**Successful Treatment of Systemic Lupus Erythematosus and Pulmonary Hypertension with Intravenous Prostaglandin I₂ Followed by Its Oral Analogue**

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**Abstract**

Systemic lupus erythematosus (SLE) is sometimes reported to complicate fatal pulmonary hypertension. A 46-year-old woman, with a ten-year history of SLE and pulmonary hypertension, was admitted to our hospital complaining of dyspnea and chest pain. She suffered pulmonary hemorrhage and after steroid pulse therapy, she underwent continuous intravenous infusion of epoprostenol (prostaglandin I₂) with corticosteroid for four weeks, which reduced the pulmonary artery pressure and resistance. Following the successful treatment, beraprost sodium, an oral PGI₂ analogue, was given and it maintained pulmonary hypertension remittance for four years. (Internal Medicine 39: 320-323, 2000)

**Key words:** epoprostenol sodium, beraprost sodium, vasoreactivity

**Case Report**

A 46-year-old woman who had SLE associated with pulmonary hypertension (PH) was admitted to our hospital, complaining of dyspnea and right chest pain. Ten years earlier, she had presented with exertional dyspnea, photosensitivity, discoid erythematosus and Raynaud’s phenomenon. Laboratory data showed leukopenia (1,800/mm³), positive antinuclear antibody (1:160), positive anti-dsDNA antibody 34 U/ml (normal <10) and a low level of CH₅₀ 17.6 U/ml (30.0< normal <40.0) and C3 36 mg/dl (60< normal <116). Markers for coagulation and fibrinolysis showed normal values including fibrinogen (314 mg/dl) and fibrinogen degradation products (FDP: <4 µg/ml). A diagnosis of SLE was made according to the criteria. Chest X-rays demonstrated enlarged central pulmonary arteries with a prominent right ventricular out-flow tract (Fig. 1A), and right-heart catheterization revealed elevation of pulmonary artery pressure (PAP) and pulmonary vascular resistance (PVR) (Table 1) with normal pulmonary capillary wedge pressure. Obvious pulmonary thromboembolism was not recognized on pulmonary angiography (Fig. 1B). She was suspected to have idiopathic precapillary pulmonary hypertension. Administration of prednisolone (PSL) was started, and then she was treated with 10 mg/day of PSL as a maintenance dose, resulting in remission of SLE for 10 years.

On the present admission, laboratory data showed moderate inflammation (C-reactive protein 2.77 mg/dl, Erythrocyte sedimentation rate 48 mm/hour) and mild reduction in hemoglobin (9.8 to 8.0 g/dl). Fibrinogen was 532 mg/dl and FDP was 5.4 µg/ml. Arterial blood gas analysis revealed PaO₂ of 62.5 mmHg, PaCO₂ of 28.8 mmHg, and pH of 7.48. Chest X-ray and computed tomography showed right pleural effusion and multiple opacities in right lower lobe (Fig. 2A, B) without the evidence of stenosis/webs/occlusion of pulmonary arteries or localized areas of decreased attenuation and vascularity sharply marginated from adjacent areas on CT. On
Figure 1. Chest X-ray (A) and pulmonary angiography (B) on first admission in 1984. Chest X-ray showed a prominent right ventricular out-flow tract (A) and major-vessel thromboembolism was not shown on pulmonary angiography (B).

Table 1. Treatment and Hemodynamic Changes: Favorable Hemodynamic Effects of Epoprostenol Followed by Beraprost were Obtained

<table>
<thead>
<tr>
<th>Treatment*</th>
<th>PAP mmHg (mean)</th>
<th>PVR dyn • sec/cm²</th>
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<tbody>
<tr>
<td>Jul. ’84 none</td>
<td>50/27 (38)</td>
<td>569</td>
</tr>
<tr>
<td>Aug. ’85 PSL 20 mg</td>
<td>40/20 (31)</td>
<td>459</td>
</tr>
<tr>
<td>Mar. ’94 after pulse therapy</td>
<td>42/23 (34)</td>
<td>319</td>
</tr>
<tr>
<td>acute effect of epoprostenol</td>
<td>41/24 (33)</td>
<td>310</td>
</tr>
<tr>
<td>Apr. ’94 4-week epoprostenol+PSL 20 mg</td>
<td>28/14 (22)</td>
<td>197</td>
</tr>
<tr>
<td>Feb. ’95 beraprost 120 µg+PSL 10 mg</td>
<td>36/13 (25)</td>
<td>220</td>
</tr>
</tbody>
</table>

acute effect of epoprostenol: just after the commencement of 10 ng/kg/min epoprostenol administration; 4-week epoprostenol: after 4-week administration of 8 ng/kg/min epoprostenol; PAP: pulmonary artery pressure; PVR: pulmonary vascular resistance, PSL: prednisolone.

echocardiography, systolic PAP was measured as 67 mmHg. Perfusion lung scintigraphy showed a defect in the right lower field (Fig. 2C). Considering the CT and the scintigraphy findings, she was diagnosed as having pulmonary hemorrhage associated with SLE. Pulse therapy (methyl-PSL 1,000 mg/day for 3 successive days), followed by 20 mg/day of PSL, was started. One week later, she complained of hemosputum and a second attack of pulmonary hemorrhage was suspected. Pulse therapy (methyl-PSL 500 mg/day for 3 successive days), followed by 20 mg/day of PSL, was again started, and chest abnormal shadows disappeared within a month.

