A Case of Chronic Renal Failure Followed by Cold Agglutinin Due to *Mycoplasma pneumoniae* Infection

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Dear Sir,

It is well known that cold agglutinin may be induced by the effect of autoimmune mechanisms [1, 2], and then hemoglobinuria and skin pain caused by disorders of the peripheral capillaries but in frequently hemolytic anemia are observed associated with cold sensitization [3]. There are three kinds of antigens against agglutinin such as I, i and Pr located on the surface of erythrocytes [4, 5], and hemolysis is induced by the activation of binding to the complement. Cold agglutinin might be formed in various diseases [6, 7] such as idiopathic, malignant lymphoma, neoplasms, and infections [8, 9] mainly such as *Mycoplasma pneumoniae*, cytomegalovirus and Epstein-Barr virus.

The presence of warm agglutinin antibody in the patient with chronic renal failure (CRF) has been reported earlier. However, this is the first case of the cold agglutinin associated with *M. pneumoniae* infection appearing in a patient with CRF derived from membranoproliferative glomerulonephritis (MPGN).

A 31-year-old male had been treated for MPGN at another hospital since June 1979. When he came to our department in July 1987, he only had CRF with the following data: daily urinary excretion of protein was 7–10 g and the serum creatinine was 4.8 mg/dl. In January 1988, he complained of a sore throat, general malaise, cough, fever (37–38 °C) and the exacerbation of azotemia, and so he was admitted for further examinations. On admission, he had a body temperature of 37.1 °C, blood pressure of 164/90 mm Hg, and the presence of a heart murmur and moist rales in his chest were observed. Regarding, laboratory data, there existed marked anemia such as RBC 140 × 10^6/mm^3, hemoglobin 5.5 g/dl and hematocrit 15.3%, but haptoglobin 112 mg/dl, serum Fe 80 µg/dl, and sugar water and Ham tests were within normal limits. Daily excretion of proteinuria was 15.8 g and serum total protein was decreased to 5.6 g/dl. Marked metabolic acidosis was observed including pH 7.30 and HCO₃ 14.3 mmol/l, and marked renal dysfunction shown as blood urea nitrogen 78 mg/dl and serum creatinine 12.3 mg/dl. For serological and immunological data, the titer of cold agglutinin showed 2,048 × at a temperature of 15 °C in vitro and Coombs tests were positive. The serum titer against various infections was only...
positive for M. pneumoniae 64 × evaluated by complement fixation test.
When the patient was treated with prednisolone 20 mg and erythromycin 1,200 mg/day, the titer
of cold agglutinin decreased, which was associated with the improvement of the symptoms of
upper respiratory tract infections, and renal function reversed almost to the same data as before
the infections. However, reduction of proteinuria was not observed.
After that the patient showed a fluctuation of the titer of cold agglutinin gradually followed by
the deterioration of renal function. On 13 November, 1988, he was readmitted to our department
for dialysis. On this second admission, the serum titer of cold agglutinin was 1,024 x , and
Coombs test and mycoplasma titer were completely negative.
To find out the isotype of the immunoglobulin class of cold agglutinin, the inhibition test was
performed by applying antihu-man immunoglobulin antibody. When antihuman IgM antibody
was applied to the in vitro system, the inhibition of agglutination of erythrocytes was observed.
A marked reduction of serum titer in cold agglutinin was recently observed and maintenance
dialysis has been performed.
Cold agglutinin syndrome (CAS) is fairly uncommon and can be induced by various diseases.
This syndrome is composed of two kinds of diseases such as chronic cold agglutinin diseases and
postinfectious CAS [10]. The former may be induced in aged patients and be slowly progressive,
and its onset is mild. Its agglutinin antibody is monoclonal and its subclass of light chain is of the
K type. The latter is usually caused by infections of M. pneumoniae or mononucleosis, and its
immunoglobulin is polyclonal. In these postinfectious CAS, the serum titers of agglutinin
reached a maximum level a few weeks after the onset, and their symptoms usually disappeared
within several months without special treatment [11].
CAS rarely occurs in kidney diseases, and there is no report of CRF followed by CAS except in
our case. Furthermore, there is a report of CAS due to membranous glomerulonephritis [12], and
our case was the first CRF followed by CAS derived from MPGN. Chronic glomerulonephritis is
thought to be induced by some immunological mechanisms, although it is not always a
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pure autoimmune disease, and is likely induced by CAS [13]. In our case CAS was associated
with M. pneumoniae which was induced by CRF followed by the immunologico-cl abnormality,
and the high titers of cold agglutinin persisted for a comparatively long time. The patient did not
complain of skin pain or lesions in the peripheral portion, which is thought to be the result of the
moderately high titer of cold agglutinin and no damaged lesions under the cold sensitization.
Furthermore, it is difficult to evaluate the presence of hemolytic anemia caused by cold
agglutinin, because anemia mostly associated with CRF was present, and sugar water and Ham
tests were within normal limits.
The patient underwent dialysis for CRF, but there was some question as to whether hemodialysis
or peritoneal dialysis was a better treatment. Indeed, the patient had been at first treated with
peritoneal dialysis to avoid the prospective trouble of hemodialysis however, the serum titers of
cold agglutination were reduced markedly with no symptoms. But specific treatment such as
plasmapheresis or immunoabsorption is necessary when the agglutinin is the warm antibody
[14].
In summary, it was suggested that our CRF case was followed by CAS due to the infection of M.
neumoniae. The agglutination was studied in detail at a temperature of 15°C in vitro, and its
immunoglobulin class was \text{IgM}(K). It was suggested that the selection of dialysis had to be considered carefully at the initiation of dialysis in the instance of a following CAS.

References


