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CASE REPORT

Congenital Toxoplasmosis in a 15 Day-Old Infant a Case Report

by

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Abstract

A case of congenital toxoplasmosis in a 15-day old infant was reported, citing the difficulties encountered in establishing the diagnosis due to the wide range of the disease's clinical spectrum. Congenital toxoplasmosis was suspected after finding hydrocephalus, cerebral calcification, and chorioretinitis. Serology tests with the ELISA technique were highly positive for antibodies against IgG, whereas anti-IgM was negative. The patient died before the second serological analysis was done. The final diagnosis of congenital toxoplasmosis was eventually established at autopsy, based on the detection of ***T. gondii*** *in the brain, testicular, liver, spleen and striated muscle tissues.*

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Introduction

Toxoplasmosis in a disease found in both humans and animals, caused by *Toxoplasma gondii,* a parasite first isolated in 1908 from the rodent *Ctedonactilus gondii* by Nicolle and Mancesaux in North Africa. In 1923 Janku found the cyst of Toxoplasma in the retina of an infant with hydrocephalus and microphthalmus; but not until 1969 was the household cat determined as a definitive host of the parasite (Remington and Desmonts, 1976), and subsequently the transplacental transmission of *T. gondii* from an infected mother established in congenital toxoplasmosis, although the majority of cases were asymptomatic (Volpe, 1987). The classic triad of symptomatic congenital toxoplasmosis are chorioretinitis, hydrocephalus, and intracranial calcification was first reported in 1939 by Wolf (Alford et al., 1974). Infants with congenital defects are not infrequently found in Indonesia, but seldom are they tested for *T. gondii* infection; this article report the effects of *T. gondii* infection on a neonate and stress on the importance of Toxoplasmosis as one of the etiologies of congenital defects.

Case Report

A 15 day-old Indonesian male infant was admitted to the paediatric ward of the Cipto Mangunkusumo Hospital in Jakarta, on the 12th of November 1987. Since 4 days old, the patient was highly irritable and by the age of one week developed a high-pitch cry and refused breastfeeding. Three days before hospitalization, the infant started to develop fever and vomited, followed by convulsions and subsequent weakness two days afterwards. The birth of the child, who was a firstborn, was uneventful, per vaginam, and the mother had not previous miscarriages. Antenatal evaluation was done regularly by a doctor, and there was no record of illness during pregnancy. The mother, however, admitted to having meals which consisted of partly-cooked meat. The mother is a 27-year old housewife with a junior high school education; the father is 30 years old, with a polytechnical school background and currently working with an income of 49.000 rupiahs a month. The family lived in a densely populated neighborhood; there were no pets in the house, but their neighbours kept cats in their homes. They did not do any gardening at home.

Physical examination: When first seen, the patient was found to be severely-ill, somnolent, the head circumference was 37 cm. Body temperature was 39°C; the respiration rate was 50/minute, shallow; the pulse rate was 14/minute. The anterior fontanel was slightly bulging, but no neck stiffness nor other signs of meningeal irritation were found. The eyes were normal, mildly sunken. No lymph gland enlargement was found. The heart and lungs were within normal limits; the liver and spleen were palpable 3 cm and 2 cm below the right and left the costal margin respectively, with a soft consistency; Skin turgor was slightly decreased. The upper and lower extremities were spastic, with slightly increased physiological reflexes, though there were but no pathological reflexes.

Laboratory examination: Hb 15.7 g/dl; WBC 11.600/ul with diff count of 1% basofil, 1% eosinofil, 62% neutrofil, and 36% of lymphocytes. Platelet count: 211.000/ul. Cerebrospinal fluid analysis: xanthochromic, Nonne rx (+), Pandy rx (++), cells 65/3, glucose 54 mg/dl, protein 441 mg/dl; bacteriological culture was negative.

A working diagnosis of bacterial meningitis with mild dehydration was made, and the patient put on a glucose 10% drip with sodium bicarbonate 1.5% (4 : 1) and 10 mEq/500 ml of potassium chloride. He was concomitantly given ampicillin 200 mg every 4 hours, phenobarbital 35 mg qid, and diazepam 5 mg bid.

