Acute and Chronic Eosinophilic Pneumonia: Clinical Evaluation and the Criteria
Shigenobu Umeki and Rinzo Soejima

The clinical courses of 11 cases of eosinophilic pneumonia which were clinico-pathohistologically diagnosed and found to be unassociated with organic disorders producing peripheral blood eosinophilia were extensively investigated and compared with various types of eosinophilic pneumonia previously reported. Five cases of acute eosinophilic pneumonia fulfilled the following criteria: 1) less than a one-month history of symptoms prior to diagnosis, 2) a short clinical course and 3) no recurrence. Six cases of chronic eosinophilic pneumonia fulfilled the following criteria: 1) more than a two-month history of symptoms prior to diagnosis, 2) a prolonged clinical course and 3) recurrence. The results suggested that various types of previously reported eosinophilic pneumonia classified by sex, the presence or absence of peripheral blood eosinophilia, the degree of clinical symptoms or peripheral blood eosinophilia, and the degree of abnormalities on chest X-ray films should be extensively reevaluated.

Key words: pulmonary eosinophilia, diagnostic criteria, bronchial asthma, steroids

Introduction

In 1932 Löffler (1) described fleeting and transient pulmonary infiltrates with peripheral blood eosinophilia (PBE) in mildly or asymptomatic patients. A number of related conditions, grouped together under the term “pulmonary eosinophilia,” by Crofton et al (2) in 1952, are 1) simple pulmonary eosinophilia (Löffler’s), 2) prolonged pulmonary eosinophilia, 3) tropical eosinophilia (Weingarten’s), 4) pulmonary eosinophilia with asthma, and 5) pulmonary eosinophilia with periarteritis nodosa. Reeder and Goodrich (3), also in 1952, preferred the descriptive phrase “pulmonary infiltration with eosinophilia” to identify these disorders and coined the term “PIE syndrome.” In 1969, Liebow and Carrington (4) defined eosinophilic pneumonia (EP) as “pulmonary infiltrations of the lung by eosinophils that may or may not be accompanied by an excess of these cells in the peripheral blood,” and Carrington et al (5) later described nine cases of chronic eosinophilic pneumonia (CEP) characterized by severe dyspnea, weight loss and fever lasting months or years with a typical roentgenogram showing peripheral pulmonary infiltrates. Recently two groups (6, 7) have described cases of acute eosinophilic pneumonia (AEP) in which many similarities with CEP exist; e.g., symptoms of cough, severe dyspnea and fever, crackles on auscultation, diffuse pulmonary infiltrates on chest X-ray films (although not always peripherally situated) and a less than one-month history of symptoms prior to diagnosis and no previous atopic illness such as asthma.

Eosinophilic lung disease, which may or may not be accompanied by PBE, has been given a multitude of names. However, the concept of this disease and its nomenclature have not yet been established. Here, we intend to present a classification which correlates with only the clinical course, including the presence or absence of recurrence of EP characterized by peculiar clinical symptoms and abnormalities on chest X-ray films.

Patients and Methods

Eleven patients with EP were seen at Kawasaki Medical School Hospital between 1980 and 1990. Patients were selected on the basis of clinical and pathologic criteria. No patients suffered from organic disorders producing PBE; e.g., collagen diseases, allergic bronchopulmonary aspergillosis, hypereosinophilic syndrome, sarcoidosis, Hodgkin’s disease, helminthic infections, and bacterial and mycotic infections with the exception...
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Table 1. A Model of Criteria for Acute and Chronic Eosinophilic Pneumonia

<table>
<thead>
<tr>
<th>major criteria (essential)</th>
<th>acute</th>
<th>chronic**</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) mild-severe symptoms (cough, fever, dyspnea)</td>
<td>less than 1 month</td>
<td>more than 2 months</td>
</tr>
<tr>
<td>2) peripheral infiltrations on chest X-ray films*</td>
<td>short</td>
<td>prolonged</td>
</tr>
<tr>
<td>(patchy, nodular, nonsegmental, shifting, recurrent)</td>
<td>(-)***</td>
<td>(+)</td>
</tr>
<tr>
<td>3) pathohistology (eosinophilic infiltrations in pulmonary interstitial tissues and alveolar spaces)</td>
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<table>
<thead>
<tr>
<th>history of symptoms prior to diagnosis</th>
<th>clinical course</th>
<th>recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>acute</td>
<td>short</td>
<td>(-)***</td>
</tr>
<tr>
<td>chronic**</td>
<td>prolonged</td>
<td>(+)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>minor criteria (not essential)</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1) blood eosinophilia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2) bronchoalveolar lavage fluid eosinophilia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3) corticosteroid responsiveness</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4) in most cases, the diseases associated with asthma are included in the chronic eosinophilic pneumonia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5) organic disorders (e.g., collagen diseases, allergic bronchopulmonary aspergillosis, bronchocentric granulomatosis, sarcoidosis, Hodgkin's disease, hyper eosinophilic syndrome, helminthic infections, bacterial and mycotic infections) associated with blood eosinophilia should be excluded from the criteria</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Sometimes pulmonary edema-like shadows and photographic negative.
** At least one of the criteria is necessary for the diagnosis of chronic disease.
*** No recurrence of disease associated with the previous eosinophilic pneumonia.

