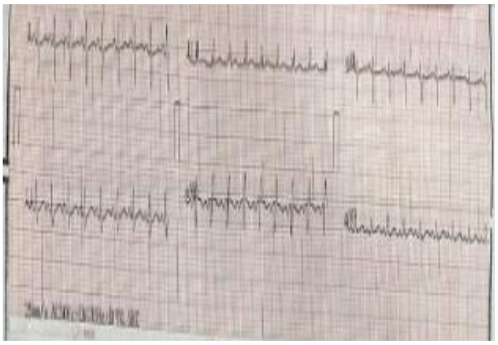

Figure 4. RSMS ECG Results (November 11, 2024)

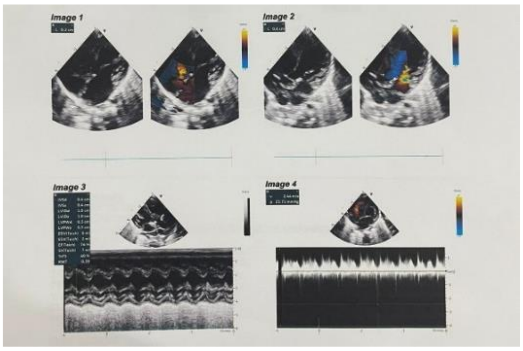

Figure 5. Echocardiogram results of W Hospital (November 6, 2024)

At the time of discharge from the maternity hospital, the patient's mother said many people visited the house, including the patient's neighbor who was coughing, visited the patient several times. However, a recent family history of coughing was denied. The patient is the second of two children (twins) and lives with her father, mother and twin sister in a residential area. The patient's mother has a master's degree and is currently working under the provincial BKKBN. The patient's father has a bachelor's degree and works in business and engineering. The patient's health financing uses BPJS non PBI class I.

The patient is the second child born by sectio caesaria (SC) to mother P2A0, 33 years old, 36 weeks 2 days gestation with a birth weight of 1900 grams, body length 45 cm and head circumference 30 cm. While the birth weight of the patient's twin sister was 2200 grams. The patient's mother was diagnosed as pregnant with twins at RSI B. In the first trimester of pregnancy, precisely at 8-9 weeks of gestation, the patient's mother often complained of severe vomiting until she lost 9 kg of weight and then sought treatment and was diagnosed with hyperemesis gravidarum. In the second trimester, the patient's mother denied any complaints. In the third trimester, the patient's mother had a cough and cold but it resolved by itself. During pregnancy, the patient's mother regularly checked her pregnancy every month with an obstetrician, and denied any abnormalities. During pregnancy, the patient's mother continued to work actively. On October 3, 2024 at 8:00 pm the patient's mother returned home from work and felt exhausted so she decided to rest. At 22:00 WIB, the patient's mother felt a large amount of clear fluid coming out of the birth canal so the patient's mother decided to go to the hospital and was diagnosed with premature rupture of membranes (KPD). After that, the patient's mother underwent SC surgery on October 4, 2024 at 02.00 WIB and gave birth to the first child then 1 minute after that the patient was born. According to the mother's statement, the patient was born

immediately crying in good condition and was placed in an incubator without an IV or oxygen. Then the patient was discharged with the mother after 3 days of post-sync care.

On initial physical examination at the emergency room, the patient was generally weak and looked yellow. Vital sign measurements obtained a pulse of 160 x/min, temperature 36.4 C, respiratory rate 59 x/min, and patient saturation levels of 95%. Anthropometric measurements of the patient obtained the results of body weight (BW) 2400 grams, body length (PB) 45 cm and head circumference 34.5 cm. From these results, the patient was found to be underweight (-3<Z<-2 SD), very short stature (-3<Z<-2 SD), good nutrition (-2 SD<Z<+1 SD) and mesocephalic with head circumference at -3<Z<-2 SD. On head to toe examination, the doctor found that the patient looked weak, apathetic consciousness and sunken fontanel, eyes were droopy, inactive movements, icteric and appeared congested. On chest inspection, there was retraction of the chest wall as the patient breathed. Noise was also heard during auscultation of the heart. The emergency room doctor then diagnosed the patient with dehydration due to low intake in infants with asianotic PJB (ASD and VSD), neonatal jaundice suspected hyperbilirubinemia dd late onset neonatal sepsis, low birth weight (LBW), premature, and gemelli. The patient received initial therapy of oxygenation with nasal cannula, IVFD dextrose 10% 1/2 NS8, ranitidine injection 2 x 5 mg intravenously (IV), ondansetron injection 2 x 1 mg IV, and continued the patient's routine medication and consulted the DSA. By DSA, the patient was diagnosed with hypovolemic shock, CHF Ross III, bronchopneumonia, jaundice suspicious of cholestasis, UTI, asianotic PJB (ASD and VSD), normocytic-normochromic anemia and history of prematurity, LBW and gemelli. The patient was then transferred to PICU for intensive care and further examination.

