POST-ADENOTONSILLECTOMY INCREASE OF IMMUNE RESPONSE IN CHILDREN WITH OBSTRUCTIVE CHRONIC ADENOTONSILLITIS

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ABSTRACT

Adenotonsillectomy (ATE) procedure may restore immune response. However, the mechanism, by which the immune response is restored, remains unknown. OCAT results in obstruction that may lead to hypoxia. Furthermore, hypoxia induces learning process in brain tissues that affect the balance between Th1 and Th2, and the latter may conversely affect the learning process of brain tissues. This reciprocal relation is known as brain-immune system bidirectional. The objective of this study was to disclose the mechanism of immune response restoration due to the effect of ATE procedure in children with obstructive chronic adenotonsillitis (OCAT) based on pyschoneuroimmunology paradigm using the concepts of Th1 and Th2. A pre-experimental study using one group pre-test post-test design was carried out to children with obstructive chronic adenotonsillitis (OCAT) admitted at the Otolaryngology Outpatient Clinic, Sebelas Maret University School of Medicine, Dr Moewardi Hospital, Surakarta. The criteria of OCAT consisted of the enlargement of Adeno-Nasopharynx (A-N) ratio of > 0.72 and tonsil enlargement to the level of T2 and T3. The independent variable in this study was ATE procedure, while the dependent variables were monocyte, neutrophil, IFN-γ, IL-1ß, IL-10, and IgG. Results of homogeneity test revealed that the moderating variables (age, body weight, A-N ratio, erythrocyte, hemoglobin, HCT, SGOT, SGPT, creatinin, total protein plasma) were homogeneous. Furthermore, homogeneity and normality tests (IIDN) were also carried out to early data of the dependent variables (monocyte, neutrophil, IFN-γ, IL-1ß, IL-10, and IgG), revealing homogeneous and normal results (p > 0.05). Since observed group was only one and without control, a cluster analysis was performed to immune response before the ATE procedure was undertaken and revealed that the immune status of the respondents were similar (p > 0.05). Further cluster analysis was done to determine immune status after ATE. Results of this latter analysis revealed two groups of immune status (p < 0.05). All samples in this study, therefore, could be assumed into two groups. Group I consisted of 5 samples, while Group II consisted of 10 samples. Results of Manova test on the response data of both new groups (i.e., data on the change before and after ATE) revealed difference (Wilks Lambda, p < 0.05). These results confirmed that ATE might induce change in immunity system. A discriminant analysis was subsequently done to find relationship between OCAT and immunity system, resulting in three discriminant variables, i.e., neutrophil, IFNg, and IgG in the immune response. Theoretical interpretation to these findings suggested that both groups demonstrated similar immune response pattern based on its magnitude in the three contributing variables. However, those patterns were differentiated only in their magnitude. In group I (5 samples) the magnitude of the pattern in three discriminant variables (neutrophil, IFN-γ, and IgG) was higher than that in group II (10 samples), while the dynamic appearance of both immune response patterns was similar. It can be concluded that ATE procedure is capable in restoring immune response.

Keywords*: adenotonsillectomy, hypoxia, Th1- Th2 concepts*

INTRODUCTION

A proportion of 60% of patients with chronic adenotonsillitis still experience recurrent infection as the effect of their disease. Additionally, those patients are also prone to the symptom of obstructive upper respiratory tract (Paradise et al, 2003), that frequently occur during bedtime (Onal et al, 1986; Spabis, 1994; Lamberg, 2001). Bedtime obstructive chronic adenotonsillitis is termed as obstructive sleep apnea syndrome (OSAS) (Suen et al, 1995; Adams, 1997; Cowan and Hibbert, 1997; Ischizuka et al, 1997), while chronic inflamed adenoid and tonsil accompanied with obstruction is named as obstructive chronic adenotonsillitis (OCAT) (Jensen et al, 1991; Salah et al, 2001). An obstruction followed by chronic inflammation may resemble a viscious circle. Infection-resulted inflammatory process may cause tonsillary and adenoid enlargement, which, in turn, contribute to the obstruction of upper respiratory tract. The latter that is developing during sleeping may result in hypoxia (Lamberg et al, 2001; Paradise et al, 2003), and such hypoxic condition may reduce immunological defense of the body (Klokker et al, 1993; Ohga et al, 2003). One procedure to overcome obstruction due to OCAT is by performing adenotonsillectomy (ATE). However, this procedure remains controversial, as both adenoid and tonsil serve immunological defense system of the body, and the enlargement of both organs may result in hypoxic condition, suppressing the defense of the body

