Glomerulopathy due to chronic infection of *Propionibacterium acnes* in a patient with Felty’s syndrome

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Introduction

Felty’s syndrome, first reported by Felty in 1924 [1], is well known as a trio of rheumatoid arthritis, splenomegaly, and neutropenia, which occurs in 1-5% of patients with rheumatoid arthritis. The nephropathy associated with Felty’s syndrome is very rare; we found only one previous case in the literature [2]. Although the pathogenesis of Felty’s syndrome is still unclear, the glomerular lesion of our patient was similar to that of systemic infection. Extensive bacterial culture revealed the presence of *Propionibacterium acnes* (*P. acnes*) in blood and bone marrow fluid at several different occasions. In this report, we discuss the relationship between *P. acnes* infection and nephropathy with a review of the literature.

Case report

A 53-year-old Japanese man with arthritis and urticarial eruption was admitted to Akita University Hospital on May 10, 1994, with proteinuria and haematuria. Twelve years before admission, he experienced polyarthralgia, and swelling and exanthema on his face and extremities. Despite visits to several hospitals, the cause of his symptoms remained unclear. When he was admitted to a local hospital for the treatment of a generalized urticaria-like skin lesion in 1993, he was found to have anaemia, proteinuria, and haematuria. Renal biopsy was performed on February 25, 1994. Light microscopic study revealed focal segmental sclerosis with reticular structure of mesangial matrix (Figure 1). An immunofluorescence study showed that the mesangial and loop granular pattern of C3 was 2(+) (Figure 2). Stainings for IgG, IgA, IgM, C1q, and fibrinogen were all negative. Electron-dense deposits were present in the mesangial area (Figure 3). He was referred to our hospital.

Physical examination on admission revealed generalized scattered pigmentation, urticarial eruption, and subcutaneous nodules on his right elbow. Blood pressure was 130/80 mmHg, pulse rate was 85/min with regular rhythm, and body temperature 35.8°C. Liver and spleen were palpable three and two finger-breadths below the costal margins, respectively. No abnormal signs were observed in the lymph nodes, lungs, or heart. Relevant laboratory data were: erythrocyte sedimentation rate 83 mm/h; red blood cell count 3490000/µl; haematocrit 37.2%; haemoglobin 7.5 g/dl; leukocyte count: 3200/µl; platelet count: 593000/µl; blood urea nitrogen (BUN): 11 mg/dl; serum creatinine: 7.3 g/dl; total protein: 7.3 g/dl; albumin: 3.8 g/dl; C-reactive protein: 4.0 mg/dl (normal range: 0–0.5); rheumatoid factor: 1(+). Anti-nuclear antibody was 80-fold positive (normal range: <40-fold) with homogenous pattern. Complement C3 was 70 mg/dl (normal range: 60–116), C4 was 53 mg/dl (normal range: 15–44), and CH50 was 43 U/ml (normal range: 30.0–40.0). Immune complex (C1q) was 1.5 µg/ml. Anti-granulocyte-specific nuclear antibody was positive on immunofluorescence study. Urinalysis showed 2+ for protein (0.7 g/day) and 1+ for blood on dipstick examination. Bone marrow aspirate showed a decreased number of mature neutrophils, suggesting maturation arrest. Chest X-ray, electrocardiogram, and ultrasonic cardiogram revealed no abnormalities. X-ray of proximal interphalangeal joints of bilateral fingers and toes showed narrowing, destruction and deformity, compatible with rheumatoid arthritis. Skin biopsy of the urticarial lesion on the left forearm demonstrated accumulation of destroyed polymorphonuclear leukocytes around the vessels (leukocytoclastic vasculitis) (Figure 4).

We diagnosed of Felty’s syndrome. Because of the similarity of the glomerular lesions to systemic infec-
Fig. 1. Light microscopic findings of renal biopsy specimen. (A) Segmental sclerosis is observed in glomeruli. It is compatible with a lesion of infectious origin (such as Lohlein's nephritis), PAS × 200. (B) Under high magnification, PAS × 400. (C) In the centre of the glomerulus, reticular structure of the mesangial area are observed (arrows). (PAM × 400.)

Fig. 2. Immunofluorescence micrograph demonstrates granular staining of C3 on the mesangial area and peripheral glomerular capillary wall, × 400.

tion, we extensively examined the bacterial cultures of blood and bone marrow fluid several times. *Propionibacterium acnes* (*P. acnes*) was consistently detected in blood and bone marrow fluid.

From June 1, 1994 we administered prednisolone (30 mg/day) for vasculitis on the skin; the arthralgia, itching, and urticaria ameliorated remarkably in parallel with the increased number of peripheral white blood cells. Several kinds of antibiotics (cefa zolin, ciprofloxacin, imipenem/cilastatin, and minocycline) were added to prednisolone in order to kill the bacteria; however, we had to stop treatment with these antibiotics after the occurrence of a hypersensitive reaction. After discharge from the hospital on June 16, 1994, he visited the clinic regularly. However, when prednisolone was reduced, the urticarial lesion recurred. Proteinuria (~1.0 g/day) and haematuria have persisted despite the administration of 20 mg/day prednisolone.
Pathogenesis of *Propionibacterium acnes* infection

Fig. 3. Electron micrographic findings. Deposition of electron-dense deposits are observed in the mesangial area (arrowheads). Bar 2 μm.