Subsequent ultrasound examination of the head revealed a hydrocephalus with possible obstruction/occlusion of the ventricles and Sylvian aqueduct (figure 1). Skull X-ray revealed intracranial calcification at the parietal region (figure 2).

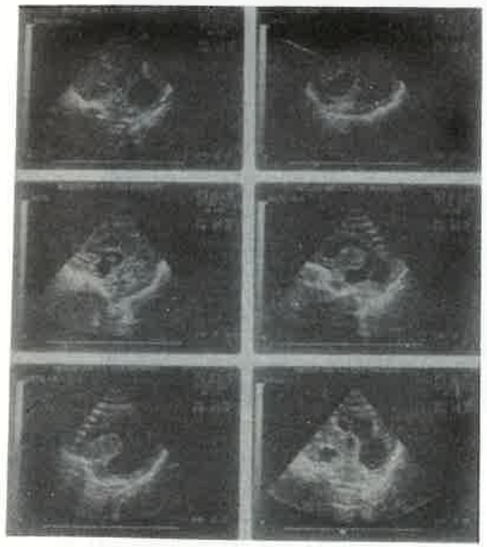

Figure 1 : *Ultra sound picture revealed hydrocephalus with obstruction of the ventricle and sylvia aquaduct*

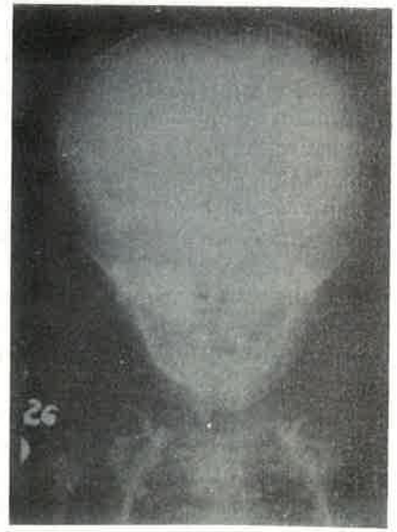

Figure 2 : *Skull X-Ray examination showed intra calcifications at the parietal region*

Head CT Scanning showed *multiple sub-ependimal calcifications of the parenchym and lateral ventricle wall with suggestive signs of a basal meningitis* (figure 3).

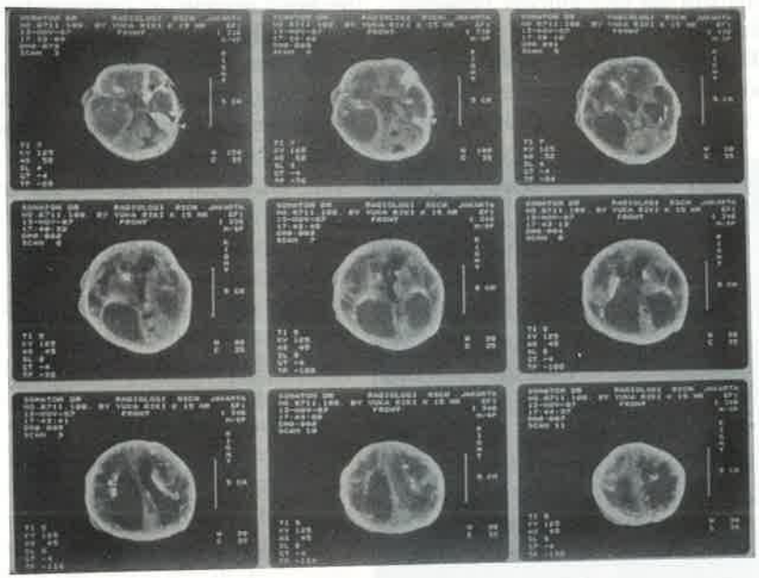

Figure 3 : *Head computered tomograph picture revealed multiple sub ependimal calcifications of the parenchym and lateral ventricle wall with suggestive signs of a basal meningitis*

Based on the presence of convulsions, internal hydrocephalus, and intracranial calcification, *congenital toxoplasmosis* was suspected in this infant; a serological investigation for toxoplasmosis was performed. A positive result was obtained for IgG (0.80, high positive) and whereas the IgM level was negative (0.19). Consultation to the Department of Ophthalmology showed that the patient had chorioretinitis, after which the treatment was consequently changed to Spiramycin 150 mg bid, dexamethasone 0.5 mg tid, and Diamox 45 mg tid.

