IRON DEFICIENCY, LOW ARTERIAL OXYGEN SATURATION AND HIGH HEMATOCRIT LEVEL AS A MAJOR MICRO-ENVIRONMENTAL RISK FACTORS IN THE DEVELOPMENT OF BRAIN ABSCESS IN PATIENTS WITH TETRALOGY OF FALLOT

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ABSTRACT

The two most serious complication of central nervous system resulting from unoperated cyanotic congenital heart disease are cerebral intravascular thrombosis and intracranial suppuration. Brain abscess is a frequent and serious complication of Tetralogy of Fallot (TF). The early diagnosis is often difficult, every patient with TF particularly with highest hematocrit (Hct) level have significant risks of the occurrence of the multiple brain abscesses. Objective: to identify that iron deficiency, oxygen saturation and hematocrit are the major micro-environmetal factors in the occurrence of brain abscess in TF. Methods: This was hospital-based case-control study where all medical records of patients hospitalized in the Dr.Soetomo Teaching Hospital from January 1989 until January 2003 were used. Data in 26 cases of TF and brain abscess were studied and compared with data in a control group with TF without brain abscess. The definitive diagnosis of brain abscess is made with the helping of CT scan. The laboratory data of TF with brain abscess were compared with of control group. The control group consisted of TF patients with a blood oxygen saturation level of less than 94 percent who had undergone routine examination at the same age and in the same year as the subjects under study. Laboratory studies use for comparison included determinations of arterial blood oxygen content and percent of saturation, hemoglobin and hematocrit. The statistical tests employed were t-test, Fischer Exact test and Mann-Whitney test. Result: The arterial oxygen saturation in this group was 67.4 percent (range 42 to 78.4 percent), significantly lower than the control group was 76.2% (range 56.7 to 86.2) ($p < 0.01$). The hematocrit in study group was 62 percent (range 48.2 to 82.4) significantly higher ($p < 0.013$) than in the control group 43.1 percent (range 37.3 to 68.9 percent. Hemoglobin values were also assessed and showed a mean of 19.8 g/dl (range 15.3 to 24.3 g/dl) significantly higher ($p < 0.016$) compared with a control group a mean of 16.7 g/dl (range 15.2 to 18.9 g/dl). Conclusion: Based on the collected data, transferrin saturation values in brain abscess group was 8.7 %, significantly lower than the control was 16.2 % ($p < 0.01$), the pertinently high prevalence of iron deficiency calls for further study. Therefore, it is strongly recommended that conservative treatment to tetralogy of Fallot patients be continuously monitored while potential occurrence of iron deficiency, low oxygen saturation and high hematocrit be anticipated as early as possible.

***Keywords**: brain abscess, tetralogy of Fallot*

INTRODUCTION

The surgical intervention is the best treatment of tetralogy of Fallot (TF), which can prevent abnormal hemodynamic consequences such as chronic hypoxia (Neches, 2001). Unfortunately, the cost of open heart surgery is very expensive, considering to the financial situation of the patient, especially who live in the developing countries such as Indonesia. So that the conservative treatment is the primary intervention while waiting the open heart surgery to increased the quality of live TF patients (Ontoseno, 2001).

Lower arterial oxygen saturation and its consequences often presents as the cause of fatal complications. These complications that mostly found at the first year of life are brain abscess, cerebral vascular disorder and cyanotic attack that may result in permanent disability and even leads to fatal outcome (Ontoseno, 1995). Brain abscess is a frequent and serious complication of cyanotic congenital heart disease especially tetralogy of Fallot (Matson, 1961; Anderson, 1997). The incidence of hematogenous brain abscess around four percent to six percent. The first case of brain abscess in relation to cyanotic congenital heart disease was reported by Farre in 1814. Ballet in 1880 emphasized the relationship between brain abscess and congenital heart disease, here were no other factors to explain the abscess (Sharer, 1986). The two most serious complication of central nervous system resulting from unoperated cyanotic congenital heart disease are cerebral intravascular thrombosis and intracranial suppuration (Neches, 2001).

The antibiotic treatment in brain abscess may promote localization of cerebral infection, it should never be considered a substitute for surgical therapy. The surgical therapy of multiple cerebral abscess is always difficult, and particularly so in this condition, because here one is

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dealing not only with intracranial pressure, often the marked degree, but also with diffuse congestion of cerebral veins with impairment of cardiac function (Anderson, 1997).

The prognosis for brain abscess has undergone a marked improvement in the past decade. Despite the availability of many antimcrobial agents, mortality from this complication remained high, with the figure of 40 - 60%. Since there is no evidence that the natural course of the disease has changed, this improvement is believed to be the result of the recent development of the new capabilities in diagnosis and management (Therrien, 2001).

This study was aimed to investigate the influence of iron deficiency, oxygen saturation and hematocrit as the major micro-environmental factors on the occurrence of brain abscess in TF patients.