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(Paradise et al, 2002; 2003). In their study, Prusek et al (1991) and Friday et al (1992) reported a post-ATE reduction of immunity. In contrast, Paulussen et al (2000) found a post-ATE increase of cellular and humoral immunity. Up to know, the mechanism of post-ATE immunity modulation remains unclear.

Inappropriate ATE procedure may result in an adverse effect to the patients. Delayed treatment may lead to recurrent infection and hypoxia (Jensen et al, 1991; Paradise et al, 2002). Other authors also reported that adenotonsillary hypertrophy may result in obstruction (Goodman et al, 1976; Franz and Mennicken, 1977; Harrington, 1978; Skevas et al, 1978; Van Somoren et al, 1990; Eike and Jorgense, 1994; Battistini et al, 1998; Litman et al, 1998), and, furthermore, hypoxic condition may reduce immunity, rendering the body susceptible to infectious diseases (Klokker et al, 1993; Ohga et al, 2003). Increased frequency of illness may impede growth and development, particularly during childhood (Paradise et al, 2002; 2003).

ATE has been frequently undertaken by otolaryngologists in Indonesia. During the year 2002, Dr Moewardi Hospital, Surakarta, had performed 220 ATE and tonsillectomy (TE) procedures among other otolaryngological procedures or operations. More than 65% of the patients receiving ATE or TE aged between 2 and 15 years old (Dr Moewardi Hospital, 2002). ATE comprised 75% of otolaryngological operations to children in Turkey (Erisen et al, 1999). Adenoid and tonsillary enlargement may result in obstruction, which may further disturb respiratory function as well as swallowing process. Due to these considerations, OCAT patients should receive ATE procedure. Otherwise, the patients' quality of life would deteriorate. The procedure is delivered based on clinical indications in each case (Bicknell, 1994). Until recently, indication for ATE is based on the results of clinical examination, thereby, the consideration for that procedure remains subjective. Obstructive symptoms disappear after the patients undergoing ATE procedure (Franz and Mennicken, 1977; Harrington, 1978; Skevas et al, 1978). OCAT may result in hypoxic condition (Eike and Jorgensen, 1994; Albert, 1997; Battistini et al, 1998; Paradise et al, 2003), which may modulate immunocompetent cells. Bodily response against stressor consists of three stages, i.e., activation, resistance and exhaustion (Putra ST, 1999). As a stressor, hypoxia may stimulate monocyte or macrophage to release much more IL-1ß (Hempel et al, 1996). Subsequently, IL-1ß stimulates Th1 to release IFN-γ, and as a MAF (macrophage activating factor), the latter may increase macrophage capability to process and to destroy immunogen. On the other hand, the increased macrophage activity may also destroy cells and tissues, leading to the occurrence of necrosis. It is expected that hypoxic stressor may disappear after the procedure is being carried out, so that the IL-1ß will be reduced. Since the benefit of ATE procedure has not been clearly disclosed, it is worth further investigation.

Psychoneuroimmunological approach is based on the understanding of non-autonomous immunoregulation (Ader, 2000). Hypoxic stressor triggers the reduction of immunological defense of the body through behavioral change of brain or nervous system. Hypoxia activates atrocyte and microglia, and, furthermore, it activates immunocompetent cells that modulate the balance of Th1-Th2, leading to the reduction of immunity modulation. Post-ATE, there is a new Th1-Th2 balance modulation, resulting in an increased modulation (Ader et al, 2001). Behavioral change in nervous system may provide regulation through the fluctuation of cytokine secretion towards immune system (Ader, 2000). This approach would be used as the parameter of a successful ATE. Research in immunopathobiology has investigated immunity changes to the extent of examining lymphocytes at subpopulation level of Th1 and Th2. The identification of Th1 and Th2 activity is observed from resulted-cytokine modulation. Some cytokines are able to carry out a complex interaction between one another, whose functions either as immunostimulator or immunoinhibitor. In recent psychoneuroimmunological studies, the investigation on immunocompetent cells-produced cytokine is performed thoroughly involving various indicators of cytokine, hormones, and polypeptides (Putra, 1999). By means of psychoneuroimmunology paradigm, ATE procedure for children with OCAT was studied to exterminate hypoxic condition, with the hope that it might improve immunity modulation. This study was focused to immunity modulation using the concept of Th1 and Th2 balance.

