Intrapulmonary Hemorrhage in Collagen-Vascular Diseases
Includes a Spectrum of Underlying Conditions

Shoko Kobayashi and Shigeko Inokuma

Abstract

Objective To elucidate the background and clinical features of intrapulmonary hemorrhage in collagen-vascular diseases (CVD) patients.

Patients and Methods The charts of collagen-vascular diseases patients who were hospitalized and had intrapulmonary hemorrhages between 1981 and 2006 were retrospectively examined for underlying diseases, clinical and laboratory features, and treatments and outcomes.

Results Of 4,017 patients, 11 females aged 52.1±12 had total of 17 episodes of diffuse or non-diffuse intrapulmonary hemorrhage. Fourteen episodes of diffuse alveolar hemorrhage (DAH) developed in 4 microscopic polyangiitis (MPA) patients having a high MPO-ANCA level, 4 systemic lupus erythematosus (SLE) patients having a high SLEDAI score, and 1 SLE/MPA patient having a high MPO-ANCA level. Among the 9 DAH patients, 2 had complicated Goodpasture syndrome, 3 had thrombotic thrombocytopenic purpura (TTP), and 1 had disseminated intravascular coagulation. In DAH the peripheral blood hemoglobin level decreased from 9.3±2.2 (n=13) to 6.8±1.5 g/dL (n=14, p<0.0001) at 0.5±0.7 g/dL/day, and the lymphocyte count decreased from 854±424 to 462±376/μL. No patient died of DAH, including 1 who spontaneously remitted. The 3 episodes of non-DAH included 2 pulmonary aneurysm ruptures in 1 SLE patient, and 1 thromboembolism that developed in 1 SLE patient who had anti-phospholipid antibody; their SLEDAI scores were low and these remitted spontaneously.

Conclusion Of intrapulmonary hemorrhage in CVD patients, DAH developed with active MPA or SLE, upon which Goodpasture syndrome or TTP was occasionally superimposed. With DAH, the magnitude of peripheral blood Hb level decrease was approximately 0.5 g/dL/day, and the lymphocyte count decreased. No patient died of DAH.

Key words: intrapulmonary hemorrhage, diffuse alveolar hemorrhage, microscopic polyangiitis, systemic lupus erythematosus, Goodpasture syndrome, thrombotic thrombocytopenic purpura

Introduction

Intrapulmonary hemorrhage, which is sometimes associated with collagen-vascular diseases (CVD), is potentially fatal (1-3). It includes both diffuse alveolar hemorrhage (DAH) typically in association with pulmonary vasculitides and hemorrhages other than DAH (non-DAH) that develop with thromboembolism or infections. We recently treated CVD patients with DAH that developed with thrombotic thrombocytopenic purpura (TTP) or with complicated Goodpasture syndrome.

Although a decrease in the peripheral blood hemoglobin (Hb) level is typical during intrapulmonary hemorrhaging, its magnitude remains unclear. While peripheral blood total leukocyte (WBC) counts have been reported to increase, lymphocyte and platelet count changes have not been reported (1, 4, 5).

In this study, we retrospectively examined our CVD patients with intrapulmonary hemorrhage, focusing mainly their underlying and associated conditions, changes in laboratory features, and therapies and outcomes.
Table 1. Background of Patients with Intrapulmonary Hemorrhage

