Clinical Manifestations and Prognosis of Wegener’s Granulomatosis

Wegener’s granulomatosis (WG), a clinicopathological entity manifested by granulomatous vasculitis, affects the upper and lower respiratory tracts as well as the kidneys. In the typical case of WG, the upper and lower respiratory tract involvement is a common initial manifestation which is followed by renal disease.

A limited form lacking the renal involvement has been reported. In contrast, we recently reported a case of WG in whom the first clinical manifestation was acute renal failure due to periglomerular granulomatosis with crescentic glomerulonephritis and the late development of respiratory lesion. The case could be a "delayed variant" or limited form of WG localized in the kidney (1). Accordingly, the combination of organ involvement is not sufficient to conclude WG.

WG has been considered to be a pathological entity (2). The typical histopathological features of WG consist of inflammation of the upper and lower respiratory tracts with necrosis and granuloma formation, systemic necrotizing angiitis, and focal granulomatous glomerulonephritis. Fauci et al (3) reported that complete remission could be obtained with the use of immunosuppressant therapy given immediately after the diagnosis. Thus, an early diagnosis is mandatory in order to improve patient outcome. That is one of the theoretical reasons to recommend repeat biopsy from the upper respiratory tract to identify typical pathological features.

Recently the recognition of the association between C (cytoplasmic: PR-3) antineutrophilic cytoplasmic antibody (ANCA) and WG has shed new light as the serological adjunct for the diagnosis of WG (4). Although it is not clear whether or not C-ANCA holds pathological significance in granulomatous vasculitis, it is at least, a specific antibody for making the diagnosis of WG.

Thus the presence of C-ANCA should be included as one of the diagnostic criteria (5). Since establishment of methods to quantitate ANCA, systemic vasculitis, especially polyarteritis nodosa (PN) and WG which affect the kidney as the major target organ, the diagnostic approach has changed dramatically. Two antibody types exist: PR-3-ANCA and MPO (myeloperoxidase)-ANCA. PR-3-ANCA is a marker antibody for Wegener’s granulomatosis. By using MPO-ANCA, systemic vasculitis can be classified as ANCA-negative classical PN and ANCA-positive microscopic PN (MPN).

Nagasawa reported that MPO-ANCA positive diseases consist of types 1 (renal alone), 2 (renal & pulmonary) and 3 (renal and systemic) (6). Type 3 disease can be classified as MPN. It has been known that MPO-ANCA is closely related to necrosis of the capillaries in the alveolar septum and renal glomerulus. Patients with a high-titer of MPO-ANCA exhibit alveolar hemorrhage and rapidly progressive glomerulonephritis (glomerulonephritis with crescent formation).

Although PR-3-ANCA is closely related to WG and is of diagnostic significance, ANCA alone cannot be used to classify all patients with various systemic vasculitis (7). From this point, the hitherto-described histopathological classification still has value for both the diagnosis and classification of systemic vasculitis (8). Histopathologically, systemic vasculitis is classified according to the size of the affected vessels, and migratory cells and to the presence of fibrinoid necrosis. However, we sometimes encounter patients with systemic vasculitis in whom different histopathological features coexist. From the clinical standpoint, we classified such patients as overlap syndrome (OL). OL typically has more advanced immunological abnormalities manifested by hyper-gamma globulinaemia, positive rheumatoid factor and anti-nuclear antibodies. More importantly, OL fails to respond conventional therapy and has a more grave prognosis.

In contrast to our clinical observations, Leavitt and Fauci described polyangiitis overlap syndrome (POL) (9). Patients with POL do not belong to a single entity of systemic vasculitis and they exhibit clinical manifestations seen in more than two diseases. Leavitt and Fauci (9) described various combinations of systemic vasculitis as POL but the most common type of POL is the overlap of PN and Churg-Strauss syndrome. They also claimed that the prognosis of POL is benign and the majority of the patients experience remission after treatment with corticosteroid and/or immunosuppressants.

In any case, the prognosis of WG is markedly improved by early diagnosis and the appropriate treatment. From this simple fact alone, it is of prime importance for the clinician to bear in mind that the systemic manifestations could be the initial symptoms of systemic vasculitis, such as PN and WG.

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References

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