

Interesting case seminar: Native kidneys

IgG4-related nephropathy

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IgG4-related sclerosing disease (IgG4SD) is a novel disease entity associated with high serum IgG4 levels. The syndrome reveals various uncommon clinical manifestations including autoimmune pancreatitis (AIP), Mickulicz's disease and Kuttner's disease, in contrast to a relatively common background pathology, i.e., interstitial fibrosis/sclerosis and lymphoplasmacytic infiltration. The kidney is a distinct target organ affected by IgG4SD, and chronic renal failure occasionally develops. Among several forms of IgG4SD in the kidney, tubulointerstitial nephritis (TIN) is a common and the severest phenotype. IgG4-related TIN is often accompanied by AIP; however, several isolated cases have also been reported. The morphology of TIN in general is non- or fairly non-specific in nature, and thus the diagnosis of IgG4-related TIN, particularly in isolated cases (without AIP) is sometimes hard to make. Since steroid therapy has been found to be effective in AIP, a proper diagnosis of IgG4SD in the kidneys is very important so that steps can be taken to impede disease progression.

This background prompted us to undertake the present study in which 20 cases considered to have IgG4-related TIN were collected from all over Japan to better define the clinical and pathological characteristics of this condition to facilitate its diagnosis and clarify its pathogenesis.

We described the histopathological features of IgG4-related nephropathy (IgG4RN). The renal lesion is relatively localized, and extends to the deep renal medulla or even beyond the renal capsule. Inflammation is mainly composed of lymphocytes and plasma cells with various numbers of eosinophils. Sclerotic fibrosis appears in the early stage, plasma cells become dominant as the disease progresses, and finally fibrotic foci remain with

disappearance of glomeruli and vessels. Hyaline deposits are detected in inflamed TBM or Bowman's capsule with IgG4 deposition demonstrated by immunofluorescence. However, these deposits are not detected in uninvolved regions of the kidneys. The percentage of IgG4 positive plasma cells is more than 50%, but decreases in the clinical course of successful corticosteroid therapy. Sometimes, glomerular immune-complex deposits are seen, and membranous nephropathy is associated in the majority of these cases. Although obliterative phlebitis is rarely seen, arteriosclerosis is evident in inflamed areas. These findings suggest that IgG4RN is a new renal interstitial disorder. Accumulation of more cases is needed to further clarify the histopathological features of IgG4RN and elucidate the underlying mechanism of this disease.

References

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Legends

Fig. 1: Low magnification of light microscopy shows tubular attenuation with diffuse interstitial infiltration and fibrosis (HE). This feature was the most common one noted in our series.

Fig. 2: Cortical involvement of fibrosis, tubular attenuation and inflammatory cell accumulation are noted (Masson trichrome).

Fig. 3: Plasma cells predominant infiltration and eosinophils infiltration on the background of diffuse connective tissue deposition are seen (HE).

Fig. 4: (Left) Small swollen-plasma cell nests are encircled by PAS-positive collagenous tissues (PAS).

(Right) Characteristic cell nests and PAM positive fibrous bundle pattern demonstrates “bird’s eye” (PAM).

Fig. 5: (Left) Eosinophilic granular depositions are present in the tubuli and interstitium (Masson trichrome).

(Right) Granular electron dense deposits are accumulated in the thickened tubular basement membrane (TBM). Note scattered particles of deposits are also seen in the interstitium (Electron microscopy).

Fig. 6: (Left) In low magnification of IgG4-positive plasma cells among severe lymphoplasmacytic infiltration, note that relatively frequent IgG4-positive cells account for approximately 60 % of the total infiltrating cells (IgG4 immunostaining).

(Right) IgG4 (red) is present in Bowman’s capsule, TBM and interstitium. Background fibrosis is composed mainly of interstitial-type collagen type III (green) (double immunofluorescent labeling demonstrating co-localization of IgG4 and collagen type III).