of bronchial asthma. All patients had peculiar clinical symptoms such as cough, fever and/or dyspnea and peripheral infiltrates (patchy, nodular, nonsegmental, shifting and/or recurrent) on chest X-ray films. The lung biopsy specimens of all of the patients revealed infiltrations of eosinophils and histiocytes in the alveolar and/or interstitial compartments acceptable for the diagnosis. The references for the diagnosis were: 1) PBE (more than 500/mm³) and 2) corticosteroid responsiveness. AEP met the following additional diagnostic criteria: a less than one-month history of symptoms prior to diagnosis, a short clinical course (of about less than one month after diagnosis) and no recurrence. CEP met the following additional diagnostic criteria: a more than two-month history of symptoms prior to diagnosis, a prolonged clinical course (of about more than two months after diagnosis) and occasional recurrence (Table 1). The diagnostic criteria are not prescribed by the presence or absence of asthma and the clinical courses of AEP and CEP are not prescribed by the presence or absence of a history of corticosteroid therapy. There were five cases of AEP (four men and one woman; mean age, 37.7 years) and six cases of CEP (four men and two women; mean age, 59.7 years).

Patient Background

Table 2 shows the characterization of five cases of AEP (Cases 1 to 5) and six cases of CEP (Cases 6 to 11). In the latter group, Case 10 developed asthma four years after the appearance of CEP and Case 11 experienced CEP simultaneously with asthma. Cases 3, 4 and 11 had a history of atopic illness or drug allergy. Cases 1, 2, 5, 6, 10 and 11 were smokers and Cases 1, 6, 7, 9, 10 and 11 were involved in dust-associated occupations. All of these cases complained of dry cough, fever or dyspnea. The mean period required for the diagnosis of EP was 15.6 days (ranging from 8 to 22 days) in AEP and 72.8 days (ranging from 32 to 155 days) in CEP. Preceding respiratory tract infections were observed in three cases of AEP and five cases of CEP. Five AEP cases and four CEP cases received drug therapy before diagnosis of EP. After diagnosis corticosteroids were given to one AEP case and 5 CEP cases.

Table 3 shows the clinical findings and laboratory data of the 11 cases of EP. Upon physical examination, fine crackles were audible in three AEP cases and four CEP cases. Rhonchi were audible in only one case of CEP. Leukocytosis (more than 10,000/mm³) on admission was observed in one AEP case and one CEP case. PBE (more than 500/mm³) was observed in four AEP cases and four CEP cases. Hyperimmunoglobulinemia E (more than 400 U/ml, normal levels are less than 400 U/ml) was observed in two AEP cases and one CEP case. C-reactive protein levels increased in four AEP cases and five CEP cases. Rheumatoid factor levels were positive in one of three AEP cases and two CEP cases. Tuberculin skin test results were negative in three AEP cases and one CEP case. In pulmonary function tests, a restrictive defect presented in three AEP cases and three CEP cases, but none of the EP patients presented with an obstructive defect. Carbon monoxide diffusion was reduced in three AEP cases and three CEP cases. Blood gases on admission while breathing room air showed significantly moderate to severe arterial hypoxia in all EP cases. Arterial blood carbon dioxide tensions,
### Table 2. Characterization of Patients with Eosinophilic Pneumonia

