Renal Vasculitis and Antineutrophil Cytoplasmic Antibody

There are controversies in the nomenclature and classification of necrotizing renal vasculitis, since the concept of antineutrophil cytoplasmic antibody (ANCA)-related vasculitis was introduced following the discovery of ANCA in 1982 (1-4). The case report of Satoh et al which appears in this issue of *Internal Medicine* (5) raises several important questions as to ① whether classical polyarteritis nodosa (PN) and microscopic PN (MPN) are the same disease? ② are MPN and microscopic polyangiitis (MPA) the same disease? ③ whether most of pauci-immune crescentic glomerulonephritis (pi-Cres.GN) is regarded as renal limited MPN or MPA? ④ what forms of necrotizing vasculitis which were described prior to the discovery of ANCA belong to ANCA-related vasculitis? ⑤ does ANCA titer rise prior to the relapse of vasculitis?

**Classical PN, MPN and MPA:** Classical PN is the disease characterized by necrotizing arteritis of medium and small muscular arteries with visible aneurysm formation. This disease was first described by Kussmaul and Maier in 1866 (6). In the kidney, arteries larger than arcuate are preferentially affected resulting in renal infarcts and glomerular ischemia. The main renal symptoms are renovascular hypertension and chronic renal failure. Most of them are ANCA negative (2, 7). MPN was described by Davson in 1948 from microscopic observation of autopsied kidneys from patients with classical PN (8). He found two distinct glomerular lesions; one is segmental necrotizing GN often with crescents, the other is glomerular ischemia. He designated the former lesion as MPN. More than 40 years has passed. Jennette and Falk noticed that most of ANCA positive patients had no arteritis, but rather vasculitis in vessels smaller than arteries; arterioles, venules and capillaries (2, 8). Thus, they proposed this type of vasculitis in ANCA positive patients as MPA, because no arteritis was found in these patients (2). Clinically, MPA is characterized by rapidly progressive glomerulonephritis (RPGN) often associated with pulmonary hemorrhage, which indicates that glomerular and pulmonary capillaries are specifically affected. Although in the report of Satoh et al (5), the term MPA was used as the abbreviation of microscopic PN, it is not adequate, because the patient is thought to be not MPN, but MPA.

**ANCA-related renal vasculitis:** Jennette et al proposed that MPA, Churg-Strauss Syndrome (CSS) and Wegener’s granulomatosis (WG) are ANCA-related vasculitis (2). This is also true in patients with renal vasculitis including pi-Cres.GN. Recently, the differences between anti-MPO and anti-proteinase-3 ANCA associated glomerulonephritis have been clearly demonstrated by Franssen et al (15).

**Renal limited vasculitis and pi-Cres.GN:** There are some reports that pi-Cres.GN represents a form of renal limited vasculitis before and after the concept of MPA or ANCA-related vasculitis was widely circulated (4, 9-15). We examined the organ involvement in 53 patients with pi-Cres.GN associated with MPO-ANCA. They were classified into 3 groups; Cres.GN only – 15 cases (28%), Cres.GN with pulmonary hemorrhage – 21 cases (40%), Cres.GN, pulmonary hemorrhage, and systemic vasculitis – 17 cases (32%) (16). This data suggests that it is reasonable to regard pi-Cres.GN as a renal limited vasculitis as the opinion of Satoh et al (5).

**Relapse of vasculitis:** There is controversy as to the relapse rate of classical PN (5, 7, 17),. Some insist there is no relapse, and others insist there is a high relapse. On the contrary, the relapse of MPA is between 15-30% in many reports, although the interval between the initial attack and second attack is variable as reviewed by Satoh et al (5). The clinical importance is that most of the relapse occurred, when maintained immunosuppressive therapy was stopped as in the case of Satoh et al. A short duration of therapy might induce a high rate of relapse, whereas long-term intensive therapy might lead to the association of serious complications related to drug toxicity. Whether the rising ANCA titer predicts the relapse of MPA or not is still a matter of debate (1, 4, 18-20), although our experience indicates that the rise of ANCA titer may be an excellent marker for the intensification of immunosuppressive therapy to prevent relapse (6). In most of the cases with MPA, serial quantitative assay of ANCA is needed to avoid relapse and to reduce drug toxicity of immunosuppressive treatment.

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**References**

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