Ca-channel blocker for elevated blood pressure was required. His last laboratory data showed that BUN was 26 mg/dl, serum creatinine was 1.3 mg/dl, C-reactive protein was 0.7 mg/dl and rheumatoid factor was negative.

**Discussion**

The findings of morning stiffness, pain and swelling in more than two joints, positive rheumatoid factor, rheumatoid nodules and bone destruction on hand X-ray fulfilled the diagnostic criteria for rheumatoid arthritis as defined by the American Rheumatism Association in 1987 [3]. The patient’s splenomegaly and leukopenia suggested Felty’s syndrome, confirmed by the detection of anti-granulocyte-specific nuclear antibody, known as a specific antibody for Felty’s syndrome [4].

Compared with the frequency of kidney involvement in patients with rheumatoid arthritis alone, glomerular abnormality is very rare in Felty’s syndrome. Maciej *et al.* [2] reported only one patient with mesangioliferative glomerulonephritis in Felty’s syndrome, and they commented that the glomerulonephritis was due to deposition of immune complexes by pneumococcal septic arthritis. In our case, we thought that the renal lesions such as segmental scar on light microscopy, immunofluorescent staining of C3 along the glomerular capillary wall, and electron dense deposits in mesangial area originated from any infection (Löhlein’s nephritis [5]). The skin biopsy revealed leukocytoclastic vascul-
P. aenes is needed. Patients with Felty's syndrome are known to have high susceptibility to bacterial infection due not only to the decreased number of white cell counts, but also to a disturbed function of neutrophils. These abnormalities suggest that P. acnes infection plays an important role as an agent of opportunistic infection. Although this combination of a chronic infection of P. acnes and glomerulopathy in Felty's syndrome may be purely coincident, the importance of bacterial infection remains to be clarified.

### References

1. Felty AR. Chronic arthritis in the adult, associated with splenomegaly and leukopenia; a report of five cases of an unusual clinical syndrome. *Johns Hopkins Hosp Bull* 1924; 35: 16-20

### Table 1. Case reports of renal dysfunction associated with *P. acnes* infection

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Sex</th>
<th>Age</th>
<th>Primary disease</th>
<th>Creatinine (mg/dl)</th>
<th>Proteinuria</th>
<th>Histology</th>
<th>Treatment</th>
<th>Outcome of renal function</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>22</td>
<td>Cerebral cyst (A-V shunt)</td>
<td>1.7</td>
<td>9 g/day</td>
<td>MPGN</td>
<td>antibiotics (shunt removal)</td>
<td>Improved</td>
<td>[6]</td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>15</td>
<td>Medulloblastoma (A-V shunt)</td>
<td>2.2</td>
<td>2(+)</td>
<td>ND</td>
<td>antibiotics (shunt removal)</td>
<td>Improved</td>
<td>[7]</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>15</td>
<td>Medulloblastoma (A-V shunt)</td>
<td>1.2</td>
<td>2(+)</td>
<td>ND</td>
<td>antibiotics (shunt replacement)</td>
<td>Improved</td>
<td>[8]</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>27</td>
<td>Pineal tumor (A-V shunt)</td>
<td>8.8 g/day</td>
<td>4(+)</td>
<td>MPGN</td>
<td>antibiotics (shunt replacement)</td>
<td>Improved</td>
<td>[8]</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>35</td>
<td>Endocarditis</td>
<td>4(+)</td>
<td>ND</td>
<td>antibiotics (valve replacement)</td>
<td>Improved</td>
<td>[13]</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>M</td>
<td>28</td>
<td>Pineal tumor (A-V shunt)</td>
<td>8.3</td>
<td>4(+)</td>
<td>MPGN</td>
<td>antibiotics (shunt removal)</td>
<td>Slightly improved</td>
<td>[9]</td>
</tr>
<tr>
<td>7</td>
<td>M</td>
<td>17</td>
<td>Hydrocephalus (A-V shunt)</td>
<td>2.2</td>
<td>9 g/day</td>
<td>ND</td>
<td>antibiotics (shunt removal)</td>
<td>Improved</td>
<td>[11]</td>
</tr>
<tr>
<td>8</td>
<td>M</td>
<td>53</td>
<td>Felty's syndrome</td>
<td>1.1</td>
<td>0.7 g/day</td>
<td>§</td>
<td>ND</td>
<td>No change</td>
<td>Current case</td>
</tr>
</tbody>
</table>

§: focal segmental sclerosis and reticular change of mesangium. ND: not done.
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