<table>
<thead>
<tr>
<th>Patient</th>
<th>Episode</th>
<th>Sex</th>
<th>Age (y)</th>
<th>Underlying disease (Duration) [SLEDAI score]</th>
<th>MPO-ANCA (EIA units)</th>
<th>Other complications</th>
<th>DAH or Non-DAH</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1-a</td>
<td>F</td>
<td>46</td>
<td>SLE (8 yr) [1], Thyroiditis</td>
<td>nd</td>
<td>Pulmonary aneurysms</td>
<td>Non-DAH</td>
</tr>
<tr>
<td>1-b</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Non-DAH</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>F</td>
<td>52</td>
<td>SLE (14 yr) [3]</td>
<td>nd</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>3</td>
<td>F</td>
<td>61</td>
<td>SLE (12 yr) [20]</td>
<td>wnl</td>
<td>Pneumonia, DIC</td>
<td>DAH</td>
</tr>
<tr>
<td>4</td>
<td>4</td>
<td>F</td>
<td>72</td>
<td>SLE (5 yr) [12]</td>
<td>wnl</td>
<td></td>
<td>DAH</td>
</tr>
<tr>
<td>5</td>
<td>5</td>
<td>F</td>
<td>25</td>
<td>SLE (10 yr) [57]</td>
<td>wnl</td>
<td>TTP</td>
<td>DAH</td>
</tr>
<tr>
<td>6</td>
<td>6</td>
<td>F</td>
<td>64</td>
<td>SLE (6 yr) [25], APS, SjS</td>
<td>wnl</td>
<td>Goodpasture syndrome</td>
<td>DAH</td>
</tr>
<tr>
<td>7</td>
<td>7-a</td>
<td>F</td>
<td>51</td>
<td>MPA (0 yr)</td>
<td>180</td>
<td>Bronchiectasis, B-P and A-P shunts</td>
<td>DAH</td>
</tr>
<tr>
<td>7-b</td>
<td></td>
<td></td>
<td>57</td>
<td>MPA (6 yr)</td>
<td>464</td>
<td></td>
<td>DAH</td>
</tr>
<tr>
<td>7-c</td>
<td></td>
<td></td>
<td>58</td>
<td>MPA (7 yr)</td>
<td>66</td>
<td></td>
<td>DAH</td>
</tr>
<tr>
<td>8</td>
<td>8</td>
<td>F</td>
<td>49</td>
<td>MPA (0 yr)</td>
<td>615</td>
<td>TTP</td>
<td>DAH</td>
</tr>
<tr>
<td>9</td>
<td>9</td>
<td>F</td>
<td>67</td>
<td>MPA (0 yr)</td>
<td>145</td>
<td>Goodpasture syndrome, TTP</td>
<td>DAH</td>
</tr>
<tr>
<td>10</td>
<td>10</td>
<td>F</td>
<td>71</td>
<td>MPA (6 m)</td>
<td>203</td>
<td></td>
<td>DAH</td>
</tr>
<tr>
<td>11</td>
<td>11-a</td>
<td>F</td>
<td>42</td>
<td>MPA (0 yr) MPA (5 yr) [4]</td>
<td>nd</td>
<td></td>
<td></td>
</tr>
<tr>
<td>11-b</td>
<td></td>
<td></td>
<td>43</td>
<td>MPA (1 yr)/ SLE (6 yr) [4]</td>
<td>18</td>
<td>Fracture of humerus</td>
<td>DAH</td>
</tr>
<tr>
<td>11-c</td>
<td></td>
<td></td>
<td>47</td>
<td>MPA (5 yr)/ SLE (10 yr) [16]</td>
<td>wnl</td>
<td></td>
<td>DAH</td>
</tr>
<tr>
<td>11-d</td>
<td></td>
<td></td>
<td>48</td>
<td>MPA (6 yr) SLE (11 yr) [8]</td>
<td>wnl</td>
<td>CMV esophagitis</td>
<td>DAH</td>
</tr>
</tbody>
</table>


Patients and Methods

Of the CVD patients who were admitted to our hospital from 1981 to 2006, patients who had intrapulmonary hemorrhage were retrospectively studied for sex, age, underlying disease and complications, clinical features, radiographic and laboratory findings, treatment and outcome. Intrapulmonary hemorrhage was diagnosed based on bloody bronchoalveolar lavage fluid (BALF), hemosiderin-laden alveolar macrophages in BALF or transbronchial lung biopsy (TBLB) specimens, autopsy findings, or massive hemoptysis. DAH was diagnosed on the basis of clinical features including diffuse alveolar filling patterns in chest images with substantial Hb level decreases without any focal hemorrhagic sites, and increased alveolar-arterial oxygen difference (A-aDO2), and pathological observation if available. Diagnoses of underlying diseases were based on the Japanese Ministry of Health Labor and Welfare criteria for micropolyangiitis (MPA) (6), and on American Rheumatism Association criteria for systemic lupus erythematosus (SLE) (7). SLE disease activity was evaluated by the SLE Disease Activity Index (SLEDAI) score (8). Goodpasture syndrome was diagnosed when patients developed both pulmonary and renal diseases and had anti-glomerular basement membrane antibody (anti-GBM) (9-11). TTP was diagnosed when a patient had more than four features among the pentad of microangiopathic hemolytic anemia, consumptive thrombocytopenia, fluctuating neurological abnormalities, renal dysfunction, and fever (12).