This study investigated whether there was post-ATE immunity heterogeneity in children with OCAT. The general objective of this study was to explain the mechanism of immunity modulation due to the effect of ATE procedure for children with OCAT. The particular objectives of this study were to prove the presence of immunity heterogeneity due to the effect of ATE procedure for children with OCAT, to find the discriminator variable from various immunity groups receiving ATE procedure for children with OCAT, and to explain post-ATE immunity modulation in children with OCAT. The theoretical benefit of this study was to obtain an explanation on post-ATE immunity modulation in children with OCAT, and its practical benefit was to obtain scientific basis for ATE procedure for those children. It was assumed in this study that there was post-ATE immunity heterogeneity in children with OCAT.

PATIENTS AND METHODS

This was a retrospective cohort study using nested case-control design. Population observed in this study was children with OCAT, and samples were those who were admitted at Otolaryngology Outpatient Clinic, Sebelas Maret University/Dr Moewardi Hospital, Surakarta, from February to September 2002. The inclusion criteria were adenoid enlargement (A - N ratio 0.72); tonsillary enlargement (T2, T3, bruised, enlarged crypt orifice with positive detritus); male; aged 5 - 15 years; normal bodyweight (height - 110) ± 10% kg; normal health status as proved by laboratory test to erythrocyte, hemoglobin, Hct, leucocyte count, blood clotting and bleeding time, hepatic function (SGOT/SGPT), renal function (creatinine), and total protein; and informed consent by the parents or family. The exclusion criteria were as follows: presence of other abnormalities that result in nasal blockade, such as polyp, deviated septum, and tumor; other causes of immunity modulation, such as allergic rhinitis, asthma, atopic dermatitis, and diabetes mellitus; and ATE contraindication, for example, blood clotting abnormalities. Sample size was based on the estimation of Hulley et al (1988) using a (one tailed) of 0.05 and b 0.20, with expectation of 0.90. Estimation revealed that the number of minimal sample was 15. Sample was recruited from all children with OCAT who met the sample criteria.

Variables observed in this study were independent, outcome, control (inclusion and exclusion), and moderator (inclusion and exclusion) variables. The independent variable was ATE procedure; the outcome variable was immunity modulation, in which we observed monocyte and neutrophil for natural or non-specific immunity, IFN-γ and IL-1ß for cellular specific immunity (representing Th1), IL-10 and IgG for humoral specific immunity (representing Th2); control variables were sex and the administration of analgetic antibiotic therapy; and finally the moderator variables were age, bodyweight, A-N ratio, hemoglobin, leucocyte, erythrocyte, thrombocyte, blood clotting and bleeding time, Hct, hepatic functions (SGOT/SGPT), renal function (creatinine), and total protein plasma.

RESULTS

Data on moderator variables in this study (hemoglobin, erythrocyte, SGOT and SGPT, serum creatinine, total protein and albumin as well as blood plasma/hematocrit) were found in normal range. Data on the dependent variable are displayed in the following table:

Table 1. Data on pre-ATE dependent variable (immunity modulation components) (in thousands)

No	Variables	N	Pre ATE		
			Mean	Standard Deviation	VC
1.	Neutrophil	15	3.49057	1.24368	35.629
2.	Monocyte	15	519.652	142.3402	27.391
3.	IFN-γ	15	4.14368	4.07259	98.283
4.	IL-1β	15	1.06125	0.78812	74.266
5.	IL-10	15	4.57778	2.13361	46.607
6.	IgG	15	1234.813	263.4341	21.334