<table>
<thead>
<tr>
<th>Case</th>
<th>Age, sex</th>
<th>Underlying diseases or complications</th>
<th>Allergy</th>
<th>Smoking (cigarette index)</th>
<th>Dust-related occupation</th>
<th>Symptoms</th>
<th>Periods from appearance of symptoms to diagnosis (days)</th>
<th>Respiratory tract infection before admission</th>
<th>Drugs before diagnosis</th>
<th>Steroid therapy</th>
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<tbody>
<tr>
<td>1</td>
<td>26, M</td>
<td>(-)</td>
<td>(+)</td>
<td>100</td>
<td>(+)</td>
<td>cough</td>
<td>12</td>
<td>(-)</td>
<td>NSAIDs, MINO</td>
<td>(-)</td>
</tr>
<tr>
<td>2</td>
<td>49, M</td>
<td>(-)</td>
<td>(+)</td>
<td>100</td>
<td>(-)</td>
<td>SOB</td>
<td>8</td>
<td>(-)</td>
<td>PIPC, MENO</td>
<td>(-)</td>
</tr>
<tr>
<td>3</td>
<td>19, M</td>
<td>(-)</td>
<td>(+)</td>
<td>100</td>
<td>(-)</td>
<td>cough</td>
<td>20</td>
<td>(+)</td>
<td>PIPC, MENO, CEZ</td>
<td>(-)</td>
</tr>
<tr>
<td>4</td>
<td>37, F</td>
<td>(-)</td>
<td>(+)</td>
<td>100</td>
<td>(-)</td>
<td>cough</td>
<td>16</td>
<td>(+)</td>
<td>PIPC, MENO, CEZ</td>
<td>(-)</td>
</tr>
<tr>
<td>5</td>
<td>56, M</td>
<td>(-)</td>
<td>(+)</td>
<td>100</td>
<td>(-)</td>
<td>SOB</td>
<td>22</td>
<td>(+)</td>
<td>PIPC, MENO, CEZ</td>
<td>(-)</td>
</tr>
<tr>
<td>6</td>
<td>73, M</td>
<td>(-)</td>
<td>(+)</td>
<td>100</td>
<td>(-)</td>
<td>cough</td>
<td>40</td>
<td>(+)</td>
<td>PIPC, MENO, CEZ</td>
<td>(-)</td>
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<tr>
<td>7</td>
<td>73, F</td>
<td>(-)</td>
<td>(+)</td>
<td>100</td>
<td>(-)</td>
<td>SOB</td>
<td>32</td>
<td>(+)</td>
<td>PIPC, MENO, CEZ</td>
<td>(-)</td>
</tr>
<tr>
<td>8</td>
<td>69, M</td>
<td>(-)</td>
<td>(+)</td>
<td>100</td>
<td>(-)</td>
<td>SOB</td>
<td>70</td>
<td>(+)</td>
<td>PIPC, MENO, CEZ</td>
<td>(-)</td>
</tr>
<tr>
<td>9</td>
<td>69, F</td>
<td>(-)</td>
<td>(+)</td>
<td>100</td>
<td>(-)</td>
<td>SOB</td>
<td>100</td>
<td>(+)</td>
<td>PIPC, MENO, CEZ</td>
<td>(-)</td>
</tr>
<tr>
<td>10</td>
<td>55, F</td>
<td>(-)</td>
<td>(+)</td>
<td>100</td>
<td>(-)</td>
<td>SOB</td>
<td>40</td>
<td>(+)</td>
<td>PIPC, MENO, CEZ</td>
<td>(-)</td>
</tr>
<tr>
<td>11</td>
<td>28, M</td>
<td>Asthma</td>
<td>Asthma</td>
<td></td>
<td>(-)</td>
<td>SOB</td>
<td>155</td>
<td>(+)</td>
<td>(-)</td>
<td>(-)</td>
</tr>
<tr>
<td>12</td>
<td>59, M</td>
<td>Asthma</td>
<td>Asthma</td>
<td></td>
<td>(-)</td>
<td>SOB</td>
<td>155</td>
<td>(+)</td>
<td>(-)</td>
<td>(-)</td>
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</table>

SOB: shortness of breath.