METHODS

Diagnostic files of the medical records of TF patients with brain abscess between January 1989 until January 2003 were collected from Cardiology Subdivision, Department of Child Health Dr Soetomo Teaching Hospital, Surabaya. The only complete data were reviewed.

Cardiac diagnosis was confirmed by echocardiography in all cases. Laboratory studies used for comparison included determinations of arterial oxygen saturation, hemoglobin and hematocrit. Diagnosis of iron deficiency was based on the level of transferrin saturation less than 13.5 %. Normal value of arterial oxygen saturation was 95 %. Normal value of haemoglobin and hematocrit in TF was 15 gr/dL and 45 % consecutively.

The definitive diagnosis of brain abscess is made with the helping of CT scan. The laboratory data of patients with brain abscess and TF were compared with those of control group of 34 patients with TF but without brain abscess. The control group consisted of patients with a blood oxygen saturation level of less than 94 percent who were admitted at the same age and in the same year as the subject under study.

The statistical tests employed were t-Test, Fischer Exact test and Mann-Whitney test.

RESULTS

Clinical observation: Thirty-four patients with TF and brain abscess were hospitalized during this study period. Only 26 of them qualified to be involved in this research. The patients range in age from 2 3/12 years to 14 years (mean 8 ¼ years). There were 10 male and 16 female. All of them had evidence of infection within a month before their admission for brain abscess: carries in eight, recurrent tonsilopharyngitis in six and a furuncle in eight. The mean interval from the initial symptoms due to brain abscess to hospitalization was 16 days (range 2 to 54 days). Nineteen patients had multiple abscesses and four had a solitary abscess. Of the 4 solitary abscesses, 3 were in the left hemisphere (frontal in 2, temporo-parietal in 1).

Treatment and course of disease: Of the 26 patients in the study, 11 (40%) were survived, 9 of these were treated with burr hole aspiration only, and two by aspiration followed by excision. There were 17 deaths (60%), all of them occurred in patients treated by antibiotic agents alone, 11 of these patients was quite drowsy on admission and shortly thereafter experienced cardiorespiratory arrest. In addition to surgical therapy all patients were treated with appropriate combination of intravenously administered ampicillin and chloramphenicol in meningitic doses. Nine of the 11 survivors were followed up for 12 months after the admission for brain abscess. Six (65%) have recovered completely, and four (35%) have some type of residual neurologic impairment related to the abscess.

Laboratory studies: The arterial oxygen saturation in 26 patients with brain abscess was 61.9% (range 44 to 68.4%), significantly lower than the control was 74.5% (range 51.4 to 82.8%) ($p < 0.001$). Hematocrit in 26 patients under study was 68 % (range 49.6 to 87.1%), significantly higher than the control group was 41.3% (range 39.7 to 62.1%) ($p < 0.0013$). Hemoglobin values were also assessed in 26 patients and showed a mean of 18.9 g/dL (range 14.9 to 22.8 g/dL) compared with a mean of 15.9 g/dL (14.9 to 17.4 g/dL) in the control group was significantly higher ($p <0.0012$). Transferrin saturation values in 26 patients with brain abscess was 8.7 % (range 5.9 % to 13.2 %), significantly lower than the control was 16.2% (range 13.1% to 18.6 %) ($p < 0.0011$).

DISCUSSION

In patients with cyanotic congenital heart disease, venous to arterial shunts within the heart allow

recirculation of poorly oxygenated venous blood to the systemic circulation. This condition causes hypoxia in the systemic circulation and the body tissues, including the brain (Anderson,1997; Calcins, 1967).

Hypoxia of the brain can cause the forming of necrotic areas which become a predisposition of brain infection. In addition that, hypoxia also cause polycythemia. The increase blood viscosity, leading to a reduction of cerebral blood flow rate, and thus worsening the brain necrosis. The forming of brain abscess in tetralogy patients is also influenced by the exposure of the brain to bacteremia. First, the bacteremia can result from the bypassing of pulmonary circulation system, because the system has a filtering affect on bacteria by phagocytosis. Secondly, the heart disease itself becomes a predisposition to the forming of vegetation on the heart valves. If bacteraemia occurs, the bacteria will harbor on the vegetations. This in turn become an effective vegetative embolus which joins into the systemic circulation. If this embolus reached the necrotic area in the brain, the development of brain abscess can occur (Carey, 1972).

It has been suggested that two conditions are necessary for brain abscess formation: (1) intermittent bacteremia, and (2) focal encephalomalacia (Matson, 1961). Patients with tetralogy of Fallot may therefore be susceptible to focal encephalomalacia because of their severe hypoxia and the increased viscosity associated with polycythemia (Therrien, 2001), and iron deficiency (Linderkamp, 1979).

