ORIGINAL ARTICLE

Congenital Anomaly Caused by Cytomegalovirus and Toxoplasma Infections

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ABSTRACT We report a case of a five-year-old child with congenital anomaly caused by maternal cytomegalovirus infection and toxoplasmosis, hospitalized in pediatric ward Sardjito General Hospital. The diagnosis was established from the history of illness, physical examination, and laboratory findings. The presence of microcephaly, failure to thrive, deaf and mute, congenitally transmitted infection was suspected. **[Paediatr Indones 1996;36:121-125]**

Introduction

Infectious disease is still a critical health problem in Indonesia and is one of the causes of infant and child mortality. Several infectious diseases in the central nervous system of infants and children which may cause physical and mental disability include toxoplasmosis, rubella, cytomegalovvirus (CMV) and herpes simplex infections. If the infection occurs intrauterine, it may cause congenital anomaly in a newborn infant. This disease may apper individually or together with other disease.

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Toxoplasosis is a disease caused by *Toxoplasma gondii*, a parasite which was first isolated in 1908 from rodent *Ctedonactilus gondii* by Nicolle and Mancesaux in North Africa. Until 1969, household cats were assumed as the hospes definitive of this parasite.[1]

Natural infection by CMV is species-specific. No vector is known in the transmission cycle. Man is supposed to be the source of infection and it happens by way of either direct or inderect contact from one person to another.[2]

Toxoplasma gondii and CMV may be transplacentally transmitted by a pregnant mother with toxoplasmosis and CMV infection and may cause congenital CMV and toxoplasmosis in her baby, but

most of the cases are asymptomatic.[3,4] The clinical symptoms depend on the gestational age: infection in the older pregnancy will associated with milder symptoms.

The aim of this paper is describe the clinical manifestations of toxoplasmosis and CMV infection.

Report of the Case

A 5-year-old child was sent form TG Hospital, with the diagnose of anemia, hepatosplenomegaly and severe malnutrition. Since he was 1 year old, the child was sometimes suffered from febrile illness and had lost of appetite. Four weeks before he was sent to the hospital his abdomen was getting bigger especially at the upper abdomen. Three months before admission he had a light fever, was weak and pale. Eleven days before admission the child was still weak and pale and he still had fever. He was then sent to TG hospital and was there for 11 days. While he was in the hospital, he got blood transfusion three times.

No such disease was found in the family. Delivery process and pregnancy were normal; there were deaf and mute problems; nutritional state was deteriorated. He had varicella and primary tuberculosis.

On physical examination, he was found weak and had anemia and somnolent. The pulse rate was 132/minute: the respiratory rate was 42/minute; and body temperature was 40°C. His weight was 11 kg, height was 82 cm; no lymph gland enlargement was found. There was no disorder of joints and neck. Heart examination revealed a systolic murmur of grade 3/6; the heart configuration was normal; the lungs were normal. The abdomen was distended with liver enlargement of 8 cm below the left costal margin; it was normal on palpation. The bowel sound was normal. The spleen was enlarged (Schuffner II). The muscle of the upper and lower extremities were hypothrophic; the physiological reflexes were normal. There was no edema. The head circumference was 46 cm (microcephaly); the eyes were normal (no xerophthalmia); he was deaf.

Laboratory examination disclosed a hemoglobin level of 8.5 g/dl; pletelet count 40.000/µl, leukocyte count 5.400/µl; PMN count 21%; lymphocte 79% with atypical lymphocytes; reticulocyte was 1%. RBC morphology showed normocytic normochromic and macrocytic hypochromic. The serum iron was 60µg/dl; TIBC 320 µg/dl; indirect bilirubin 0.8 mg/dl; direct bilirubin 0.4 mg/dl, albumin 2,7 g/dl; globulin 3.4 g/dl; AST 60 µ/l; ALT 18 µ/l; GGT 88 u/l; cholesterol 47 mg/dl. The electrocardiogram was normal; echocardiography showed a moderate ASD (atrial septal defect).

Based on the presence of fever, hepatosplenomegaly and thrombocytopenia, the initial diagnosis was sepsis, and ampicillin 100 mg/kgBW/day and gentamicin 5 mg/kgBW/day were given. Results further laboratory examination showed that IgG CMV was 164 iu/ml, IgG toxoplasma was 94 iu/ml, and IgM toxoplasma was 204 iu/ml. Cranial CT-scan showed cerebral atrophy without evidence of calcification. Consultation with the Department of Opthalmology showed that there was no chorioretinitis or xer-

ophthalmia found.

Based on the history, clinical manifestations and laboratory data the diagnosis of congenital CMV and toxoplasmosis infection, anemia, severe malnutrition of marasmus type, failure to thrive, deaf and mute, and ASD were made.

The patient was then put on diet for severe malnutrition. Spiramycin 50 mg/kg BW/day and isoprinosin 50 mg/kgBB/day were given for toxoplasmosis and CMV. Consultation with the Department of Ear, Nose and Throat for the treatment of hearing disorder was shown that there was 30dB hearing left. From the Department of Psychology it was found that the child's intelligence was still normal. The patient was the referred to the Department of Rehabilition for speech therapy.