### Table 3. Laboratory Data

<table>
<thead>
<tr>
<th>Breath sounds</th>
<th>Case 1</th>
<th>Case 2</th>
<th>Case 3</th>
<th>Case 4</th>
<th>Case 5</th>
<th>Case 6</th>
<th>Case 7</th>
<th>Case 8</th>
<th>Case 9</th>
<th>Case 10</th>
<th>Case 11</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC (10^3/mm³)</td>
<td>6,300</td>
<td>7,100</td>
<td>7,800</td>
<td>6,200</td>
<td>14,000</td>
<td>9,400</td>
<td>9,200</td>
<td>4,200</td>
<td>16,600</td>
<td>8,100</td>
<td>7,300</td>
</tr>
<tr>
<td>Eosinophils (%)</td>
<td>2</td>
<td>11</td>
<td>20</td>
<td>9</td>
<td>4</td>
<td>3</td>
<td>5</td>
<td>16</td>
<td>44</td>
<td>15</td>
<td>19</td>
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<tr>
<td>IgE (U/ml)</td>
<td>180</td>
<td>206</td>
<td>531</td>
<td>113</td>
<td>922</td>
<td>209</td>
<td>156</td>
<td>936</td>
<td>47</td>
<td>263</td>
<td>10</td>
</tr>
<tr>
<td>CRP (mg/dl)</td>
<td>2.3</td>
<td>0.3</td>
<td>2.2</td>
<td>14.7</td>
<td>18.0</td>
<td>5.2</td>
<td>20.2</td>
<td>5.0</td>
<td>15.2</td>
<td>0.3</td>
<td>1.4</td>
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<tr>
<td>ESR (mm/h)</td>
<td>20</td>
<td>17</td>
<td>17</td>
<td>95</td>
<td>142</td>
<td>70</td>
<td>100</td>
<td>17</td>
<td>98</td>
<td>3</td>
<td>17</td>
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<tr>
<td>RA (%)</td>
<td></td>
<td></td>
<td>95</td>
<td>95</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>P.P.D. (mm)</td>
<td>9×8</td>
<td>30×25</td>
<td>2×0</td>
<td>0×0</td>
<td>4×4</td>
<td>32×22</td>
<td>5×5</td>
<td>5×5</td>
<td>30×21</td>
<td>60×40</td>
<td></td>
</tr>
<tr>
<td>VC (l)</td>
<td>3.7</td>
<td>3.2</td>
<td>3.4</td>
<td>2.7</td>
<td>2.4</td>
<td>2.9</td>
<td>1.1</td>
<td>3.3</td>
<td>1.8</td>
<td>3.4</td>
<td>3.7</td>
</tr>
<tr>
<td>%VC (%)</td>
<td>92</td>
<td>77</td>
<td>78</td>
<td>93</td>
<td>67</td>
<td>96</td>
<td>55</td>
<td>107</td>
<td>71</td>
<td>79</td>
<td>110</td>
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<tr>
<td>FEV₁,0, (%)</td>
<td>91</td>
<td>75</td>
<td>82</td>
<td>93</td>
<td>83</td>
<td>77</td>
<td>77</td>
<td>75</td>
<td>90</td>
<td>70</td>
<td>72</td>
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<tr>
<td>DLCO (ml/min/mm Hg)</td>
<td>18.4</td>
<td>25.9</td>
<td>17.8</td>
<td>17.5</td>
<td>14.0</td>
<td>12.6</td>
<td>5.8</td>
<td>14.7</td>
<td>11.5</td>
<td>24.5</td>
<td>20.1</td>
</tr>
<tr>
<td>%DLCO (ml/min/mm Hg)</td>
<td>77</td>
<td>146</td>
<td>69</td>
<td>89</td>
<td>64</td>
<td>73</td>
<td>43</td>
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<td>66</td>
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<td>104</td>
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<td>PaO₂ (mm Hg)</td>
<td>73</td>
<td>69</td>
<td>64</td>
<td>61</td>
<td>64</td>
<td>65</td>
<td>55</td>
<td>72</td>
<td>54</td>
<td>68</td>
<td>69</td>
</tr>
<tr>
<td>PaCO₂ (mm Hg)</td>
<td>42</td>
<td>36</td>
<td>39</td>
<td>41</td>
<td>36</td>
<td>32</td>
<td>37</td>
<td>34</td>
<td>37</td>
<td>41</td>
<td>38</td>
</tr>
<tr>
<td>DLTR</td>
<td>all (-)</td>
<td>all (-)</td>
<td>N.D.</td>
<td>all (-)</td>
<td>CPZ (+)</td>
<td>N.D.</td>
<td>IPM/CS (+)</td>
<td>N.D.</td>
<td>INH (+)</td>
<td>N.D.</td>
<td>N.D.</td>
</tr>
</tbody>
</table>

however, were all within normal limits in all 11 cases. In all of the EP patients who received drugs before admission, the drug-stimulating lymphocyte transformation rate (DLTR) was measured. In Case 5 the DLTRs of cefoperazone (CPZ, 597%) and doxycycline (DOXY, 243%) were positive. The DLTR of imipenem/cilastatin (IPM/CS, 206%) was positive in Case 7 and that of isoniazid (INH, 275%) was positive in Case 9.