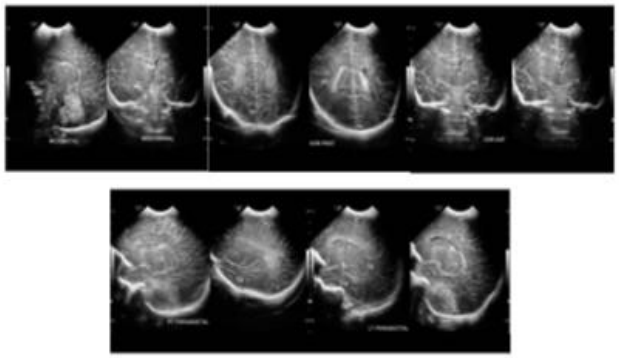

Figure 7. Head Ultrasound (RSMS November 13, 2024)

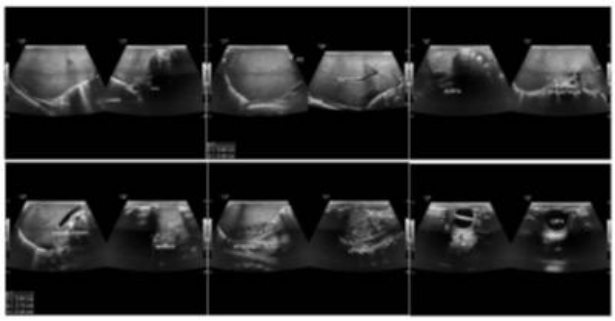

Figure 8. RSMS Abdominal Ultrasound (November 13, 2024)

Supporting examinations such as complete blood tests, blood chemistry, electrolytes, urinalysis, sputum culture and blood culture, TORCH infection examination, ultrasound, and peripheral blood picture examination were performed to help establish the diagnosis and evaluate the patient's condition. Figure 6 is an ultrasound of the patient's head which shows no bleeding, cystic lesions, or hydrocephalus.

Figure 7 shows the results of abdominal ultrasound showed no dilation of the biliary ducts both intra-and extrahepatic and the choledochal ducts. Sonography of other intra-abdominal

organs was also within normal limits. Testicular ultrasound examination was also performed to confirm the diagnosis of enlarged testicular size. The ultrasound showed a dextra hydrocele, while the location and size of other structures were within normal limits.

The patient was hospitalized at RSMS for 14 days starting from 09/11/2024 in the emergency room, then from 10/11/2024 to 16/11/2024 the patient was treated in the PICU for 6 days and from 16/11/2024 to 22/11/2024 the patient was treated in the Aster ward for 7 days. While in the PICU, the patient received intensive care. The patient received oxygenation with a nasal cannula, ventolin nebulizer + NaCl 0.9% 3cc every 12 hours, dopamine 0.1 cc / hour, ranitidine injection 5 mg every 12 hours, ondansetron injection 1 mg every 12 hours, ursodeoxycholate per oral 2x24 mg and continued the patient's routine medication and enteral and parenteral nutrition based on the calculation of the patient's fluid needs which were met by feeding breast milk / formula milk 30cc every 3 hours and D10% ¼ NS 4 cc / hour and installing a dower catheter (DC). Before the blood culture results were released, the patient received first-line antibiotics, namely ampicillin 100 mg/8 hours IV given for 6 days, gentamicin 12 mg/24 hours for 5 days. Along the way, there was a change in the antibiotic regimen given along with the results of sputum culture and blood culture which showed the growth of Eschericia coli bacteria with ESBL (+) and blood culture which showed the growth of Staphylococcus hominis MRSA (+) bacteria so that tigecycline injection was given with a loading dose of 5 mg IV followed by a maintenance dose of 2.5 mg/12 hours IV.