Hematocrit had been corrected in these data

Note:
Units for:
1. Neutrophil (μL)
2. Monocyte (μL)
3. IFN-γ (pg/dL)
4. IL-1β (pg/dL)
5. IL-10 (pg/dL)
6. IgG (mg/dL)

Table 2. Data on post-ATE dependent variable (immunity modulation components) (in thousands)

No	Variables	N	Post ATE		
			Mean	Standard Deviation	VC
1.	Neutrophil	15	3.32172	0.98567	29.673
2.	Monocyte	15	354.8816	203.4122	57.318
3.	IFN-γ	15	4.19812	3.06640	73.042
4.	IL-1β	15	1.45498	2.12837	146.281
5.	IL-10	15	4.15106	1.74764	42.101
6.	IgG	15	1196.453	208.5431	17.430

Hematocrit had been corrected in these data

Note:
Units for:

1. Neutrophil (μL)
2. Monocyte (μL)
3. IFN-γ (pg/dL)
4. IL-1β (pg/dL)
5. IL-10 (pg/dL)
6. IgG (mg/dL)

Results of Cluster analysis on post-ATE immunity revealed two different immunity groups, i.e., group 1 (5 samples) and group 2 (10 samples) (Wilks' Lambda, estimated F value = 0.199, p = 0.017) (see the following Table).

Table 4. Results of post-ATE cluster

Total samples	Group	
	1	2
	5 (33 %)	10 (67%)

After the results of cluster analysis have been revealed, the following step was to identify pre- and post-ATE immunity change. Results of immunity change, which was designed as immunity modulation, were obtained from the difference of pre- and post-ATE data in each sample. Manova test was carried out to immunity modulation data in both groups post-ATE resulting from post-ATE cluster analysis. Results of the Manova test on immunity modulation between group 1 and group 2 revealed significant difference (Wilks' Lambda, estimated F value = 0.266, p= 0.026). Therefore, ATE procedure in this study resulted in two different immunity modulation groups. However, results of Manova test between pre- and post-ATE immunity in group 1 (5 samples) revealed no difference (Wilks' Lambda, estimated F value = 0.216, p = 0.334). Results of Manova test between pre- and post-ATE immunity in group 2 (10 samples) also revealed no difference (Wilks' Lambda, estimated F value = 0.594, p = 0.259). To obtain the difference of post-ATE immunity modulation, a discriminant analysis was carried out in group 1 and group 2, revealing neutrophil, IFN-γ and IgG as discriminator with 100% power. Therefore, the dynamics of biological immunity modulation in ATE procedure or the disappearance of hypoxic condition was played particularly by neutrophil, IFN-γ and IgG. Results of discriminant analysis can be seen in the following table.

Table 5. Results of Discriminant Analysis on Immunity Modulation in Both Groups

No	Variable	Wilks' Lambda	
		F	Sig.
1.	IFN-γ	6.919	0.021
2.	IgG	6.840	0.010
3.	Neutrophil	10.144	0.002

The contribution of each discriminator variable is shown in Table 6.

Table 6. The contribution of each discriminator variable

No	Variables	Groups	
		1	2
1.	IFN-γ	3.0463	0.4331
2.	IgG	1.9663	0.1138
3.	Neutrophil	1.7036	-0.021

The discriminant pattern is a description of the contribution of the three variables (discriminators) in immunity modulation due to ATE procedure. This pattern was needed to explain the mechanism of post-ATE immunity modulation.