**Case Reports**

Case 1 (Fig. 1, upper). A 26-year-old man consulted a local doctor because of a persistent headache which appeared in December 1985 and received non-steroidal antiinflammatory drugs (NSAIDs, diclofenac, serrapeptidase and pronase) for nine days. Although the patient's headache disappeared, he was referred to our hospital because of appearance of a low-grade fever and mild dyspnea. A chest X-ray film on admission revealed peripheral nonsegmental infiltrates in the bilateral lung fields. After clinico-pathological diagnosis, a drug-free natural course for 20 days produced disappearance of the clinical symptoms and the abnormality on a chest X-ray film. There has been no recurrence since then.

Case 2 (Fig. 1, lower). A 49-year-old man given minocycline (MINO) for an atypical pneumonia by a local doctor because of cough and fever which appeared in July 1989. Seven days later, the patient's symptoms disappeared. However, he was referred to our hospital because of deterioration of the abnormality on his chest X-ray film. A chest X-ray film on admission revealed peripheral infiltrates in the bilateral lower lung fields. Laboratory data on admission revealed PBE (781/mm$^3$). After clinico-pathological diagnosis, a drug-free natural course for two weeks produced disappearance of the abnormality on his chest X-ray film. There has been no recurrence since then.

Case 3 (Fig. 2, upper). A 19-year-old man was given cefalexin (CEX) and piperacillin (PIPC) by a local doctor because of sputum and a low-grade fever which appeared in February 1982. A twenty-day course of this drug therapy improved the patient's symptoms. One week later, however, the patient again complained of cough, fever and dyspnea, and received MINO for pneumonia based on an abnormality on his chest X-ray film. The patient was referred to our hospital because of continuation of clinical symptoms and the abnormality on his chest X-ray film. A chest X-ray film on admission revealed peripheral patchy/nonsegmental infiltrates over the bilateral lung fields. Laboratory data on admission showed PBE (1,560/mm$^3$). After clinico-pathological diagnosis, a drug-free natural course for 10 days produced disappearance of the clinical symptoms and improvement of the abnormality on his chest X-ray film. Twenty days after that, the abnormality on the chest X-ray film disappeared. There has been no recurrence since then.

Case 4 (Fig. 2, middle). A 37-year-old woman received
MINO because of fever and cough occurring in May 1984 and was temporally released from these symptoms. However, she was given cefazolin (CEZ) because of recurrence of the fever and appearance of dyspnea and an abnormality on her chest X-ray film. This treatment led to deterioration of the abnormality on her chest X-ray film. The patient was referred to our hospital. A chest X-ray film on admission revealed peripheral patchy/nonsegmental infiltrates over the bilateral middle/lower lung fields. Laboratory data on admission revealed PBE (558/mm³). After clinico-pathological diagnosis, the patient was followed under a drug-free condition. Four days later, the patient's symptoms disappeared and 12 days after that, a chest X-ray film showed the lung field to be normal. There has been no recurrence since then.

Case 5 (Fig. 2, lower). A 56-year-old man was admitted to a local hospital because of cough and fever occurring in August 1984. He received antibacterial chemotherapy for pneumonia based on leukocytosis and an abnormality on his chest X-ray film. Ten days later, dyspnea and deterioration of the abnormality on the chest X-ray film occurred. Two weeks after that, the patient was referred to our hospital because of further deterioration on the chest X-ray film. A chest X-ray film on admission revealed peripheral patchy/nonsegmental infiltrates over the bilateral lung fields. Laboratory data on admission revealed PBE (560/mm³). After clinico-pathological diagnosis, the patient was treated with 30 mg of prednisolone (PSL), tapering to a low dose over two weeks. This led to disappearance of the patient's symptoms and the abnormality on the chest X-ray film. The patient showed no evidence of recurrent disease for more than one year.

Case 6 (Fig. 3, upper). A 74-year-old man was referred to a local hospital because of cough and fever occurring...
to our hospital because of cough, fever and dyspnea for 40 days which appeared in January 1986. A chest X-ray film on admission revealed peripheral nonsegmental infiltrates over both middle/lower lung fields. After clinico-pathological diagnosis, the patient was treated with 30 mg of prednisolone, tapering to a low dose over two weeks, and then was discharged when the clinical symptoms and the abnormality on his chest X-ray film improved. One week later, however, the patient experienced recurrent disease with dyspnea, cough and shifting infiltrates on his chest X-ray film. At that time the patient was followed under a drug-free condition, which led to improvement. After that, there was no recurrence for more than one year.