Table 1. RSMS Laboratory Test Results

Check	10/11	11/11	15/11	18/11	25/11	Reference Value
Hemoglobin	9.1	9.1	8.8	12	10.4	9-16.6 g/dL
Leukocytes	6840	13940	10270	7850	6320	5000-19500/mm³
Hematocrit	28.3	28.2	27.2	36.9	30.9	30-54%
Erythrocytes	2.83	2.87	2.79	4.10	3.53	3.1-5.1 10^6/µL
Platelets	375000	334000	476000	297000	269000	217000-497000/mm³
MCV	100	98	97.6	90	87.5	98-122 fL
MCH	32.2	31.5	31.5	29.4	29.5	25-37 pg
MCHC	32.1	32.2	32.3	32.6	33.7	26-34 6/dL
RDW	14.7	14.1	14.5	16.9	16.3	11.5-14.5%
MPV	9.2	8.9	9.2	8.7	8.6	9.4-12.4 fL
Basophils	0.1	0.0	0.2	0.1	0.1	0-1%
Eosinophils	3.5	2.3	3.1	4.9	3.7	1-5%
Trunk	0.0	0.3	0.1	0.1	0.1	0-8%
Segment	24.5	47.7	25.8	33.8	26.9	17-60%
Lymphocytes	66.4	38.2	62.5	52.5	68.2	20-70%
Monocytes	5.5	11.5	8.3	8.6	1	1-11%
Neutrophils	24.5	48	25.9	33.9	27	35-60%
Granulocytes	1670	6650	2650	2650	1700	3000-9500/µl
SGOT	98	-	56	-	30	<50 U/L
SGPT	36	-	22	-	16	<41 U/L
Total Bilirubin	9.76	-	4.09	-	2.08	<1 mg/dl
Bilirubin Direk	1.11	-	0.74	-	1.,11	<0.2 mg/dl
Indirect Bilirubin	8.65	-	3.35	-	0.97	0-1 mg/dl
Glucose At Time	137	-	64.3	-	75.2	80-139 mg/dl
Sodium	136	-	136	-	-	136-145 mmol/L
Chloride	103	-	100	-	-	97-107 mmol/L
Calcium		-	9.6	-	-	8.6-10.3 mg/dl
Potassium	5.59	-	5.53	-	-	3.5-5.1 mmol.L
Ureum	8.71	-				11-36 mg/dL
Creatinine	0.37	-		-	-	0-0.85 mg/dL
Albumin	-	3.30		-	-	3.97-4.94 g/dL
Free T-4	-	1.45		-	-	0.89-2.2 ng/dL
TSH	-	2.72		-		0.72-11 uIU/mL
CRP	-		1.6	-	-	<5
Anti Toxoplasma IgG		411				<1 IU/mL: *Non reactive*; 1-30 IU/mL: *Intermediate*; >30 IU/mL: *Reactive*
Anti Toxoplasma IgM		0.209				<0.8 COI: *Non reactive*; 0.8-1.0: *Intermediate*; >1.0 *Reactive*

Table 2. RSMS Urinalysis Results

Inspection	10/11	15/11	Reference Value
Physics			
Color	Colorless	Light yellow	-
Clarity	Clear	Somewhat cloudy	-
Smell	Typical	Typical	-
Chemistry			
Urobilinogen	Normal	Normal	0.2-1.0
Bilirubin	Negative	Negative	Negative
Urine Glucose	Negative	Negative	Negative
Ketones	Negative	Negative	Negative
Specific gravity	1000	1.010	1.002-1.03
Erythrocytes	1+/10	1+/10	Negative
pH	7.0	8.0	4.8-7.4
Urine Protein	Negative	Negative	Negative
Nitrite	Negative	Negative	Negative
Leukocytes	1+/25	1+/25	Negative
Urine Sediment			
Erythrocytes	0-3	1-3	Negative
Leukocytes	1-5	0-4	Negative
Crystal	Negative	Negative	Negative
Bacteria	1-10	1-10	Negative
Mushrooms	Negative	Negative	Negative
Trichomonas	Negative	Negative	Negative
Epithelium	0-5	0-1	Negative
Leukocyte Cylinder	Negative	Negative	Negative
Erythrocyte Cylinder	Negative	Negative	Negative
Hyaline Cylinder	Negative	Negative	Negative
Candle Cylinder	Negative	Negative	Negative
Fine Granular	Negative	Negative	Negative
Coarse Granular	Negative	Negative	Negative

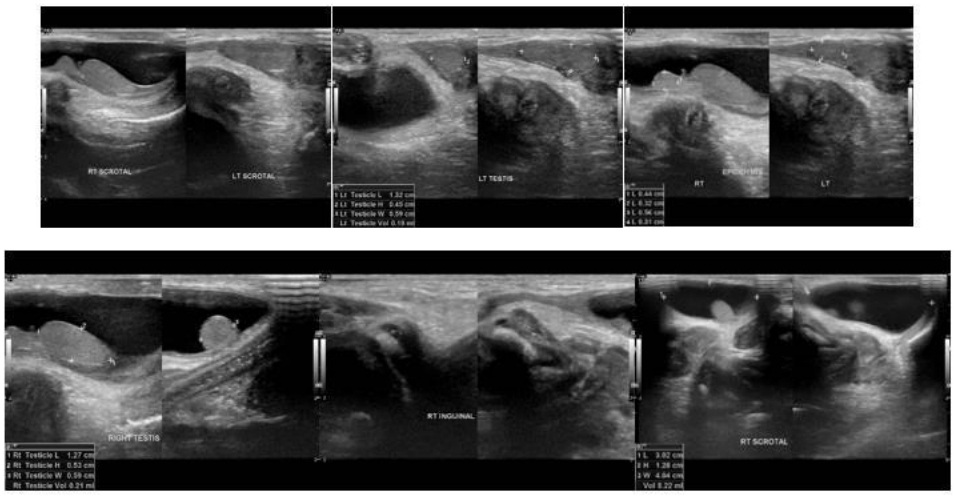

Figure 9. RSMS Testicular Ultrasound (November 13, 2024)

The results of the TORCH examination showed high levels of IgG anti-CMV and IgG anti-toxoplasma, then the patient was given therapy for CMV infection with valganciclovir 40 mg twice

a day taken orally starting from 12/11/2024. While for toxoplasmosis, the patient received clindamycin 30 mg three times a day. After the patient's IgG anti-CMV and anti-toxoplasma titers were declared reactive, the patient's mother conducted a TORCH examination and obtained reactive IgG anti-CMV and IgG anti-toxoplasma results.