Numeric data are shown as mean±standard deviation (S. D.). The statistical comparisons were made by paired and unpaired t tests.

Results

Seventeen episodes of intrapulmonary hemorrhage were observed in 11 patients among a total of 4,017 hospitalized patients. The prevalence rate was 1.8% among total hospitalized patients, and 12.5% among total hospitalized MPA patients, respectively. All 11 patients were female, and episodes occurred at the age of 52.1±12.8 years (range, 25-72 years) (Table 1).

Non-DAH episodes

Patient 1 (SLE) had acute massive hemoptysis caused by ruptures of preexisting pulmonary aneurysms two times. Patient 2 (SLE) with anti-phospholipid antibody developed substantial hemoptysis with chest pain and high fever caused by pulmonary thromboembolism. SLEDAI scores were low in these 2 patients with non-DAH (Table 1). The peripheral blood Hb level decreased from 12.6±1.2 to 10.8±2.2 g/dL at 0.3±0.4 g/dL/day (n=3) (Fig. 1). Platelet, WBC and lymphocyte counts and serum C-reactive protein (CRP) levels did not change. These patients recovered only with supportive therapy.

DAH episodes

Fourteen DAH episodes developed in 9 patients. The major underlying diseases were SLE and MPA (Table 1). DAH was diagnosed on autopsy in Patient 3 (SLE), on transbronchial lung biopsy in Patient 4 (SLE), 7 (MPA), 8 (MPA) and 10 (MPA), by bronchoalveolar lavage in Patient 5 (SLE), 9 (MPA) and 11 (MPA/SLE), and by clinical findings including hemoptysis and infiltrates in Patient 6 (SLE). The second DAH episode of Patient 11 (MPA/SLE) was noted by chance on tracheal tube insertion for a bone fracture operation. Eight patients other than Patient 11 had a fever. XP/CT revealed mottled ground-glass opacities (GGOs) distributed diffusely in the lungs (Fig. 2); GGOs were most severe in Patient 6 (SLE) who had complicated Goodpasture syndrome.

SLE was diagnosed at least 5 years previously in all 5 patients, and the SLEDAI score became high at DAH onset (Table 1).

All 4 MPA patients had already ongoing signs or symptoms of MPA of 6 episodes, before a high titer of serum myeloperoxidase-anticytoplasmic antibody (MPO-ANCA)
Figure 1. Peripheral blood hemoglobin level and lymphocyte count before and at onset of intrapulmonary hemorrhage. DAH means diffuse alveolar hemorrhage. Bars show mean±S.D.

Figure 2. a: Chest CT of Patient 4 at hemorrhage onset. b: Plain chest X-P (b-1) of Patient 8 taken two months before the CT scan (b-2).

(279±213 EIA units, n=6, Table 1) was noted. Patient 8 (MPA) had chronic severe anemia and multiple wandering lung infiltrates for about six months before hysterectomy specimen showed MPA (Fig. 2). Patient 10 already developed MPA nephropathy five months prior to DAH. Patient 11 (MPA/SLE) had interstitial pneumonitis in addition to lupus nephritis that was confirmed by biopsy five years earlier.

**Goodpasture syndrome and TTP complicated with DAH**

Goodpasture syndrome and TTP were complicated in 2
and 3 patients, respectively (Table 1).

Patient 5 (SLE) had exacerbation of SLE with fever, urinary abnormalities, and increased anti-ds-DNA antibody and decreased complement levels. Within two weeks, the peripheral blood schistocyte level increased to 5.6% of the total RBC count, the serum haptoglobin level decreased, and neurological disorders including fluctuating deafness, severe headache, and cramps developed, with a resulting diagnosis of TTP. Renal failure also developed simultaneously with DAH.

In Patient 6 (SLE), Goodpasture syndrome with a >300 EU anti-GBM antibody level was noted just before apparent intrapulmonary hemorrhage developed.

In Patient 8 (MPA) whose hysterectomy revealed anagistis, 2.4% schistocytes were already noted before starting pulsed steroid and intravenous cyclophosphamide (IVCY) therapy. One and a half months later, acute microangiopathic hemo-lytic anemia with schistocyte level of 6.5% was observed, and thrombocytopenia, renal dysfunction, and a high fever developed. Fresh frozen plasma infusion rescued her from TTP.