On follow-up, the anterior fontanel was found to be bulging and taut, with worsening (decrease) of consciousness. The child became convulsive again and a repeated lumbal puncture disclosed an increase in cell number (248/3 with 96 percent of lymphocytes) and protein (750 mg/dl) and staining of the smear showed positive for negative-Gram rod bacteria. A ventricular puncture was performed. Analysis of the ventricular fluid was showed cells 415/3 with 92 percent of segments, and protein 1733 mg/dl. Ampicillin 200 mg qid, cefotaxime 500 mg bid, and intraventricular garamycin 20 mg were added to the treatment regimen. The patient's condition improved until the third week of hospitalization, when he suddenly became dyspneic. Chest X-ray revealed pneumatocele. He subsequently developed pneumothorax, necessitating the use of water sealed drainage. The infant condition became worse and death ensued not long afterwards. Post mortem analysis of the cerebrospinal liquid revealed cells 512/3 (lymphocytes 94 percent), protein 1750 mg/dl and a negative Gram staining. An autopsy was done with consent of the parents (figure 4a).

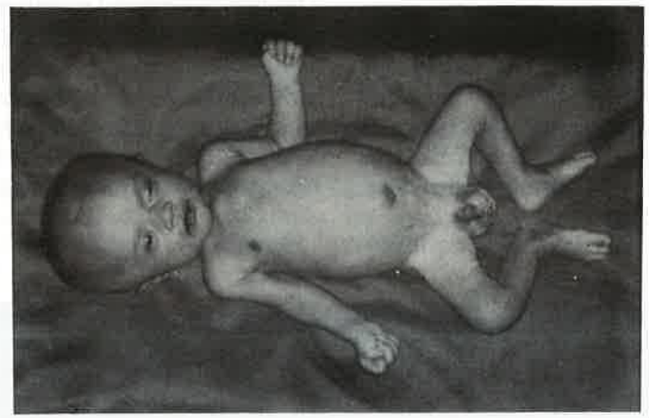

Figure 4a : *Picture of case on the time of autopsi.*

Autopsy Report: The intracranial space contained 10 ml of yellowish cloudy liquid. Yellowish spots were seen on the surface of the brain, with clearly-defined vasculature. Cross-section study of the brain showed the presence of yellowish-coloured necrotic parts which were brittle, especially in the vicinity of the ventricle, medulla oblongata, and brain stem. There was partial occlusion of the third ventricle space, parital distension of the left lateral ventricle, and thinning of the cortex. Microscopically, the leptomenix tissue, especially at the basal part of the brain, was edematous with accumulation of plasma cells and lymphocytes. Necrosis and calcification were found especially in the periventricular region. Groups of toxoplasma were seen, both intra and extracellularly (figure 4b).

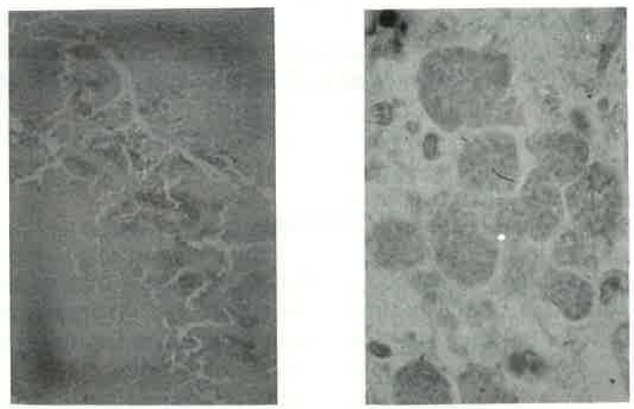

Figure 4b : *Cross section of the brain showed the presence of yellowish coloured necrotic parts, vicinity of the ventricle, medulla oblongata, and brain stem. Necrosis and calcifications were found in the periventricular region. Groups of toxoplasma were seen, both intra and extra cellularly.*

