Acute Eosinophilic Pneumonia Following Cigarette Smoking

**Key words:** cigarette smoke, acute respiratory failure, eosinophilia, tolerance, provocation test

Acute eosinophilic pneumonia (AEP) is an acute febrile illness that can result in acute respiratory failure (ARF) (1–3). Since AEP was first described in the literature, many cases have been reported, and many factors have been incriminated as a cause of this disease process (4). Unfortunately, however, the relationship between AEP and cigarette smoking is not well recognized.

A relationship between cigarette smoking and AEP has been suggested by some investigators based on the finding that some young patients have developed AEP after they began to smoke. In 1993, Hashimoto et al (5) and thereafter Nakamura et al (6) and Hoshino et al (7) suggested a possible relationship between cigarette smoke and AEP, however direct and definitive evidence for cigarette smoke-induced AEP (CS-AEP) could not be provided. There has been evidence against it; 1) Even when patients with AEP resumed cigarette smoking after recovery, AEP did not recur. 2) Results showed that provocation tests using cigarette smoke did not always induce respiratory symptoms or pulmonary lesions. 3) After improvement of AEP, the patient experienced a recurrence of symptoms and pneumonia when they returned to their homes or entered specific rooms, suggesting positive evidence for an environmental provocation test. 4) Positive skin test results and positive serum antibody titers for fungi as a causative antigen. 5) Limitation of the condition to only Japanese is unusual if cigarettes are the cause. 6) All cases of AEP followed after cigarette smoking appeared between April and September, when summer-type hypersensitivity pneumonitis is common in Japan, (suggesting a weather-related cause for the development of AEP). 7) Some patients had been treated with antibiotics and drugs for fever, cough, and respiratory failure; thereby a drug-induced cause has been suspected.

In 1997, we reported the first case of CS-AEP with positive results on a provocation test (8, 9). The patient manifested a high fever (39°C) and severe dyspnea, which were associated with an abnormal WBC count, decrease of PaO₂, and abnormal results on a pulmonary function test after a provocation test with cigarette smoke (three cigarettes). Fifteen hours after the provocation test, the patient’s WBC count abruptly increased to 9,600/mm³ (10,100/mm³, 21 hours after the provocation test) from 5,700/mm³, PaO₂ decreased to 56 mmHg from 93 mmHg, DLco (diffusing capacity of the lung for Co) decreased to 59% from 97%, and FEV₁% (expiratory volume in 1 second/forced vital capacity) decreased to 61% from 83%.

After the first report, we encountered six cases in which ARF and/or AEP began after patients smoked cigarettes for the first time in their lives. At Japanese Respiratory Society annual meetings in 1998 and 1999, we presented clinical, laboratory, and pathological findings and positive results for provocation tests. A diagnosis of CS-AEP was made for these patients based on clinical and laboratory findings and the results of provocation tests regarding these cases. In two cases, the provocation test induced respiratory symptoms, high fever, a low PaO₂ level, and a low level on pulmonary function tests (DLco and/or FEV₁%). Severe cough with or without serious sputum and abrupt elevation of eosinophils in the peripheral blood (acute eosinophilia) were induced in 3 cases. The cigarette brands were of both American (Lark® and Lucky Strike®) and Japanese products (Mild Seven®). In 1997, Kawamura et al (10) described a second case of CS-AEP. In 1998 and 1999, Nitsuma and Saito (11) and Ito et al (12) also described CS-AEP patients with positive results on a provocation test using the same method as we performed (8). These provocation tests resulted in abnormal laboratory data such as low PaO₂ levels, an increase in the white cell count, dyspnea, fever, and cough. Therefore, cigarette smoke is now believed to be a cause of AEP.

Shiota and colleagues present a patient with AEP following cigarette smoking in this issue (13).

They describe the recurrence of CS-AEP one month after discharge from hospital and the resumption of cigarette smoking. Regarding the recurrence of CS-AEP, we encountered not only two CS-AEP patients with AEP induced by a provocation test (cigarette smoke), but also had two patients with no recurrence after resumption of smoking. In 1999, we reported a CS-AEP case in whom cigarette smoke did not induce a recurrence, and discussed the possibility of tolerance induced by resumption of cigarette smoking in a CS-AEP patient (14). We think that the number of cigarettes smoked, the duration of smoking, the degree of tolerance, and unknown factor(s) may influence the recurrence of CS-AEP. Although cigarette smoking may induce tolerance, physicians should be aware of the danger of developing respiratory failure following a provocation test. In fact, Shiota et al (13) and some other investigators have reported that AEP might have recurred following cigarette smoking and that a provocation test might have induced respiratory failure in once improved CS-AEP patients.

Regarding peripheral eosinophilia, it is absent during the
acute stage of AEP, but usually appears during the recovery stage. CS-AEP patients may also develop eosinophilia during the recovery stage, which has been reported in this issue (13). Although some investigators have reported a relationship between cigarette smoking and eosinophilia (15–19), it is not well known that cigarette smoke can induce acute eosinophilia. In 1999, we reported the apparent first reported case of cigarette smoke-induced acute eosinophilia (sudden elevation of peripheral eosinophils within a week) (14). We performed a provocation test (once a day, with three cigarettes each time for two days) in an AEP patient, who developed cough and chest pain about 13 hours later and abrupt eosinophilia (42% of the total white blood cell count) for a few days. After the development of these symptoms and eosinophilia, he resumed cigarette smoking, but neither symptoms nor peripheral eosinophilia reappeared. Thereafter, we encountered another patient with CS-AEP with no recurrence after resumption of cigarette smoking. We think that tolerance may be induced by resumption of cigarette smoking in CS-AEP with only acute eosinophilia or with no abnormal laboratory data and/or no symptoms.

Shiota et al (13) in this issue examined previous literature on AEP, and found a high incidence in the initial cigarette smoking in young AEP patients. In 1998, we also reviewed the English and Japanese literature on AEP to search for histories of smoking in AEP cases (9), using the following criteria [modified AEP criteria of Allen et al (3)] for the diagnosis of AEP; 1) onset of any symptom occurring 7 days before visit to physician, 2) BAL differential with ≥25% eosinophils or pathologically proven eosinophilic pneumonia, 3) mild-to-severe symptoms of cough, dyspnea, and fever, 4) bilateral infiltrate shadows on chest X-ray, 5) a recovery in a short clinical course of less than a week, and 6) no apparent causes of AEP detectable. With these criteria, we collected 58 AEP cases. They ranged in age from 14 to 80 years (mean age: 30 years); 26 were under 22 years of age. Surprisingly enough, 35 out of 56 cases revealed a history of cigarette smoking, and 26 cases were patients under 22 years. The duration of smoking was described in only 25 cases reported from Japan. Of these 12 cases (48%) showed a short duration of cigarette smoking; namely, two days to one month before the development of AEP. Although we first recognized and reported on CS-AEP, a number of cases must have previously gone unrecognized as such and thus unreported. We agree with one of the conclusions of Shiota et al (13) that the high incidence in the literature of AEP occurring within a month after initial cigarette smoking is not merely coincidental.

References


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