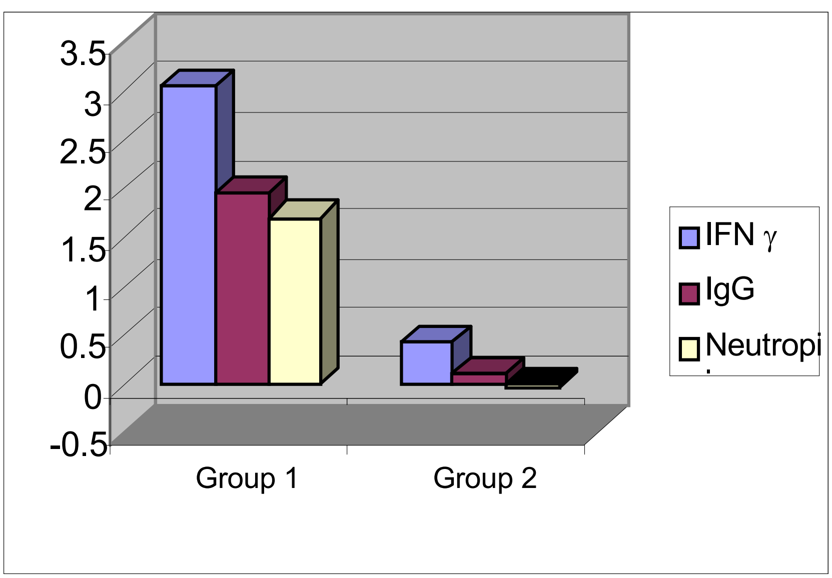

Figure 1. Discriminant Pattern of the Immunity Due to the Effect of ATE

Based on the pattern of immunity due to the effect of ATE and results of analysis on Manova discriminant test in immunity pre- and post-ATE procedure in each group, immunity change due to eradicated hypoxia might result in immunity modulation, particularly in group 1 (5 samples), reflecting post-ATE recovery of immunocompetent cells activity.

DISCUSSION

A number of authors had undergone hypoxic measurement in OCAT, and even the most severe airway obstruction may ensue repeatedly during sleeping (Onal et al, 1986; Jensen et al, 1991; Salah et al, 2001). Onal et al, (1986) found that in sleeping normal individual airway blockade occurred due to muscular relaxation in laryngeal and pharyngeal area. Hypoxic assumptions were based on previous studies in OCAT (Spabis, 1994; Lamberg, 2001; Salah et al, 2001; Paradise et al , 2002). Results of observation and grade analysis on OCAT samples revealed the A-N ratio of 0.72 and tonsillary grade T2-T3. These facts supported the assumption of obstructive condition as a stressor in children with OCAT. Results of moderator variables showed that nutritional status (total erythrocyte, hemoglobin, protein), hepatic function (SGOT, SGPT, and serum albumin), and renal function (serum creatinine) remained under the confidence limits and in normal range. Hematocrit measurement (Hct) was carried out to find the accuracy of serum material level, particularly those from the dependent variables. Results of Hct discriminant test pre- and post-ATE revealed significant difference ($p < 0.05$). Therefore, the level of the dependent variables in blood should be corrected by means of Hct factor to prepare the subsequent data analysis (Setyawan S, 1996). As to hypoxic eradication, it has been recognized that OCAT may result in hypoxic condition (Jensen et al, 1991; Salah et al, 2001). Morphological picture based on A-N ratio also supported OCAT, and the severity of the latter based on A-N ratio was also subjected to measurement and test. Results of A-N ratio homogeneity were found to be under the confidence limits. Therefore, the obstructive degree in those patients was similar, so that it could be assumed that there was no difference in hypoxic condition of the patients with OCAT.

Correction to the data of the dependent variables was carried out based on the fact that the results of hematocrit examination on blood analysis unit were not similar (Setyawan, 1996). The subsequent analysis was that to meet the analysis requirement. Preliminary data on all observed dependent variables were subjected to homogeneity test. Results of IIDN were found under the confidence limits. This indicated that data on the dependent variables in preliminary condition were at normal and homogeneous distribution. Results of analysis on all variables of immune status revealed that samples in this study were homogeneous with normal data distribution. The data therefore met the requirement to use in multivariate statistical assessment.