Examination of the testes showed necrotic faci with plasma cells and lymphocytes; toxoplasma was seen especially in the seminiferous tubules. A cyst with a fibrotic wall was found at the upper lobe of the right lung. The liver weighed 245 g, with hydropic degeneration of the hepatocells; a limited number of toxoplasma was seen in the liver cells. The spleen weighed 39 g, with no microscopically definable red pulp structure; extramedullary hemopoeiesis and groups of toxoplasma were seen (figure 4c). The thymus weighed 1 g, with an increase in interlobular fibrotic tissue and decrease in lymphocytes. Toxoplasma was also found in the psoas muscle. No inflammatory reaction nor toxoplasma were found in the left posterior ocular tissue obtained for autopsy. The autopsy diagnosis was *congenital toxoplasmosis*.

Figure 4c : *Picture of lung, liver and spleen: a cyst with a fibrotic wall was found at the upper lobe of the right lung. Hydropic degeneration of the hepatocells.*

Discussion

The relatively large number of antibody-positivity to toxoplasma in the healthy population showed that the acute infection of toxoplasmosis occurs without symptoms, and that only a few present with clinical manifestations (Beverly, 1973; Remington & Desmonts, 1976). Toxoplasmosis can be congenital or acquired, with the almost damage seen in neonates who received the infection through the tranplacental route from the infected mother. After primary infection of the mother, parasitemia developed, followed by a placentitis and hematogenous spread to the fetus. The factors determining infectivity to the fetus are the mother's immunologic state, the strain of the toxoplasma, the condition of the placenta, and the age of gestation when the toxoplasma infects the mother (Swartzberg and Remington, 1975). The age of gestation will also determine the severity of clinical manifestations (Beverly, 1973). At birth or shortly afterwards (sometimes for years), these infants usually will show signs of chorioretinitis, cerebral calcification and occasionally hydrocephalus; psychomotor disturbances might also be found during this period. In the United States, the majority of newborn infants with congenital toxoplasmosis have no clinical manifestations, the presentation of which will be found somewhat later (Beverly, 1973; Remington and Desmonts, 1976). This was also the case with the patient presented in this article. The infant appeared to be normal at birth and was brought to the attention of the doctor only after the emergence of convulsions at 14 days.

In Indonesia, studies involving the detection of antibodies for *T. gondii* in man was undertaken only after the year of 1976 by Cater and colleagues in Java and Bali (cited by Nelwan, 1975). The result of the study, comprising of skin tests and serological analyses, showed a *T. gondii* prevalence of 2 to 63 percent. There has been no report on the incidence of congenital toxoplasmosis in Indonesia (Gandahusada, 1978; Gandahusada and Endardjo, 1980; Nelwan, 1975).

The diagnosis of congenital toxoplasmosis in suspected if a neonate is found to have congenital defects such as hydrocephalus, chorioretinitis, hepatosplenomegaly, and calcification of the brain. The clinical diagnosis is often difficult due to the range of varied manifestations; more than 60 percent of cases are even much more difficult to diagnose due to the absence of clinical findings (Frenkel, 1985). In this case, a working diagnosis of purulent meningitis was established based on the presence of seizures, fever, a high-pitch cry accompanied by vomiting. The analysis of cerebrospinal fluid obtained by lumbar puncture showed xantochromia, pleiocytosis, and increased in protein level. Congenital toxoplasmosis was suspected after further evaluation disclosed signs of hydrocephalus, intracranial calcification, and bilateral chorioretinitis, eventually supported with other findings such as liver and spleen enlargement, jaundice, thrombocytopenia. Even than, viral intrauterine infections with the herpes simplex virus, as well as rubella, cytomegalovirus (CMV), and syphilis could also produce similiar manifestations. Therefore, the importance of laboratory and serological tests was deemed to be vital in confirming the diagnosis. On analysis of the cerebrospinal fluid, pleiocytosis and protein increase were found, and the demonstration of tachyzoits in tissue and body fluids eventually confirmed an acute infection. On the other hand, the finding of a cyst was of no help in differentiating between an acute and chronic infection. Isolation of the parasite in a biopsy specimen could have established the presence of an acute infection, but the pathological result there of would have taken too long.