Case 7 (Fig. 3, lower). A 73-year-old woman was treated with various antibacterial antibiotics for pneumonia by a local doctor whom the patient consulted because of the appearance of cough, sputum and fever occurring in October 1987. Ten days later, however, the patient complained of dyspnea, and a chest X-ray film taken at that time revealed deterioration. The patient was referred to our hospital because of continuation of the clinical symptoms and the abnormality on his chest X-ray film. A chest X-ray film on admission revealed peripheral patchy/nonsegmental infiltrates over the bilateral lung fields. Laboratory data on admission showed PBE (672/mm³) and hyperimmunoglobulinemia E (936 U/ml). After clinico-pathological diagnosis, he was followed under a drug-free condition for one month. This led to improvement of his clinical symptoms and the abnormality on his chest X-ray film. Then the patient was discharged. However, the patient had two recurrences of disease 55 and 110 days after diagnosis. On those occasions, the patient was treated with prednisolone (30 mg/d), tapering to a low dose over 80 and 110 days, respectively. There have been no further recurrences since those episodes.

Case 9 (Fig. 4, lower). A 55-year-old woman who consulted her local doctor because of fever and sputum occurring in April 1990 was treated with amoxicillin (AMPC) and ofloxacin (OFLX) for pneumonia based on an abnormality on her chest X-ray film. Thereafter the patient received antituberculosis drugs for suspected pulmonary tuberculosis because no improvement in the
Criteria of Eosinophilic Pneumonia

**Fig. 4.** Clinical courses of cases 8 and 9. A1: the first admission, D1: the first discharge, A2: the second admission, D2: the second discharge, A3: the third admission, D3: the third discharge.

<table>
<thead>
<tr>
<th>Case 8</th>
<th>Days</th>
<th>Therapy</th>
<th>Temp. (°C)</th>
<th>Symp.</th>
<th>WBC (/μl)</th>
<th>Eosino. (%)</th>
<th>IgE (U/ml)</th>
<th>Chest X-R</th>
<th>Days</th>
<th>Therapy</th>
<th>Temp. (°C)</th>
<th>Symp.</th>
<th>WBC (/μl)</th>
<th>Eosino. (%)</th>
<th>IgE (U/ml)</th>
<th>Chest X-R</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>30 60 90</td>
<td>D1 120</td>
<td>A2 270</td>
<td>A3 340</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>30 60 90</td>
<td>D1 120</td>
<td>A2 270</td>
<td>A3 340</td>
<td></td>
<td></td>
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**Fig. 5.** Clinical courses of cases 10 and 11. A1: the first admission, D1: the first discharge, A2: the second admission, D2: the second discharge.

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<th>Case 10</th>
<th>Days</th>
<th>Therapy</th>
<th>Temp. (°C)</th>
<th>Symp.</th>
<th>WBC (/μl)</th>
<th>Eosino. (%)</th>
<th>IgE (U/ml)</th>
<th>Chest X-R</th>
<th>Days</th>
<th>Therapy</th>
<th>Temp. (°C)</th>
<th>Symp.</th>
<th>WBC (/μl)</th>
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abnormality on her chest X-ray film occurred in spite of antibacterial chemotherapy. Sixty days after the treatment, however, the patient complained of dyspnea, leading to consultation at our hospital. A chest X-ray film on admission revealed peripheral patchy/nonsegmental infiltrates over the bilateral lung fields. Laboratory data on admission revealed leukocytosis (16,600/mm³) with PBE (7,304/mm³). After clinico-pathological diagnosis, the patient received prednisolone (30 mg/d), tapering to a low dose over one month. She had recurrent disease when the drug was discontinued, leading to retreatment with prednisolone (20 mg/d). During tapering to a low dose there was one more recurrence, which led to an increase of the prednisolone dosage with tapering to a low dose over two months. There has been no further recurrence since those episodes.