Symptom and signs of brain abscess in our patients with tetralogy of Fallot did not differ from those reported by others. The youngest patient in our series was 3 1/3 years old. An abscess in a patient under age 2 years is very rare, explanation of this phenomenon is not clear, several authors have suggested that episodes of bacteremia are less common in infants than in children. Others have attributed this age-related phenomenon to the fact that the teeth act as a common source of bacteremia, and patients in the younger age group do not have fully developed dentition.

Laboratory: In our patients with tetralogy of Fallot and brain abscess the arterial oxygen saturation was significantly lower ($p < 0.001$) than that of comparable control group.

Berthrong and Sabiston suggested that the important role of polycythemia in the production of intravascular thrombosis is as a cause of the infarct (Sharer, 1986). Blood viscosity has been mentioned as a factor affecting cerebral blood flow (Anderson, 1997). An increase in viscosity will result in decreased blood flow, and relative hypoxia of brain tissue may develop, thereby predisposing that tissue to brain abscess formation in the presence of bacteremia. Although blood viscosity was not measured in our patients, it is known to be directly related to hematocrit (Rosenthal, 1970). Our data suggest a higher hematocrit value for the patients with a brain abscess than for the control group ($p < 0.0013$).

Risk Factors: The present study pointed that iron deficiency, oxygen saturation and hematocrit as major micro-environmental risk factors in the development and prognosis of brain abscess in patients with tetralogy of Fallot. Actually, this condition drives compensatory mechanism represented in the increasing activities of the erythropoietic system to combat the hypoxia (Behrman, 1992).

Clinical implication: Although brain abscesses have been reported in patients without congenital heart disease, cyanotic congenital heart disease remains the single common correlate with brain abscess formation in the childhood years (Calcins, 1967). The persistent high morbidity and mortality rates of brain abscess have been attributed to delay in diagnosis and treatment (Snyder, 1971). This study demonstrates the relation between the severity of the hypoxemia and the development as well as prognosis of brain abscess in patients with tetralogy of Fallot.

Tetralogy of Fallot patients with low oxygen saturation levels, high hematocrit and iron deficiency are more likely to have brain abscess than those with higher saturation levels, lower hematocrit and without iron deficiency.

CONCLUSION AND RECOMMENDATION

Thus, to reduce the morbidity and mortality of brain abscess, the predisposing cardiac lesions should be correction at an early age. Based on the collected data, the pertinently high prevalence of iron deficiency, low arterial oxygen saturation and high hematocrit level calls for further study with interest pay attention to validity. Therefore, it is strongly recommended that conservative treatment to tetralogy of Fallot patients be continuously monitored while potential occurrence of iron deficiency in addition to lower oxygen saturation and higher hematocrit be anticipated as early as possible.

REFERENCES

Anderson RH, Mc Carthey FJ, Shinebourne EA, Tunan M. 1997. Tetralogy of Fallot. Pediatric Cardiolgy. Vol. 2 Churchill Livingstone. London. 774-775.

Behrman RE, 1992. Polycythemia. In: Behrman RE, Kliegman RM. Nelson Textbooks of Pediatrics. 14th.ed. Philadelphia: WB Saunders Co. 1257.

Calcins RA, Bell WE. 1967. Cerebral abscess and cyanotic congenital heart disease. Lancet 87: 403-410.

Carey ME, Chou SN, French IA. 1972. Experience with brain abscesses. J.Neurosurg (4): 36-9.

Linderkamp O, Close HJ, Betke K, Broder-Heberlien S, Buhlmeyer K, Kelson S, 1979. Increased blood viscosity in patients with cyanotic congenital heart disease and iron deficienc. J Pediatr 95:567-9.

Matson DD, Salam M. 1961. Braain aabscess in congenital heart disease. Pediatrics 27:772-780.

Neches WH, Park SC, Ettedguy JA. 1997. Tetralgy of Fallot and Tetralogy of Fallot with Pulmonary Atresia. In: The Science and Practice of Pediatric Cardiology. Ed: Garson A, Bricker JT, Fisher DJ, Neish SR. 2 ed. Williams & Wilkins A Waferly C. Baltimore.Philadelphia.London.Paris.Bangkok. Vol I: 1383-1411.

Ontoseno T. 1995. Factors Associated with the Occurrence of Cyanotic Spells in Tetralogy of Fallot Patients. Paediatr Indone; 35:227-230.

Rosenthal A, Nathan DG, Marty AT. 1970. Acute hemodynamic effects of red cell volume reduction in polycythemia of cyanotic congenital heart disease. Circulation 42: 297-307.

Sharer RM, Deuchar DC. 1986. Hematogenous Brain Abscess in Cyanotic Congenital Heart Disease. Am J Med 2: 349-54. Snyder BD, Farmer TW .1971. Brain abscess in children. South Med J 64: 687-690.

Therrien J and Webb GD. 2001. Congenital Heart Disease in Adults. In Heart Disease. Ed by Braunwald. Zipes. Libby. WB Saunders Co. 6th ed. 1592-1621.