In observing immunity change due to ATE procedure, cluster analysis was done towards post-ATE immunity, resulting in two groups (Wilks' Lambda, estimated F value = 0.199 p = 0.017). Group 1 consisted of 5 samples (post 1), and Group 2 10 samples (post 2). Furthermore, to test the post-ATE immunity difference in both groups (post and post 2), Manova test was carried out, which was based on (1) the application of multivariate concept, (2) immunity difference between groups, comprising multivariable measurement to neutrophil, monocyte, IFN-γ, IL-1ß, IL-10, and IgG (Sharma, 1996). Results of Manova test to both groups revealed significant difference (Wilks' Lambda, estimated F value = 0.266 p = 0.026). These results confirmed that ATE procedure brought about immunity modulation (Paradise et al, 2003), and that OCAT also lead to hypoxic condition (Onal et al , 1986), particularly during bedtime (Jensen et al, 1991; Salah et al, 2001) which may result in the reduction of immunity (Ohga, 2003). Furthermore, Paradise et al (2003) suggests that immunity may increase post-ATE. Conclusively, ATE procedure in this study had revealed two immunity groups. This confirmed previous studies that ATE procedure could improve immunity. This can be elaborated as follows: (1) ATE procedure may eradicate hypoxia, since in hypoxic condition, quantitative and functional reduction of neutrophil, monocyte, T lymphocyte, and B lymphocyte occurs (Klokker et al, 1993; Lahat et al, 2003). Immunocompetent cells are sensitive to hypoxic condition (Migone et al, 2001; Keel et al, 1997). (2) Hypoxia-eradicating ATE procedure may increase or restore immunity as reflected in the concept of Th1 and Th2 balance, while, conversely, in a previous study it was found that immunoglobulin secretion also reduced in hypoxic condition (Lardner, 2001).

It is well-recognized that the balance of immunity system, either cellular or humoral, is taking place dynamically (Banz et al, 2002). Using Th concept, the balance is maintained by Th1 (cellular) and Th2 (humoral) cells (Estaquier and Ameisen, 1997). Th1 and Th2 lymphocyte may experience balance modulation through the mechanism of signaling transduction of cytokines, hormones, and polypeptide (Elenkov et al, 2000; Banz et al, 2002). Hypoxic condition may reduce the function and activity of immunocompetent cells, particularly lymphocyte, monocyte, and neutrophil (Lahat et al, 2003). Results of other studies revealed that in hypoxic condition the secretion of IFN-γ and IL-8 is reduced (Carta et al, 2001; Ohga et al, 2003). From the pattern of immunity in group 1, it can be analyzed that ATE procedure could restore Th1 activity. The restoration of Th1 activity can be reflected from predominant IFN-γ contribution in immunity pattern. In addition, the contribution of neutrophil was also remarkable in the immunity pattern of group 1. Based on both phenomena in those variables in the biological response of immune system, it can be assumed that the elimination of hypoxic condition may restore innate immunity activity. Innate immunity is also based on the role of IFN-γ that may enhance the increase of macrophage and monocyte activity (Sigel and Ron, 1994; Estaquier and Ameisen, 1997; Goldsby et al, 2000). However, the pattern of immunity in group 1 also showed the recovery of Th2 activity. The recovery is indicated by remarkable IgG secretion by plasma cells. Thereby, immunity pattern in group 1 demonstrated both innate and adaptive (humoral) immunity modulation. The phenomenon of predominant innate and cellular (Th1) immunity may be reflected by predominant role of IFN-γ. The role of Th1 and Th2 was less in group 2, probably because the immunity in monocyte has experienced chronic apoptosis in OCAT or hypoxia (Klokker et al, 1993; Shi et al, 1997; Lahat et al, 2003). The balance between Th2 and Th1 is also maintained by the predominant role of Th2, as reflected by IgG secretion that suppresses Th1, monocyte, or macrophage (Yeatman et al, 2000).

The pattern of immunity in group 2 (10 samples) was similar to that in group 1. However, the contribution of the three variables (IFN-γ, IgG and neutrophil) was not as large as that of immunity in group 1. Based on obtained data on immunity, the immunity pattern in group 2 could be assumed as identical to pre-ATE immunity. It could also be assumed that ATE procedure in group 2 immunity for a period of 2 weeks was unable to restore the immunity of OCAT patients. The reduction of Th1 activity, as reflected by the contribution of IFN-γ secretion, could reduce the activity of macrophage, monocyte, and neutrophil due to chronic apoptosis in OCAT or hypoxia (Klokker et al, 1993; Lahat et al, 2003).