During the treatment, the patient's weight was evaluated, where it was found that the patient's weight decreased from 2400 grams to the smallest weight of 2275 grams and a height of 47.5 cm. At the end of treatment, the patient's weight was again measured and found to have increased to 2335 grams with a body length of 48.4 cm and head circumference of 34.5 cm. During the course of treatment, the patient's clinical UTI improved where on the 7th day of treatment, there was no clinical UTI so the patient's DC was released.

During the 6 days of treatment in the PICU, the patient's clinical condition improved so the patient was transferred to the Aster ward. In Aster, the patient's clinical condition generally improved, the patient was willing to breastfeed even though the duration was less than 10 minutes. On the 11th day of treatment, the patient's mother complained of mushy stools accompanied by mucus and a little foam every time the patient finished breastfeeding. Therefore, a routine stool examination was carried out and bacteria were found. The patient was then given zinc 1 x ½ measuring spoon, after 3 days of administration, clinical diarrhea improved. On 11/22/2024, the patient was discharged with discharge medications, namely ursodeoxycholate 2x24 mg, valgovir 2x40 mg, clindamycin 3x30 mg and zinc 1x ½ measuring spoon as well as the patient's routine medications, namely furosemide 2x1 mg and captopril 2x1 mg. The patient was also educated on post-treatment controls, education on medication consumption, education on the potential for bronchopneumonia transmission to the patient's twin and education to increase the patient's weight and length to reach the ideal anthropometric status target.

The patient visited the pediatric clinic of RSMS on 25/11/2024 and 9/12/2024. The patient's condition improved, no longer looked yellow, chest retraction was reduced, the patient looked more active. Based on the patient's mother's statement, the patient was also actively breastfeeding and able to suck strongly. However, after breastfeeding the patient's breathing becomes faster. Anthropometric measurements at the clinic showed an increase in the patient's weight where the patient's weight at control was 2375 grams and 2764 grams respectively. The patient's mother said the patient was currently breastfed and formula fed.

3. RESULT AND DISCUSSION

Congenital malformations are defined as morphological anomalies in the formation of tissues, organs, or body parts that arise from abnormal development during embryonic or fetal life, making congenital malformations one of the most common causes of disability and mortality in children (Ardi et al., 2024; Barycheva et al., 2019). Congenital malformations can occur due to various factors during pregnancy. TORCH infection (Toxoplasma, others, Rubella Cytomegalovirus, Herpes simplex) has been widely studied to be one of the causes of congenital malformations. These infections can interfere with the process of organ formation (organogenesis), causing congenital defects/deformities (Barycheva et al., 2019). Congenital heart disease (CHD) is one of the most common congenital malformations with a cumulative incidence of 0.8% or estimated between 8-12 cases per 1000 live births with an annual mortality rate of 300,000 deaths worldwide (Ascher et al., 2014; Singampali et al., 2021). Congenital heart disease is defined as a macroscopic structural abnormality of the heart or intrathoracic great vessels that has a significant definite or potential function. Broadly speaking, CHD is divided into two groups, namely cyanotic and asianotic CHD (PNPK Management of Pediatric Heart Failure, 2021).

It is called cyanotic PJB because it causes cyanosis, which is a bluish discoloration of the skin, lips and nails. Cyanosis occurs because the blood pumped to the body contains low oxygen levels due to the mixture of unoxygenated blood with oxygenated blood. Asianotic PJB comes from the word "a-" which means "without" and "cyanotic" which refers to the condition of cyanosis (blueness) so that it is defined as the presence of structural abnormalities in the heart that are congenital in nature that do not cause cyanosis (Hinton and Ware, 2017).