Discussion

Toxoplasma and CMV infections in a pregnant woman may be transmitted to her fetus. This disease may have a fatal result if it attacks the embryo. If the infection occurs in the first trimester, pregnancy may terminate. CMV infection in the second and third trimester may result in brain disorder.[5]

Most babies with congenital CMV infection in the prenatal period is asymptomatic. Asymptomatic infection may be detected by serologic examination of mothers and children.[2] In the longitudinal research on a newborn baby with subclinical infection, clinical symptoms may appear in the future.[2,7,8] More than 90% of congenital CMV infection in newborn babies is asymptomatic.[9] In our patient, the presentation of symptoms after birth did not attract the parents. Microcephaly, mute, and deaf problems were not known early. According to Williamson et al,[10] children with neurosensoric hearing loss as a result of congenital CMV infection at birth are mostly asymptomatic.

Hepatoslenomegaly is frequently the first sign of toxoplasmosis and CMV infections, that bring the parents to seek medical help. According to Alfort,[2] hepatoslenomegaly is the sign mostly found in CMV or toxoplasma infection.

In this case the disease was thought as a result of congenital toxoplasmosis and CMV infection. This was based on the positive IgG CMV (204 iu/ml) and IgG toxoplasm (94 iu/ml) in the mother in the presence of multiple congenital anomalyas (microcephaly, failure to thrive, deaf, and mute). The diagnosis of congenital toxoplasmosis may be ensured by the detection of specific IgG or IgM that persists even when the mother's IgG has disappeared.[11]

Positive toxoplasm IgM in children may be caused by toxoplasm reinfection. If re infection happens, anti IgG tether w.. increase.[11] Acute infection diagnosis may be confirmed by repeated examination, that is, if the negative IgG tether seroconversion changes into positive one; or if IgG increases significatly; or if specific anti-IgM is found.[11]

Early congenital toxoplasmosis treatment is expected to decrease or avoid brain demage after birth.[12] Length of treatment is not known yet. Volpe[1] assume that the treatment is about 21 days and is repeated several times within one year both in symtomic and asymptomic infection. Most treatment using the combination of pyrimethamin and sulfadoxin

combined is effective.[13] The use of spiramisin for the sufferer is chosen because it is less toxic than others. Antiviruses are useful to stop viruses but it has no effect on neurological diseases coused by CMV.[14] Several antiviruses used for the treatment of congenital CMV infection and viruses obtained are deoxyrridine, cytosine arabinose, adenine arabinoside and acyclovir.[9] In this case they are only given immunodulator, i.e. isoprinosin which is expected to increase protective tether so as to prevent virus replication. In a research in Italy, it was shown that the use of high-dose gancyclovir for a long time is effective for a baby with symptomatic congenital CMV infection,[14] but this medicine is not available in Indonesia.

Growth disorder in this case predicted to happen when the baby was 1 year old as the height of the baby was similar to a one-year old child. This is possibly because the child often has fevver and no appetite. The frequent fever and decreasing appetite may result in malnutrition and anemia. It's perhaps relates to the existing CMV replication. Anemia found in this case was deficiency anemia which was probably the result of poor feeding.

References

1. RemingtonJS, Desmond G. Toxoplasmosis, In: Remington JS, Klein JO, eds. Infection Diseases of the newborn Infant. Philadelpia: WB Saunders Company, 1982: 143-263.
2. Alfort CA, Chronic congenital and perinatal infections. In: Avery GB, Ed. Neonatology: Pathophysiology and management of the Newborn. Philadelphia : J.B. Lippincott Company, 1987;874-916.
3. Haksohusodo S. Viral infection on CNS of the neonates. Seminar on the Progress of Molecular Genetics and Perinatology , Yogyakarta, August 2-3, 1994.
4. Volpe JJ. Intracranial infections. In: Texbook of neurology of the newborn. Philadelphia: WB Saunders Company, 1987: 556-56.
5. Moore K. Before we are born: Basic embriology and birth defects; 3th ed. Philadelphia: WB Saunders company, 1989; 122.
6. Overall JC. Infection of the newborn. In: Behrman RE. Vaughan VC, eds. Nelson texbook of pediatrics. Philadelphia: WB Saunders Company, 1987: 422-35
7. Koppe JG. Loewer-Sieger DH, de Roever-Bonnet H. Result of 20-year follow-up of congenital toxoplasmosis. Lancet 1986: 254-6.
8. Wilson SB. Remington JS. What can be done to prevent congenital toxoplasmosis. Am J Obstet Gynecol 1980; 138: 357-63.
9. Hanshaw JB. Cytomegalovirus infection. In: Behrman RE, Vaughan VC, eds. Nelson texbook of pediatrics, Philadelphia: WB Saunders Company, 1987:668-70.
10. Williamson WD, Demmler GJ, Percy AK, Catlin FI. Progressive hearing loss in with asymtomatic congenital cytomegalovirus infection. Pediatrics 1992:90: 862-6.
11. Gandahusada S. Toxoplasmosis : Epidemiologi, patogen esis dan diagnostik. Kumpulan Makalah Simposium Toxoplasmosis, Jakarta, August 11, 1990.
12. Saxon SA, Knight W, Reynold DW, et al. Intellectual deficits in children born with subcinical congenital toxoplasmosis: A preliminary report. J Pediatr 1973;82: 792-7.
13. Zubaidi J, Sukarban S. Pengobatan toksoplasmosis ditinjau dari segi farmakologi, Kumpulan Makalah Simposium Toxoplasmosis, Jakarta, August 11, 1990.

14. Nigro G, Scholz H, Bartmann U. Ganciclovir therapy For symtomatic canginital cytomegalovirus infection in infants: A two regimen experience, J Pediatr 1994; 124:318-21.