In Patient 9 (MPA), Goodpasture syndrome was revealed by renal biopsy when anti-GBM antibody level was 220 EU, and concurrently, TTP with a schistocyte level of 7.4% were noted after DAH.

ADAMTS13 activity was only slightly decreased (26% in Patient 5 and 48% in Patient 9).

**Laboratory findings in DAH patients**

Regarding the data analysis, the blood cell counts prior to the onset of hemorrhage in Patient 8 (MPA), who had repeated blood transfusions, were excluded. In DAH patients, the Hb level decreased from 9.3±2.2 (n=13) to 6.8±1.5 g/dL (n=14, p<0.0001) at 0.5±0.7 g/dL/day (Fig. 1); from 10.7±2.2 (n=5) to 7.1±1.8 g/dL (n=6, p<0.005) at 0.3±0.4 g/dL/day in MPA patients, and from 8.4±1.3 to 6.0±1.0 g/dL (n=4, p<0.05) at 1.1±1.1 g/dL/day in SLE patients. The decrease in Hb level in Patient 11 (MPA/SLE) was from 8.6±2.2 to 7.0±1.3 g/dL at 0.2±0.2 g/dL/day (n=4). The Hb level at the onset of DAH was significantly lower than that at non-DAH (p<0.005).

In the 4 SLE patients with DAH, the platelet count decreased from 26.6±7.1x10^9 to 3.2±0.8x10^9/μL (p<0.05), and returned to prehemorrhage levels on recovery. The platelet count did not change in MPA patients.

The WBC count increased from 7,140±2,528 (n=5) to 8,083±3,116/μL (n=6, p<0.05) in MPA patients with DAH, in contrast, it decreased from 7,625±5,976 to 7,200±2,652/μL (n=4, p=0.8347) in SLE patients. The WBC count increased from 6,700±4,402 to 11,400±5,755/μL (n=4, p<0.05) in an SLE/MPA patient.

The peripheral blood lymphocyte count in patients with DAH decreased from 854±424 (n=13) to 462±376/μL (n=12, p<0.001) (Fig. 1).

The serum C-reactive protein (CRP) level reached as high as 10.5±6.3 mg/dL in DAH (n=14, range 2.7-22.1), even when excluding the data of Patient 3 (SLE) with severe pneumonia.

MPO-ANCA and anti-GBM levels were as described above.

Hypoxemia at 67.4±16.9 Torr (n=14) and an increased A-aDO₂ of 64.3±61.1 Torr (n=14) were observed at the onset of hemorrhage. DLco measured 28 days after DAH onset in Patient 7 was 124.3% of the predicted value in contrast to 52.5% before the onset; in Patient 10, it was 133.6% at 7 days after the onset in contrast to 65.4% before. DLco decreased again concomitantly with recovery from hemorrhage.

Hematuria or albuminuria had already been observed in 7 patients with DAH [Patients 3 (SLE), 5 (SLE), 6 (SLE), 7 (MPA), 8 (MPA), 10 (MPA), and 11(MPA/SLE) prior to hemorrhage onset. Only in patients 4 (SLE) and 9 (MPA), DAH preceded renal dysfunction, the latter of whom had later complicated Goodpasture syndrome.

**Treatments for and outcomes of DAH**

Blood transfusions were required for 4 DAH episodes in 4 patients (Table 2).

Patient 3 (SLE/DIC), who required mechanical ventilation, died of respiratory failure. Autopsy findings included diffuse alveolar hemorrhage with *Pseudomonas* pneumonia and lupus nephritis.

Two DAH episodes in Patient 11 (MPA/SLE) remitted spontaneously (Table 2). Excluding these 3 episodes in 2 patients, 11 episodes of DAH were treated with intravenous pulsed steroids and/or intravenous pulsed or daily oral cyclophosphamide (Table 2). Responses were favorable, though mechanical ventilation was required in Patients 5 (SLE/TTP) and 6 (SLE/Goodpasture syndrome) (Table 2). Patient 5 (SLE/TTP) recovered from DAH after repeated plasma infusions and phereses; however, multiple brain infarctions were observed with increasing schistocyte count and she eventually died of multiorgan failure. Patient 6 (SLE/Goodpasture syndrome) recovered from DAH after hemodialysis.