The aetiology of CHD is still a controversial discussion. The main cause is a genetic trait, but there are several risk factors that increase the likelihood of CHD. One of these is TORCH infection. TORCH is one of the most dangerous pathogens for the fetus. When a pregnant woman is infected for the first time, because the body does not have corresponding antibodies and cannot resist the invasion of pathogens, pathogenic microorganisms easily spread to the fetus, resulting in abortion, IUGR, congenital abnormalities, prematurity, and so on. In addition, the teratogenic effect of TORCH infection on the embryo is more obvious in pregnant women during the early stages of pregnancy and decreases with infection at later gestational ages (Wang, et al., 2019). The pathogenesis of congenital infections is multifactorial and not well understood. In essence, fetal damage results from several mechanisms including chorionic villous epithelial necrosis, apoptosis of infected cells by direct viral damage, inhibition of mitosis, and development of precursor cells restricted by the virus, and cytopathic damage to vascular endothelial cells resulting in ischemia of developing organs (Zhang, et al., 2022). Cytomegalovirus (CMV) is the largest herpes virus with a double-stranded DNA component and a size of 150 - 200 nm2. It is called congenital CMV infection because this infection occurs in pregnant women who are then transmitted through the placenta (transplacental) to infect the fetus (Dioverti et al., 2016; Congenital Infection Consensus, 2019). The most common manifestations found in infants born with CMV infection are hepatosplenomegaly, hemolysis anemia (44%), thrombocytopenia (67%), conjugated hyperbilirubinemia (44%) and cholestasis (100%) as well as organ defects (Tehsin et al., 2019). Meanwhile, congenital toxoplasmosis is defined as Toxoplasma gondii infection in infants acquired in utero from infected mothers. Toxoplasma gondii is a protozoan parasite with domestic cats of the Felidae family as its definitive host and birds and rodents as its intermediate hosts.

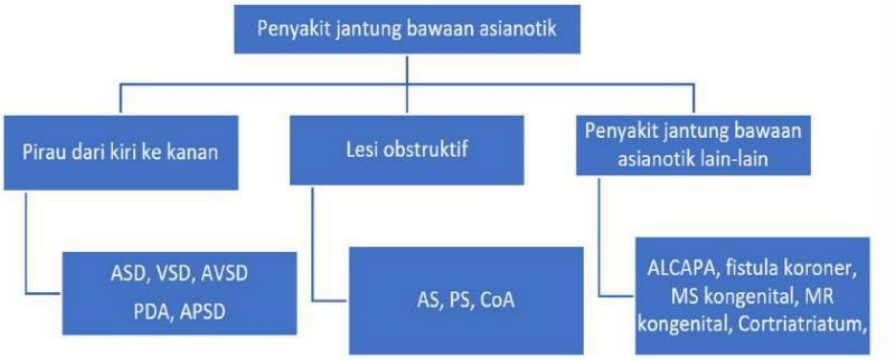

Figure 10. Asianotic Congenital Heart Disease

Figure 11. Cyanotic Congenital Heart Disease

Toxoplasmosis infects fetuses more frequently in the late trimester (80%) than the early trimester (<2%) (Dioverti et al., 2016; Congenital Infection Consensus, 2019). Toxoplasmosis has a classic triad of manifestations, namely hydrocephalus, chorioretinitis, and intracranial calcification (Supit, 2021). About 90% of toxoplasmosis cases are asymptomatic, but some cases have other manifestations such as anemia, DIC, tombocytopenia, hepatitis, jaundice, hepatic

calcification, hepatosplenomegaly, skin rash, lymphadenopathy, myocarditis, pneumonitis, sepsis-like illness, temperature instability, prematurity, and failure to thrive (Consensus on Diagnosis and Management of CMV Infection and Toxoplasmosis, 2019).

Transmission of TORCH infection can occur prenatally (transplacental), perinatally (blood contact and vaginal secretions during labor), and postnatally (breast milk). Other risk factors include maternal immunization history, history of sexually transmitted infections (STIs), and exposure to animals during pregnancy (Supit, 2021). In this case, the patient's mother denied any poor prenatal history and history of STIs. However, the patient's mother mentioned that there were stray cats around the office where the patient's mother worked and the patient's father often interacted with stray cats.

The diagnosis of CMV infection and Toxoplasmosis in the patient was based on the results of history taking, physical examination, and supporting examination. The results of anamnesis in the patient's mother showed symptoms in the form of yellow skin and tended to be weak, a history of babies born prematurely and LBW (1900 grams). In addition, there was a history of cough and cold during pregnancy, a history of HEG during pregnancy, and the possibility of indirect contact with cats by the patient's mother and father. The results of the history were also supported by the results of the physical examination which showed that the patient appeared icteric (Kramer 2) and looked weak. The presence of heart disease in the patient is also a form of manifestation of congenital congenital infection. Based on research by Barycheva et al in 2019, the manifestations of heart defects due to congenital CMV are a history of fibroelastosis (13%), VSD (5%), ASD (3%), and dextracardia (3%). Meanwhile, congenital toxoplasmosis can cause manifestations in the heart in the form of ASD (7%), VSD (2%), aortic stenosis (1%) and PDA (1%).