Serological analysis will reveal the presence of IgG in a newborn infant, passively transferred transplacentally from the mother who has been antibody-positive for *T. gondii* (Broadbent, 1973). The high titer of IgG will not determine whether or not the infant has an acute infection; on the other hand, IgG cannot pass through the placenta due to its large molecul weight, so the detection of IgM in an infant will mean that an acute infection is present. If IgM is not detected, the analysis will have to be

repeated when the child is three and six months old. At three months, the mother-derived IgG will have disappeared and the baby will produce his own if a toxoplasmosis infection is present, the levels of which will reach its peak in six months. Antibody to the IgG can be detected using various serological tests: the Sabine & Feldman test, the indirect haemaglutination test, and the complement fixation test. The indirect immunofluorescent and ELISA (*Enzyme-Linked Immunosorbent Assay*) tests can detect both IgM and IgG.

Treatment

Sulphadiazine and pyrimethamine in combination are still considered to be the treatment of choice, ever since Eyles and Coleman first used them in 1955 to prevent Toxoplasma infection in rats. However, pyrimethamine is toxic to the bone marrow, so the less-toxic spiramycin is used as an alternative. Sulphadiazine is also said to enhance the development of kernicterus in patients with hyperbilirubinemia at moderate levels of serum bilirubin (Bell and McCormick, 1981), hence the choice of spiramycin for this case in view of coexisting jaundice, anemia, and thrombocytopenia.

In Europe, due to its relatively low teratogenicity, spiramycin is frequently the drug of choice when the doctor is confronted with toxoplasmosis in pregnancy; however, since the drug cannot pass the placental barrier, it is not effective against toxoplasma infection in the fetus (Desmonts and Couvreur, 1974). Other authors have reported that the clinical efficacy of Spiramycin is inferior to pyrimethamine. The American Academy of Paediatrics, in its *Report of The Committee on Infectious Diseases* (1986) advocated the use of sulphadiazine and pyrimethamine for congenital toxoplamosis. The current trend is to use pyrimethamine 15 mg/m^2 or 1 mg/kb BW every 2 days, plus sulfadiazine or trisulfapyrimidine 100 mg/kg BW/day in 2 doses, plus folinic acid 5 mg every other day (Remington and Wilson, 1983). The blood and platelet counts should be monitored twice weekly. Twenty one day courses of pyrimethamine plus sulfadiazine may be alternated with 4 to 6-week courses of spiramycin, 100 mg/kg BW per day in three doses.

Corticosteroids (prednisone, with the initial dosage of 1.5 mg/kg/day) may be added in patients with active chorioretinitis with involvement of the macula. The Committee on Infectious Diseases (1986) recommends prednisolone for active ophthalmic involvement of the disease to prevent further destruction of the choroid and retina.

The efficacy of postnatal treatment of infants with congenital toxoplasmosis infections is meager, and a treatment duration of six months or more is recommended. However, each treatment regimen should be determined on an individual basis. Upon suspicion of toxoplasmosis in an apparently-healthy and serologically unconfirmed infant, pyrimethamine and sulfadiazine sould be given for 21 days, followed by spiramycin or sulfadiazine alone until the diagnosis is established (Wilson and Remington, 1980).

Prognosis of the disease will greatly depend on the severity of disease, the time elapse at start of treatment, and the distribution of lesions. Fortunately, only about 0.9 percents of cases eventually died of the disease. Fofar and Arneil (Forfar, 1984) in 1984 have reported that treatment will not produce satisfactory results if tissue destruction has already taken place at commencement of therapy. As also seen in our case report, there was clinical improvement in the early phase of treatment, but brain tissue involvement was already evident

(proven by postmortem lumbar aspiration and autopsy), and the patient eventually died. Although only 30 percent of infected mothers will transmit the disease to their offsprings through the transplacental route (Wilson, 1980), congenital toxoplasmosis is a potentially fatal disease which also cause disabilities. There is no doubt that the prevention of the primary infection in pregnancy is of paramount importance (Beverly, 1973; McCarty, 1983).

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