Epoprostenol sodium (prostaglandin I₂; PGI₂) was adopted to remit PH as a clinical trial for pulmonary hypertension after informed consent. She underwent continuous intravenous epoprostenol at the rate of 8 ng/kg/min with 20 mg/day of PSL for 4 weeks. Although the acute effect of epoprostenol was unsatisfactory (Table 1; cardiac index and pulmonary capillary wedge pressure were 5.16 l/min/m² and 6 mmHg, respectively, before the epoprostenol administration and cardiac index was unchanged, 5.13 l/min/m², after the administration), the catheterization, at the endpoint of 4-week epoprostenol administration, revealed a favorable chronic effect: PAP 28/14 (mean 22) mmHg (−35.3%), PVR 197 dyn • sec/cm² (−38.3%). Following the treatment, 120 µg/day of beraprost sodium, oral
PGI₂ analogue, was started. Ten months later, follow-up catheterization was performed, which revealed the lasting favorable hemodynamic effect of beraprost: PAP 36/13 (mean 25) mmHg, PVR 220 dyn  sec/cm⁵. During treatment with epoprostenol and beraprost, a dramatically-increased exercise tolerance was noted, although she sometimes had a headache, knee-joint pain and diarrhea. The remittance of pulmonary hypertension has continued until now.

**Discussion**

Various types of treatment for PH associated with SLE have been reported, such as immunosuppressive therapy, corticosteroid pulse therapy or heart/lung transplantation (2–4). In many cases, however, this condition is refractory and the mortality is high (5). The pathogenesis includes pulmonary thromboembolism, pulmonary fibrosis or pulmonary vasculitis, that is an idiopathic lesion. In one report, most patients with SLE and PH were classified as idiopathic (5). In several autopsied cases, plexogenic pulmonary arteriopathy was revealed, which is characteristic of primary pulmonary hypertension (PPH) (6), and the idiopathic PH may be very similar to PPH. Although the differential diagnosis between chronic pulmonary thromboembolism (CPTE) and idiopathic pulmonary hypertension is sometimes difficult, the present case was diagnosed as having idiopathic pulmonary hypertension rather than CPTE, due to the lack of evidence of arterial stenosis/webs and localized areas of decreased attenuation and vascularity sharply marginated from adjacent areas on CT (7), and the lack of evidence of coagulation and fibrinolysis on laboratory data at anytime. The remittance of pulmonary hemorrhage only by administration of corticosteroid without anticoagulation therapy on the second admission also supported the diagnosis. Data on lupus anticoagulant and antiphospholipid antibody may have supported our diagnosis, but we failed to examine them.

PGI₂ is a potent vasodilator and inhibitor of platelet aggregation (8), in addition, it has a protective action against increased pulmonary vascular permeability in experimental acute pulmonary edema as we previously demonstrated in dogs (9). For PPH, continuous epoprostenol (PGI₂) has been shown to improve hemodynamic abnormalities and survival of the patients (10). Beraprost sodium is an oral PGI₂ analogue, which has similar effects to PGI₂. A recent report described that in 10 PPH patients treated with beraprost for two months, the average reduction rate of PAP and PVR was 12% and 26%, respectively (11), and oral administration of beraprost showed beneficial effects on the survival of outpatients with PPH (12). However, it is said that oral vasodilators should not be used without evidence of a patient’s vasoreactivity to acute challenge, while therapy with epoprostenol may be initiated without an acute challenge, since long-term therapy with epoprostenol produces sustained hemodynamic responses even in patients who have little or no response to acute infusion (8).

The present patient is the first case of SLE with PH who was successfully treated with epoprostenol followed by beraprost. Although this case was treated by these vasodilators with corticosteroid, epoprostenol and beraprost, rather than simply corticosteroid, this combination was likely more responsible for the remittance of pulmonary hypertension, since conventional treatment for pulmonary hypertension associated with SLE is widely accepted to be unsatisfactory (13) and corticosteroid was not effective before the administration of epoprostenol in this case. Interestingly, this case showed an unsatisfactory effect of epoprostenol in acute challenge, while there was a significant response after 4-week administration. Continuous epoprostenol sometimes causes serious complications in its delivery system, such as sepsis or pump malfunction, and in addition, the cost of epoprostenol is high (10). Thus, treatment relaying from intravenous epoprostenol to oral beraprost with evidence of the patient’s vasoreactivity to short-term epoprostenol, not necessarily to acute challenge, may be favorable from the cost-benefit viewpoint and should come into
PGI₂ for SLE with Pulmonary Hypertension

consideration for this condition.

References