Based on the Consensus book Diagnosis and Management of Congenital Toxoplasma and CMV Infections, CMV diagnosis is based on clinical and laboratory features. Clinical features of congenital CMV infection include:

Table 5 Clinical Features of Congenital CMV Infection

System	Manifestation	Freq (%)
Skin	Petechie	75
	Purpura	10
	Icteric	67
Hepatobilier	Direct bilirubine	80
	Increasing transaminase enzyme	80
	Hepatosplenomegaly	60
Hematopoeietic	Thrombocytopenia	77
	Anemia	59
	Splenomegaly	60
CNS	Microcephaly	53
	Intracranial Calsification	54
	Letargy	37
	Seizure	7
Auditory	SNHL	50
Visual	Chorioretinitis	10

Meanwhile, laboratory criteria for confirming the diagnosis of congenital CMV are PCR examination with urine/saliva samples in the first 3 weeks of life (sensitivity >97.4% and specificity 99.9%) or blood PCR (sensitivity 100%) with the gold standard being virus isolation in the first 3 weeks of life. In addition, the diagnosis can also be made by CMV blood antigenemia examination (sensitivity 89.18% and specificity 90-100%) and anti-CMV IgM antibody serology examination (sensitivity 72.97% and specificity 62.06%). Another source states that the diagnosis

of CMV infection is considered if one of these examinations is found, namely (1) seroconversion with the appearance of anti-CMV IgM; (2) a 4-fold increase in IgG titer; (3) detection of CMV antigens in infected cells; (4) detection of CMV DNAemia using molecular techniques; (5) and/or virus isolation using throat culture, buffy coat, or urine (Karyanti et al., 2018).

In this case, supporting examinations were carried out for the diagnosis of CMV in the form of blood laboratory tests, and anti-CMV IgM and IgG serology, head ultrasound, and abdominal ultrasound. Other supporting examinations such as PCR and antigenemia were not performed due to limited facilities. The results of head ultrasound showed no bleeding, cystic lesions, or hydrocephalus as well as abdominal ultrasound results which did not show any abnormalities. Serologic examination showed non-reactive IgM anti-CMV. Meanwhile, the IgG anti-CMV showed reactive results. The presence of anti-CMV IgG in newborns may indicate the possibility of intrauterine CMV infection in infants (Teimouri et al., 2020).

Routine blood tests and peripheral blood smears showed normochronic normocytic anemia (hemoglobin 9.1 and 8.8 mg/dL) which was a marker of hemolytic process due to infection. The patient also had hyperbilirubinemia indicating cholestasis and elevated transaminase enzymes indicating hepatic insufficiency.

Indications for CMV therapy according to the Consensus book Diagnosis and Management of Congenital Toxoplasma and CMV Infections are infants with severe symptomatic aged < 6 months. Severe symptomatic means there are at least 2 symptoms/signs: thrombocytopenia (<100.000/µL), ptekiae, hepatomegaly, cholestasis, splenomegaly, IUGR, hepatitis, ALT increase >3x the upper limit of normal or central nervous system (CNS) involvement: microcephaly; radiology: ventriculomegaly, intracerebral calcification, periventricular echogenicity, cortical cerebellar malformation; abnormal cerebrospinal fluid (CMV DNA found), chorioretinitis, SNHL. Antiviral therapy should also be considered in infants with serious organ disorders (Triono et al., 2020).

Although the patient's anti-CMV IgM level showed non-reactive results, the high level of anti-CMV IgG and the presence of severe manifestations in the patient became a consideration for this patient to be given therapy. In this case, the patient received valganciclovir therapy at a dose of 16mg/kgBB taken twice a day for virus eradication. The selection of this regimen is in accordance with the 2019 congenital CMV infection management consensus where there are 3 types of CMV infection therapy patterns, namely: (1) Ganciclovir IV for 6 weeks; (2) Oral valganciclovir for 6 months; and (3) Ganciclovir IV for 2 weeks followed by oral valganciclovir 4 weeks. The second option was chosen due to drug availability and ease of administration after hospitalization. In addition, oral valganciclovir administration at a dose of 16 mg/kgBB.day provides the same effect as ganciclovir 6mg/kgBB IV (Pata et al., 2023).

Meanwhile, therapy for congenital toxoplasmosis in this case was given based on confirmation of the diagnosis of toxoplasmosis in the form of detection of high levels of toxoplasma IgG in the patient's serum and manifestations such as anemia, jaundice, temperature instability/fever, prematurity, and failure to thrive. The presence of anti-toxoplasma IgG in the patient cannot be used as a specific marker of toxoplasma infection at this time so it is necessary to conduct serial anti-toxoplasma IgG examinations to confirm whether the anti-toxoplasma IgG in the patient is a form of active infection in the patient or is a maternal antibody transferred to the patient. The IgG titer in infants from the mother will decrease by half every month. Meanwhile, the IgG titer of congenitally infected infants will remain/persist or increase. The diagnosis of congenital toxoplasmosis can be made laboratorically if: (1) Toxoplasma IgG increases and persists until more than 12 months of age (gold standard); (2) Toxoplasma IgG (+) and toxoplasma IgM (+); (3) Toxoplasma PCR (+) from amniotic fluid, peripheral blood, cerebrospinal fluid, urine, or other body fluids; (4) Neonate toxoplasma IgG (+) (but IgM negative) and there is serologic evidence of acute maternal infection during pregnancy, and evidence of clinical manifestations suggestive of congenital toxoplasmosis (Consensus on Diagnosis and Management of Congenital Toxoplasma and CMV Infections, 2019). In this case, although the anti-toxoplasma IgM was non-reactive, the presence of anti-toxoplasma IgG and clinical manifestations suggestive of congenital

toxoplasmosis became the basis for establishing the diagnosis of congenital toxoplasmosis in the patient.

