phocytes alveolitis of granulomatous lung disorders are polyclonal or oligoclonal, we analyzed DNA extracted from T cells obtained by bronchoalveolar lavage in patients with sarcoidosis and farmer's lung disease. Southern blot hybridization with T cell receptor gene probe gave no signals derived from the specific rearrangement, indicating polyclonal expansion of lung T cells (Fig. 1).

5. Enhanced expression of cluster of differentiation (CD) 2 antigen on lung T cells

It has recently been established that, in the immune system, cell adhesion molecules, such as CD2 and lymphocyte-function associated antigens, are involved in leukocyte-endothelial cell contact, lymphocyte recirculation, and lymphocyte accessory cell interactions. To investigate the role(s) of CD2 molecules in the accumulation of lung T cells, using a monoclonal antibody and a flow cytometer, we examined CD2 antigen expression on lung and blood T cells in a variety of pulmonary and extrapulmonary diseases. In contrast to the results regarding TCR antigen, the expression of CD2 antigen on lung T cells in pulmonary sarcoidosis and farmer's lung disease was significantly increased compared with that on blood T cells (Fig. 2). These results suggest that CD2 molecules play an important role in the accumulation and activation of lung T cells.

6. Restriction fragment length polymorphism (RFLP) of HLA-DR beta gene in pulmonary sarcoidosis

We have previously reported an association between pulmonary sarcoidosis and HLA-DRw52 (3). In the present study, RFLP analysis was performed on HLA gene of patients with pulmonary sarcoidosis. Preliminary study revealed different frequencies of some HLA-DR β bands between patients and control subjects.

REFERENCES


(3) A Double-blind Placebo-controlled Study of OKY-046 for the Treatment of Chronic Asthma

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Six oral prophylactic anti-asthma agents, tranilast, oxatomide, ketotifen, azelastin, repirinast and amlexanox, have been marketed and used in the treatment of asthma in Japan based on clinical efficacy demonstrated in double-blind, placebo-controlled multicenter trials, a methodology used to establish efficacy of cromoglycate. Recently, Miyamoto et al (1) have conducted a dose-finding study of OKY-046 (2, 3), a specific thromboxane (Tx) synthetase inhibitor, in 240 adult patients with asthma on a similar design and revealed that the drug is most effective in a daily dosage of 400 mg given in two divided doses in the morning and before bedtime. In order to see if it is possible to assess the usefulness of the drug with high accuracy in a smaller number of subjects at a single institution, we have conducted a placebo-controlled double-blind study in a small series of patients at our
PATIENTS AND METHODS

The study excluded those patients who take a large amount of a steroid continuously, regardless of severity and type of the disease. It consisted of a 4-week observation period and a 12-week treatment period. The clinical data were collected from 25 cases in the OKY-046 group and 24 cases in the placebo group, totaling 49 cases. Of these, statistical analysis was made in 42 cases, and final overall improvement rating could be done in 40 cases. No significant difference was observed between the two groups in the type of disease, atopic, infectious and mixed type, and the severity of disease.

A tool used to evaluate the efficacy of the two study regimens was the patient’s diary which recorded symptoms and concomitant medication. An asthma score was calculated based on these records. Physician assessment of the clinical state of the patient was done by the same investigator who directed the whole study and followed up on all the subjects over the course of treatment.

RESULTS

The proportions of moderately to markedly improved cases and slightly to markedly improved cases in the OKY-046 group were 33.3 and 66.7%, respectively, and those in the placebo group were 10.5 and 21.1%. Thus the OKY-046 group showed a significantly higher improvement rate. This improvement rate was lower than that observed in the previous report of Miyamoto et al. (1) (Fig. 1). This is likely due to a smaller number of subjects in the present study and the fact that this study included many patients with an infectious type or mixed type of asthma, although the efficacy in patients with either type was similar to that with an atopic type. The asthma score remained unchanged or increased in the placebo group even after the start of the treatment, while that of the OKY-046 group decreased at weeks 9–12 of treatment. No significant difference, however, was noted statistically.

The main urinary metabolite of TxA2, 2,3-dinor-TxB2 was measured before and after administration of the drug to study any relationship between the treatment and the improvement rating in asthma. Among the cases of the OKY-046 group showing slight to marked improvement, the main urinary metabolite decreased significantly, while it did not change significantly in the cases showing no change or aggravation in the disease, thus suggesting that
Active Drug Group

Slightly improved (n=13)

No change or aggravated (n=5)

P<0.01

NS

NS

NS

Placebo Group

Slightly improved (n=4)

No change or aggravated (n=12)

NS

NS

NS

Fig. 2. Change in urinary 2,3-dinor-TxB₂ level.

Active Drug Group

Slightly improved (n=13)

P<0.1

NS

NS

NS

Placebo Group

Slightly improved (n=3)

No change or aggravated (n=10)

P<0.1

NS

NS

Fig. 3. Effect of OKY-046 on PD₃₅-Mch.

The present study also included a methacholine-inhalation challenge test to investigate the effect of the drug on airway hypersensitivity. In the cases of the OKY-046 group showing slight to marked improvement, PD₃₅-Mch values tended to increase and it was demonstrated that OKY-046 inhibits acceleration of airway hypersensitivity (Fig. 3).

CONCLUSIONS

Forty patients with chronic asthma completed a double-blind, placebo-controlled trial of Tx synthetase inhibitor OKY-046, 200mg twice daily, conducted in a single institution in the prophylaxis of asthma. Throughout the study, the same physician rated the individuals receiving the drug for clinical
improvement from their pretreatment condition. The OKY-046 group showed a significantly higher improvement than the placebo group. The result was similar to that shown in the previous multicenter study in a larger number of subjects.

REFERENCES