Several studies showed that hypoxic exposure could lead to the increase of neutrophil, monocyte, and TNF (Klokker et al, 1993; Schimmer et al, 2001; Lahat et al, 2003). The reduction of Th1 activity can also result from the reduction of IFN-γ, leading to the reduced role of monocyte (Klokker et al, 1993; Schimmer et al, 2001; Lahat et al, 2003), particularly in hypoxic condition. In contrast, the predominant role of Th2, as reflected by the secretion of IgG, could suppress monocyte (Yeatman et al, 2000).

The modulation of Th1 and Th2 balance can be induced through the mechanism of sudden perfusion change from hypoxic condition. This sudden condition results in the increase of Th1 and Th2 activity, which was undergoing through cytokine transduction signaling, and designed as withdrawal effect (Lee et al, 1999; Migone et al, 2001). Due to the withdrawal effect, Th2 can secrete IL-10 and IL-4. The increase of IL-4 secretion could modulate IgG secretion, while the secretion of IL-10 could regulate the activity of Th1 and monocyte. The regulating mechanism of Th1 and monocyte reduction can work through apoptotic process (Lee et al, 1999; Goldsby et al, 2000; Yeatman et al, 2000). The predomination of Th2 leads to the suppression of Th1 by the increase of IL-10 secretion (Keel et al, 1997; Wurster et al, 2002; Doseff et al, 2003). IL-4 predominant role, which may modulate Th1 apoptosis, has been recognized as being able to antagonize Th1-secreted IL-1ß (Poe et al, 1997; Doseff et al, 2003). Therefore, the modulation of immune system may work without the use of epitope, but through the change of behavior modulation of cells in nerve system by various cytokines. This phenomenon is a mechanism that can be explained by the concept of psychoneuroimmunology. This approach was needed in this study since post-ATE immunity modulation resulted from reduced or even eradicated hypoxic stressor, which brought about a learning process that affected to the balance of Th1-Th2 as reflected by post-ATE immunity modulation (Ader, 2000).

In addition to its design, the shortcomings in this study were as follows:

1. This study used cohort retrospective design. The obstacles in the use of this design in investigating ATE procedure for children with OCAT were (1) the difficulties in obtaining samples that meet the criteria, since the psychoneuroimmunology concept used in this study was so sensitive to the change of condition in human body, (b) not all parents agreed to provide informed consent for ATE, resulting in remarkable rate of drop out, (c) control group was difficult to obtain, because the subjects should have medically been operated. However, this operational restraint had been overcome by using cohort

retrospective design without involving control group.
2. Pre- and post-ATE hypoxic condition was not appropriately measured due to ethical reasons to obtain sampling unit of blood gas analysis from paediatric patients, because not all the OCAT patients agreed to undergo blood gas analysis examination.
3. The observation of immunity modulation was carried out in a short period (two weeks), and it was also done once, two weeks after operation (De Weese, 1982; Ranidewi, 1995), while the development of immunity condition was not observed.
4. Physical condition of post-ATE OCAT patients was only assessed from general impression. Post-ATE laboratory examination, such as that for hemoglobin level, erythrocyte, hepatic and renal functions, was not undertaken. However, this examination should be done as the principle for managing OCAT patients in the future.

CONCLUSIONS AND RECOMMENDATIONS

Conclusions

The results of ATE procedure for children with OCAT can be concluded as follows:
1. ATE procedure for children with OCAT may modulate immunity in two different immunity groups.
2. Discriminant variables in immunity modulation due to the effect of ATE procedure in children with OCAT are IFN-γ, IgG, and neutrophil.
3. ATE procedure in children with OCAT results in two immunity patterns. However, a part of the patients have not experienced immunity modulation recovery two weeks post-ATE.

Recommendations

1. Children with OCAT should be subjected to ATE procedure.
2. Similar study should be undertaken involving serial observation for more than two weeks to post-ATE immunity modulation in children with OCAT.
3. Further studies should involve variables that may disclose more detail mechanism in revealing immunity modulation due to the effect of ATE procedure in children with OCAT.

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