In the 13 remitted DAH episodes, lung opacities and hypoxemia clearly improved within 65 days and 125 days, respectively. However, in patients 7 (MPA), 8 (MPA), and 11 (MPA/SLE), who had preexisting pulmonary symptoms as described above, the lung fibrosis worsened. No patients died directly of DAH.

**Discussion**

In this study, MPA patients who developed DAH showed a substantially higher MPO-ANCA level than the normal upper limit (9.0 U/mL), and SLE patients who had it showed a high SLEDAI score, as defined as ‘severe’ or ‘active’ in the literature (13, 14). Moreover, concurrently developed Goodpasture syndrome with a clearly positive anti-GBM antibodies, or TTP with clearly apparent schistocytes were observed. DAH developed in MPA or Goodpasture syndrome.
syndrome, hardly being differentiated from each other, was reported occasionally (15, 16). Goodpasture syndrome or positive GBM has been reported in several CVD cases (17-20).

Three patients had TTP when DAH developed. Although DAH in Patient 5 (SLE) could be related to active SLE, concurrent clear development of the TTP pentad was highly indicative of its association with DAH. TTP has so far been thought to spare the lungs, but recent autopsy reports showed hyaline thrombi, edema, and hemorrhage in the lungs of TTP patients (1, 3, 21-25). Recently, in contrast to that deficient ADAMTS13 activity causes idiopathic or hereditary TTP, endothelial involvement has been shown to contribute to TTP pathogenesis in CVD patients (26, 27).

Despite the scarcity of patients with MPA complicated with TTP, several cases that developed TTP have been reported who showed a high MPO-ANC Atiter or small arteritis and arteriolitis, although they were defined as having polyarteritis nodosa (28-30). MPA and SLE involving endothelial cells, and endothelial pathology could relate to TTP development, and could cause DAH. One patient in this study was diagnosed as having both SLE and MPA. Whenever a CVD patient develops DAH, ANCA, anti-GBM and tests for TTP should be properly examined.

The Hb level decrease during DAH was first shown by this study to be around 0.5 g/dL/day, resulting in the level of 6.8 g/dL, that was lower than the 8.1±1.8 g/dL observed in 29 cases of MPA with DAH (31).

A clear decrease in lymphocyte count at DAH onset was also shown for the first time in this study. The influence of steroids or immunosuppressants was not likely responsible, as the doses were not changed in SLE patients, and no therapy was performed in MPA patients prior to DAH onset. In Wegener’s granulomatosis, T cell participation in the active phase has been suggested from lower lymphocyte counts at diagnosis and relapse than during remission (32). Initial lesions of ANCA-associated vasculitis are thought to be polymorphonuclear leukocyte-dependent, with subsequent T cell recruitment and infiltration occurring as a secondary event (33). Although this phenomenon should be further examined, lymphocyte participation might be a key to elucidating the mechanism underlying DAH.

Decreased platelet counts only in SLE with DAH could indicate SLE exacerbation as shown by a high SLEDAI score.

Pulmonary diffusion capacity was reported as unlikely to increase when tested more than 48 hours after DAH development (1, 2). However, our observations showed that testing DLco would be useful even when carried out considerably later.

Pulsed steroids and/or cyclophosphamide were mostly effective for DAH in this study. No patients died of DAH itself, although Patient 3 died of DAH caused by DIC complicated with pneumonia. However, in contrast to that MPA patients survived even after renal failure required hemodialysis, a SLE patient died of multi-organ failure after surviving DAH, and another SLE patient died of pneumonia. Preexisting immunosuppression might relate to a poor outcome as indicated in the literature (34).

DAH in a SLE/MPA patient twice remitted spontaneously, including one observed by chance during tracheal intubation. She already had pulmonary fibrosis. Patient 8 (MPA), who had recurrent spontaneous remission of DAH, also had lung fibrosis. Recurrent clinical or subclinical DAH may in time cause pulmonary fibrosis, at least in MPA of which feature frequently includes it. Subclinical alveolar bleeding in pulmonary vasculitides is also known to occur in Wegener’s granulomatosis and Churg-Strauss syndrome (35). The spontaneous remissions suggest that DAH may not always require intensive therapy.