Based on this, the patient received clindamycin therapy at a dose of 20-30 mg/kgBB divided into 2-3 doses. The 2019 Congenital Toxoplasmosis Infection Management Council states that the first line therapy that can be given is pyrimethamine with a loading dose of 2 mg / kgBB / day orally divided into 2 doses and continued at 1 mg / kgBB / day orally for 2 months and if there is no clinical improvement the treatment is extended to 6 months. Then sulfadiazine 100 mg/kgBB/day PO can be divided into 2 doses for up to 1 year, leucovorin 10 mg PO three times a week given for 1 week and corticosteroids if chorioretinitis is found. The second line is trimethroprim-sulfametoxazole or alternatively with pyrimethamine + clindamycin + leucovorin or pyrimethamine + claritomycin + leucovorin. If sulfadiazine regimen is not available, trimethroprim-sulfamethoxazole or a combination of pyrimethamine and clindamycin can be given. In this case, the patient was only given clindamycin in consideration of the availability of drug regimens. Although there is no randomized control trial (RCT) study on the use of clindamycin as a single agent of toxoplasmosis therapy, a case report written by Madi et al. in 2012 showed that clindamycin therapy as a monoagent for cerebral toxoplasmosis in a 30-year-old patient showed clinical improvement within 48 hours and complete recovery in 3 weeks.

During the administration of therapy for CMV and toxoplasmosis, it was found that the patient's clinical condition improved where the hemoglobin level was 12 mg/dL, no icterus skin was found with the last bilirubin level of 2.08 mg/dl, and the patient was willing to breastfeed with the mother.

The diagnosis of PJB in the patient was made 4 days before the patient was brought to RSUD Margono Soekarjo. Initially, the patient's mother complained that the patient did not want to breastfeed and the history of breastfeeding was intermittent, appeared weak, and the frequency of breathing appeared fast. By the DSA of the previous hospital, the patient was also diagnosed with failure to thrive. Growth failure in children can be a sign of congenital heart disease. This is because children with CHD will have central venous anoxia and congestion which causes malabsorption of food. Peripheral anoxia also causes nutritional inadequacy and increased metabolic rate, causing growth failure in children (Samudro, 2012). A repeat physical examination at RSMS for this patient also showed poor anthropometric status. On auscultation, the patient's heart sounded noisy throughout the systolic phase. Heart noise is an important sign in determining congenital heart disease (CDC, 2020). On echocardiogram examination, there was an abnormality in the form of an atrial septal defect of 2mm and a ventricular septal defect of 7mm. Based on these results, the patient was also found to have heart failure with Ross III criteria.

Nutritional adequacy and fluid and electrolyte balance are things that must be considered in patients with heart failure. In children with heart failure, fluid restriction up to 80% of basal metabolic needs should be done. However, if the clinical severity of heart failure has improved, fluid needs are again adjusted and maintained so as not to exceed basal metabolic needs. Meanwhile, nutritional adequacy in children with heart failure can be adjusted to the optimal nutritional parameters of infants with CHD. The use of an orogastric or nasogastric tube is also a consideration, especially in infants with low sucking ability, non-optimal chewing or frequent vomiting and reflux (PNPK Management of Heart Failure in Children, 2023).

In this case, the patient received therapy in the form of Furosemide 1mg/8 hours IV and Captopril 2x1 mg PO. The administration of furosemide as a diuretic agent aims to reduce cardiac load by lowering preload. In addition, furosemide has a vasodilator effect and increases systemic venous capacitance. The administration of captopril as an angiotensin enzyme inhibitor aims to lower blood pressure and improve cardiac function. In addition, captopril administration can also reduce the risk of hypokalemia due to furosemide administration (PNPK Management of Heart Failure in Children, 2023; Ali et al., 2024).

The patient received nutrition and fluids from breast milk/formula milk as much as 300cc which was divided into 10 feedings, and the rest was fulfilled by infusion of 10% dextrose ¼ normal saline at a rate of 4cc/hour. The choice of breast milk feeding in patients with CHD is recommended because of its easily absorbed composition. In addition, breast milk contains macronutrients and micronutrients, and has a high protective power that reduces the risk of

necotizing enterocolitis (NEC), intolerance, and osmotic diarrhea (PNPK Management of Heart Failure in Children, 2023). After receiving the above therapy, the patient's clinical condition gradually improved, the sunken head was reduced, the patient looked fitter, and the eye discharge was reduced.