Case 10 (Fig. 5, upper). A 28-year-old man visited a local hospital because of a dry cough and dyspnea occurring in May 1986 and was diagnosed clinico-pathologically as EP. Prednisolone of 30 mg/d, tapering to a low dose over one month, produced disappearance of the patient's symptoms. Recurrence of disease occurred twice over the next year and a half. The patient was referred to our hospital because of recurrent dyspnea and deterioration of an abnormality on his chest X-ray film, in spite of treatment with prednisolone with tapering to a low dose over three months. A chest X-ray film on admission revealed peripheral nonsegmental infiltrates over the bilateral upper/lower lung fields. Laboratory data on admission showed PBE (1,215/mm³). The patient was diagnosed clinico-pathologically again as EP, and followed under a drug-free condition for one month. This led to disappearance of the clinical symptoms and improvement of the abnormality on his chest X-ray film. Three months after his discharge, the patient had recurrent disease and was readmitted to our hospital. A natural drug-free course for five months produced disappearance of the patient's symptoms and the abnormality on his chest X-ray film. There was no evidence of recurrent disease for more than three years. Four years after the initial diagnosis, however, the patient developed bronchial asthma with a cough and wheezing, but without any abnormality on his chest X-ray film.

Case 11 (Fig. 5, lower). A 59-year-old man had received beta-2-stimulants and theophylline for bronchial asthma because of a cough, wheezing and dyspnea appearing in September 1986. The patient was referred to our hospital because of continuation of the clinical symptoms and an abnormality on a chest X-ray film taken four months after antiasthmatic therapy was initiated. A chest X-ray film on admission revealed peripheral infiltrates (fluffy nodules) over the bilateral lung fields. Laboratory data on admission showed PBE (1,387/mm³). After clinico-pathological diagnosis, the patient was followed under only bronchodilators, with no steroid therapy. The patient was discharged on the 40th hospital day when a chest X-ray film revealed improvement of the abnormality. Thereafter clinical symptoms such as mild dyspnea and wheezing and the abnormality on his chest X-ray film continued for more than two years. A chest X-ray film taken three years after discharge revealed no abnormal shadows. The patient has shown no evidence of recurrent disease since then, but has complained of wheezing.

Discussion

Eosinophilic lung disease has been given a multitude of names on the basis of each etiology and pathophysiology with or without PBE: Crofton et al (2), for example, divided it into five categories (containing Löffler syndrome), while Reeder and Goodrich (3) coined the term “PIE syndrome.” In 1969, Liebow and Carrington (4) defined EP pathohistologically as “pulmonary infiltrations of the lung by eosinophils that may or may not be accompanied by an excess of these cells in the peripheral blood.” Based on pathohistological findings consistent with EP, Carrington et al (5) later clinically demonstrated that CEP is a disease entity consisting of a chronic and ultimately life-threatening illness with high fever, night sweating, weight loss and severe dyspnea. The additional diagnostic criteria are as follows: 1) progressive, dense infiltrates arranged in a peculiar peripheral pattern, 2) surprisingly rapid resolution with corticosteroid medication, 3) recurrence of lesions in the same unusual locations during relapse, and 4) pulmonary infiltration best described as a “photonegative” or “reversal” of the shadow seen in pulmonary edema or alveolar proteinosis. On the other hand, two groups (6, 7) have recently described cases of AEP in which there are many similarities with CEP, e.g., the symptoms of cough, severe dyspnea and fever, the crackles on auscultation and the diffuse pulmonary infiltrates on chest X-ray films, although these are not always peripherally situated. Badesch et al (7) reported the following diagnostic criteria for AEP: a less than one-month history of symptoms prior to diagnosis, no evidence of asthma, the absence of other organic disorders, no obvious etiology, and no evidence of recurrent disease.

The results obtained here suggest that if EP pathohistologically exists in a disease not consistent with an organic disorder causing EP or PBE, it should be diagnosed clinically using a diagnostic criteria including 1) clinical symptoms (cough, fever and dyspnea), 2) characteristics on chest X-ray films, and 3) clinical courses characterized by a short-term or long-term, the presence or absence of recurrence, and corticosteroid responsiveness. Cases 1 and 2 in our study are considered to be consistent with simple pulmonary eosinophilia (Löffler's) as classified by Crofton et al (2) based on mild symptoms, transient pulmonary infiltrates on chest X-ray films, and short clinical courses. The fact that some of the
Criteria of Eosinophilic Pneumonia

