中文題目：隱匿於血清 ANCA 陽性-快速進展腎小球腎炎下的疾病：亞急性細菌性心內膜炎

英文題目：A hidden cause of ANCA-positive rapidly progressive glomerulonephritis: subacute bacterial endocarditis

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Introduction:

Rapidly progressive glomerulonephritis (RPGN) is known as acute renal failure in a short period. A prompt identification of underlying etiology following an effective treatment strategy might reverse renal function. Here, we describe a case of proteinase-3 antineutrophil cytoplasmic antibodies (PR3-ANCA)-positive RPGN concealed subacute bacterial endocarditis (SBE).

Case presentation:

A 74-year-old male suffered from progressively exertional dyspnea and bilateral lower extremities edema for months. An unexpected renal function decline was noted during clinic visits, translating eGFR decline from 76.57 ml/min 1.73m^2 to 10.71 ml/min 1.73m^2 (Figure 1-A). Furthermore, newly developed proteinuria (1289 mg/gm urinary protein-creatinine ratio) combined with persistent microscopic hematuria was identified (Figure 1-B). Considering highly suspected RPGN, hospitalization for examination was arranged by the nephrologist.

Vital signs upon admission revealed no fever. Physical examination presented a grade III/IV systolic heart murmur at the apex and bilateral lower limbs edema. Hemogram disclosed anemia (hemoglobin of 6.8 g/dL), increased white blood cells (10,710/μL), and thrombocytopenia (platelet counts of 93,000/μL). Clinical biochemistry showed increased levels of BUN (blood urea nitrogen) (141.0 mg/dL), creatinine (8.86 mg/dL) and C-Reactive protein (CRP) (63.52 mg/dL), as well as hypoalbuminemia (2.82 g/dL). Bilateral kidney showed neither shrinking in size nor polycystic change on renal sonography. A high titer of the antinuclear antibody (ANA) (1:640) and an increased level of PR3-ANCA (7.4 IU/mL) were presented. Decreased complement C3 level (32.8 mg/dL), normal C4 level, and positive cryoglobulin were found. Other immune-associated profiles were negative, including Myeloperoxidase-antineutrophil cytoplasmic antibodies (MPO-ANCA), anti-glomerular basement membrane antibody (anti-GBM), anti-double stranded DNA antibody (ds-DNA), Anti-streptolysin O antibody (ASLO), and hepatitis C. Due to the rapid progression of renal failure and abnormal immunology profiles, renal biopsy was recommended for further RPGN diagnosis. However, shock was identified, and a left frontal intracranial hemorrhage was found on the third hospitalization day. During the following days, bacterial blood cultures grew *Streptococcus parasanguinis*. Transthoracic echocardiography revealed an 18.4 mm vegetation on the mitral valve and a small vegetation on the aortic valve (Figure 2). According to Duke's criteria of infective endocarditis, a highly suspected infective endocarditis was considered. No cardiac surgery was performed due to severe neurological sequelae resulting from intracranial hemorrhage. Regrettably, the patient died due to

endocarditis-related multi-organ failure.

Discussion:

The PR3-ANCA are commonly detected in ANCA-associated vasculitis (AAV), or specifically, granulomatosis with polyangiitis (GPA). Serum ANCA was positive in 25% of endocarditis-associated glomerulonephritis (GN). The SBE presenting as ANCA-positive RPGN has been described. Since the treatment plan for two ANCA-positive diseases was entirely different, it is important to recognize SBE in suspicious AAV cases.

To date, no diagnostic criteria were established for SBE-associated ANCA-positive RPGN. Bonaci-Nikolic et al. proposed that low-titer ANCA expression and rarely pulmonary or sinusoidal involvement were clinical manifestations in ANCA-positive populations with infection compared with classic AAV. Cryoglobulin, ANA, RA factor, and hypocomplementemia might be presented on serologic tests. In studies for pathologic change of endocarditis-associated GN, 47% of cases exhibited necrotizing and crescentic GN, and 37% displayed diffuse proliferative GN. Intense complement deposition and occasional immunoglobulin deposition differed from AAV, representing negative staining for immunoglobulins and complement components.

Another issue is the mechanism of intracranial hemorrhage. There are three main hypotheses. One hypothesis is a fragment of huge vegetation leads to an ischemic infarct following hemorrhagic transformation. Another one is the rupture of the mycotic aneurysm. The last one is erosion or necrosis of septic arteritis.

The following conditions made diagnostic pitfalls in our case. First, a rapid decline of renal function accompanying an elevating serum ANCA level gave the clinical concern of ANCA-associated RPGN. Second, infectious symptoms and signs, such as fever, might be absent in subacute infectious conditions. Third, the typical endocarditis features according to Duke Criteria, like Janeway lesion or Osler's node, were not identified. The clue of SBE was a positive blood culture, following the confirmation by valvular vegetation disclosed from echocardiography. Poor oral hygiene was considered the contributing cause of endocarditis in this patient.

Conclusion:

We reported a subacute bacterial endocarditis, presenting a seropositive PR3-ANCA RPGN. The indolent clinical course made it a challenge for clinical diagnosis. Awareness of infective endocarditis in an atypical presentation of PR3-ANCA RPGN should be considered.