A blood culture was performed on this patient to look for the cause of sepsis. Sepsis is a lifethreatening organ dysfunction caused by immune dysregulation against infection (PNPK Management of Sepsis in Children, 2021). The incidence of sepsis is increased in infants born prematurely and is closely associated with immune immaturity. However, the incidence is also increased in children with CHD due to changes in cardiac structure and function which may affect the immune system, blood circulation and hemodynamic balance. Sepsis in infants with CHD can often exacerbate an already compromised heart, leading to organ failure and increased mortality (Melit et al., 2024). Susceptibility to sepsis in infants with CHD occurs due to circulatory changes resulting from structural abnormalities of the heart such as atrial septal defect (ASD), ventricular septal defect (VSD), or patency of the ductus arteriosus (PDA), causing abnormal blood flow between parts of the heart. As a result, low-oxygen blood may mix with oxygen-rich blood, leading to hypoxia (lack of oxygen) and impaired blood flow to various vital organs, including the lungs, kidneys and brain. As a result, the body becomes more susceptible to infection. In this case, the patient had bronchopneumonia as well as pulmo edema as evidenced by the patient's thoracic photograph. This correlated with her pre-existing CHD. In many cases, PJB alters blood flow patterns throughout the heart as it produces low pressure pathways that disrupt normal flow, this can pose a significant risk of morbidity as it affects oxygenation and systemic/lung volume status, which in turn can lead to reactionary inflammation. In this case, the increased right-sided flow of the heart can lead to pulmonary edema (Singampalli et al., 2021). In addition, the presence of blood flow stagnation increases the risk of lower respiratory tract infections due to the decreased ability of the body to effectively clear pathogens. As a result, microorganisms multiply more easily, and bronchopneumonia results. If this infection persists and sepsis occurs, the infant's body will become hypotensive, which exacerbates cardiac and circulatory dysfunction (Ascher et al., 2013; Melit et al., 2016). In the sputum culture examination, a positive result of Escherichia coli bacterial growth was found. Variations in bacterial colony growth in adults and children are different where in children, the most common bacteria causing lower respiratory tract infections found in sputum culture results are Streptococcus pneumoniae, Haemophilus influenza and Escherichia coli (especially in infants) (Popova et al., 2019).

Sepsis in this patient was suspected based on the clinical condition of the patient who appeared weak, lazy to suckle and there was temperature instability during treatment. Blood culture results showed positive Staphylococcus hominis spp hominis and MRSA (Methyciline Resistance Staphylococcus Aureus) organisms. Staphylococcus hominis is a gram-positive bacterium and is a skin commensal bacterium that is often the cause of infection in hospitalized children. S. hominis infections are associated with secondary infections in patients transferred to the intensive care unit (Frickmann et al., 2018). Staphylococcus hominis is a class of coagulase-negative staphylococci (CoNS). Infections caused by these bacteria are often challenging to treat because of their ability to cause antibiotic resistance (Szemraj et al., 2024). A positive result on blood culture does not fully explain whether the bacteria is a true infection or just a contaminant that is usually present on the baby's skin. Thus, clinical judgment is important in determining this bacterial infection. MRSA positivity is a challenge in eradicating sepsis-causing bacterial infections (Rose et al., 2023). In this case, initially the patient was given an injection of ampicillin and gentamicin antibiotics with consideration of the use of empirical therapy with broad-spectrum antibiotics for the initial treatment of sepsis as in the PNPK book Management of Sepsis in Children in 2021, the selection of empirical antibiotic combinations that can be given is the penicillin group combined with the aminoglycoside group with the choice of gentamicin. After the culture results came out, the patient was given antibiotic therapy in the form of Tigecyclin with an initial dose of 2mg / kgBB and a maintenance dose of 1mg / kgBB given twice a day. The selection of tigecyclin as a therapeutic option is based on the results of antibiotic resistance

testing. After receiving the appropriate antibiotic, the patient's clinical improvement began to appear, the patient's temperature tended to stabilize, the patient was also more active in moving and willing to breastfeed.

4. CONCLUSION

Congenital malformations are one of the most common causes of disability and mortality in children. PJB as the most common form of congenital malformation is closely related to congenital infection. Manifestations of congenital infection in infants are usually found in cholestasis, anemia, thrombocytopenia and hyperbilirubinemia. In this case, CMV and Toxoplasma infections contributed to the incidence of CHD resulting in heart failure. In addition to immune immaturity, previous infections with CHD may increase the child's susceptibility to opportunistic infections leading to sepsis. The administration of valganciclovir for CMV infection, single clindamycin for congenital toxoplasmosis, captopril and furosemide for heart failure condition, and tigecycline for sepsis patient showed a good response where the patient's clinical condition immediately improved supported by the results of supporting examinations that improved..

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