reported AEP patients (6, 7) naturally improved, led us to conclude that AEP should be not distinguished from simple pulmonary eosinophilia on the basis of whether the patient's symptoms are mild or severe. Cases 3 to 5 in our study meet the diagnostic criteria for AEP demonstrated by Badesch et al (7). We would like to propose that the term “AEP” be used for illness in patients with pathologically-proven EP characterized by 1) mild to severe symptoms (cough, fever and dyspnea), 2) peripheral infiltrates (patchy, nodular, non-segmental, or shifting) on chest X-ray films, 3) a less than one-month history of symptoms prior to diagnosis, 4) a short clinical course, 5) no evidence of recurrence and 6) no evidence of organic disorders producing EP or PBE (Table 1). Our diagnostic criteria of AEP includes two categories of Löffler syndrome and previously-reported AEP but not the following conditions: 1) no evidence of asthma and 2) no obvious etiology proposed by Badesch et al (7). In addition, references for diagnosis of AEP include the following conditions: 1) PBE (more than 500/mm³) and 2) corticosteroid responsiveness.

Carrington et al (5) proposed that the segregation of patients with asthmatic symptoms is the least defensible part of the classification of Crofton et al (2). From the cases of Carrington et al (5), it is apparent that the presence of wheezing with pulmonary eosinophilia has little consequence in terms of the clinical course and response to therapy. Cases 6 to 11 met the diagnostic criteria for CEP proposed by Carrington et al (5). From several reports (8–11) containing the cases of Carrington et al (5), we would like to propose that the term “CEP” be used for illness in patients with pathologically-proven EP characterized by 1) mild to severe symptoms (cough, fever and dyspnea), 2) peripheral infiltrates (patchy, nodular, non-segmental, shifting or recurrent) on chest X-ray films, 3) a more than two-month history of symptoms prior to diagnosis, 4) a prolonged clinical course, 5) occasional recurrence and 6) no evidence of organic disorders producing EP or PBE (Table 1). Our diagnostic criteria of CEP includes three categories (prolonged pulmonary eosinophilia and asthmatic pulmonary eosinophilia proposed by Crofton et al (2) and CEP proposed by Carrington et al (5)). In addition, references of CEP include the following conditions: 1) PBE (more than 500/mm³) and 2) corticosteroid responsiveness. In most cases of PBE, EP associated with asthma is included in CEP. Although CEP is usually responsive to corticosteroid therapy, the present cases were recurrent after tapering or discontinuation of corticosteroids, suggesting that corticosteroid responsiveness in CEP differs from case to case. Jederlinic et al (9) recommended at least six months of corticosteroid therapy beginning with a high dose tapering to a low, alternate day dose. If the disease recurs when medication has been discontinued or while tapering is under way, treatment should be continued for another year before a second attempt is made to discontinue the drug. In our study, the mean period from the diagnosis to disappearance of the abnormality on chest X-ray films in CEP patients was 15.5 months (ranging from 3 to 40 months) despite the presence or absence of drug therapy. CEP patients reported by Carrington et al (5) were all females. Out of 19 CEP patients reported by Jederlinic et al (9), however, 10 were males ranging from 43 to 79 years of age (mean age, 61.7 years). From our cases and those of Jederlinic et al (9), CEP should not be considered as a disease seen only in females.

In regard to the etiology of EP, Patterson et al (12) demonstrated a list of agents that have been implicated in the production of EP: 1) Aspergillus, 2) helminthic infections, 3) drugs or chemicals, 4) bacterial and mycotic infections, 5) pollens, and 6) sarcoidosis or Hodgkin’s disease. Although EP is produced by a variety of agents, as pointed out by Carrington et al (5) and Badesch et al (7), EP should be separated from many organic disorders producing EP or PBE, such as collagen diseases, allergic bronchopulmonary aspergillosis, sarcoidosis, Hodgkin’s disease, helminthic infections, hypereosinophilic syndrome, and bacterial and mycotic infections. Eosinophilic lung disease refers to poorly understood and ill defined disorders assumed to represent some altered immunological response or allergic reaction. Now eosinophilic lung diseases are classified or defined by the degree of severity of clinical symptoms and abnormality on chest X-ray films, or by the presence or absence of PBE and its degree. Pathologically-proven EP should be restricted to two categories, i.e., AEP and CEP, if it is satisfied that there are no organic disorders producing EP or PBE. AEP and CEP should each be recognized as a disease category (or syndrome) but not as an independent disease entity. The classification of eosinophilic lung disease of Crofton et al (2) should be carefully reevaluated.

References

8) Gaensler EA, Carrington CB. Peripheral opacities in chronic eosinophilic pneumonia: the photographic negative of pulmonary
Umeki et al