Table 2. Duration from Symptom Onset to Diagnosis of Intrapulmonary Hemorrhage, Treatments and Outcome

<table>
<thead>
<tr>
<th>Patient</th>
<th>Symptom Onset to DAH</th>
<th>Treatment</th>
<th>Outcome</th>
<th>Diagnosis</th>
<th>Remission</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>DAH</td>
<td>NSAIDs</td>
<td>DAH</td>
<td>NSAIDs</td>
<td>DAH</td>
</tr>
<tr>
<td>2</td>
<td>MPA</td>
<td>NSAIDs</td>
<td>MPA</td>
<td>NSAIDs</td>
<td>MPA</td>
</tr>
<tr>
<td>3</td>
<td>Pulmonary Fibrosis</td>
<td>NSAIDs</td>
<td>Pulmonary Fibrosis</td>
<td>NSAIDs</td>
<td>Pulmonary Fibrosis</td>
</tr>
<tr>
<td>4</td>
<td>Pulmonary Fibrosis</td>
<td>NSAIDs</td>
<td>Pulmonary Fibrosis</td>
<td>NSAIDs</td>
<td>Pulmonary Fibrosis</td>
</tr>
<tr>
<td>5</td>
<td>Pulmonary Fibrosis</td>
<td>NSAIDs</td>
<td>Pulmonary Fibrosis</td>
<td>NSAIDs</td>
<td>Pulmonary Fibrosis</td>
</tr>
<tr>
<td>6</td>
<td>Pulmonary Fibrosis</td>
<td>NSAIDs</td>
<td>Pulmonary Fibrosis</td>
<td>NSAIDs</td>
<td>Pulmonary Fibrosis</td>
</tr>
<tr>
<td>7</td>
<td>Pulmonary Fibrosis</td>
<td>NSAIDs</td>
<td>Pulmonary Fibrosis</td>
<td>NSAIDs</td>
<td>Pulmonary Fibrosis</td>
</tr>
<tr>
<td>8</td>
<td>Pulmonary Fibrosis</td>
<td>NSAIDs</td>
<td>Pulmonary Fibrosis</td>
<td>NSAIDs</td>
<td>Pulmonary Fibrosis</td>
</tr>
<tr>
<td>9</td>
<td>Pulmonary Fibrosis</td>
<td>NSAIDs</td>
<td>Pulmonary Fibrosis</td>
<td>NSAIDs</td>
<td>Pulmonary Fibrosis</td>
</tr>
<tr>
<td>10</td>
<td>Pulmonary Fibrosis</td>
<td>NSAIDs</td>
<td>Pulmonary Fibrosis</td>
<td>NSAIDs</td>
<td>Pulmonary Fibrosis</td>
</tr>
<tr>
<td>11</td>
<td>Pulmonary Fibrosis</td>
<td>NSAIDs</td>
<td>Pulmonary Fibrosis</td>
<td>NSAIDs</td>
<td>Pulmonary Fibrosis</td>
</tr>
<tr>
<td>12</td>
<td>Pulmonary Fibrosis</td>
<td>NSAIDs</td>
<td>Pulmonary Fibrosis</td>
<td>NSAIDs</td>
<td>Pulmonary Fibrosis</td>
</tr>
</tbody>
</table>

DAH: diffuse alveolar hemorrhage; NSAIDs: non-steroidal anti-inflammatory drugs; MPA: microscopic polyangiitis; MPE: monoclonal protein; TTP: thrombotic thrombocytopenic purpura; DIC: disseminated intravascular coagulation; AR: acute respiratory distress syndrome; CV: cyclophosphamide; IVCC: intravenous cyclophosphamide; TTP: thrombotic thrombocytopenic purpura; MPA: microscopic polyangiitis; AR: acute respiratory distress syndrome; CV: cyclophosphamide; IVCC: intravenous cyclophosphamide; TTP: thrombotic thrombocytopenic purpura; MPA: microscopic polyangiitis; AR: acute respiratory distress syndrome.
In conclusion, intrapulmonary hemorrhage in CVD patients included non-DAH and DAH. DAH developed with active MPA or SLE, upon which Goodpasture syndrome or TTP was sometimes superimposed. In DAH, the magnitude of peripheral blood Hb level decrease was approximately 0.5 g/dL/day, and the lymphocyte count clearly decreased. Pulsed steroid and cyclophosphamide therapies were effective for DAH, although spontaneous remission may also occur.

Acknowledgement
We thank for every doctor in charge of the patients in this study.

References

32. Izzedine H, Cacoub P, Launay-Vacher V, Bagnis C, Deray G.

