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LETTER TO THE EDITORS

Primary Sjögren syndrome that developed after IgA nephropathy

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Sirs,

We read with great interest the article entitled "Primary Sjögren's syndrome with mesangial proliferative glomerulonephritis and IgA deposits in a child" by Jung et al. [1]. These authors reported a boy with immunoglobulin A nephropathy (IgAN) concomitant with primary Sjögren syndrome (SjS). We have treated two female patients also presenting with both conditions (Table 1). However, our patients developed IgAN followed by SjS with a long time lag. Patient 1 developed IgAN at the age of 10 years and later developed SjS when she was 19 years old. Patient 2 developed IgAN at the age of 12 years and SjS at the age of 32 years. A renal biopsy revealed focal mesangial proliferative IgAN in both patients. At the time the SjS was diagnosed, the disease activity of IgAN was low in both patients, and they did not have any other autoimmune diseases, suggesting primary SjS. The IgAN was successfully treated with an anti-platelet agent, angiotensin-converting enzyme inhibitor, or angiotensin II receptor blocker. Renal function remained normal at their last visits. In patient 1, SjS was treated with prednisolone 5 mg daily, resulting in a dramatic amelioration of the clinical manifestations, a normal erythrocyte sedimentation rate, and normal serum IgG and IgA levels. The prednisolone treatment also improved her residual hematuria. Patient 2 has been followed up without medication, but we are planning to use prednisolone for treatment of her SjS.

It is difficult to elucidate whether IgAN is a likely complication of SjS. Plasma cells producing IgA rather than IgG or IgM are dominantly observed in the salivary glands of SjS patients [2]. Enrichment of anti-Sjögren's syndrome B (anti-SS-B) IgA antibodies in the saliva of patients with SjS may suggest enhanced local synthesis of anti-SS-B IgA [3]. The presence of IgA autoantibodies against M3 muscarinic acetylcholine receptors is also considered to be a pathophysiological factor of primary SjS [4]. These basic findings may suggest that both IgAN and SjS are attributable to abnormal immunity in terms of IgA production.

With the exception of the patient reported by Jung et al. [1] and the two patients reported here, there has been only one report of IgAN being associated with SjS: this was a 61-year-old Japanese woman who was diagnosed with SjS after an 8-year history of IgAN [5]. However, as Jung et al. suggested, SjS may be under-diagnosed in patients with recognized IgAN or a history of IgAN. We initially suspected complications from an autoimmune disease based on the clinical manifestations as well as the elevated erythrocyte sedimentation rate and serum IgG level. These abnormal values may be clues that will facilitate the diagnosis of SjS in patients with IgAN. A routine urinary check is also necessary for patients with SjS. More extensive investigations will be needed to further support our hypothesis.

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Table 1 Summary of the characteristics of two patients with primary Sjögren syndrome that developed after IgA nephropathy

Patient/clinical characteristics	Case	
	Patient 1 (female)	Patient 2 (female)
Age at onset of IgAN	10 years	12 years
Initial symptoms of IgAN	Proteinuria, microscopic hematuria	Proteinuria, macroscopic hematuria
Renal biopsy	Focal MPG with positive IgA staining	Focal MPG with positive IgA staining
Treatment for IgAN	Lisinopril, candesartan, mizoribine, dipyridamole	Dipyridamole, Saireito, tosilectomy
Prognosis of IgAN	Micro-hematuria, normal renal function	Complete remission, normal renal function
Age at onset of SjS	19 years	32 years
Initial symptoms of SjS	Malaise, headache	Malaise, fever, arthralgia, dry eyes
Diagnosis of SjS	Schirmer's I test: positive, minor salivary gland biopsy: grade 4	Schirmer's I test: positive, abnormal salivary scintigraphy decreased whole salivary flow
Results of laboratory tests at diagnosis of SjS		
Anti-SSA/SSB antibody (IU/ml)	170/negative	>10,000/190
Serum IgG (mg/dl)	2017	2353
Serum IgA (mg/dl)	404	220
Erythrocyte sedimentation rate (mm/h)	57	51
Treatment for SjS	Low dose prednisolone	None

IgAN, Immunoglobulin A (Ig) nephropathy; SjS, Sjögren syndrome; MPG, mesangial proliferative glomerulonephritis; Saireito, Chinese herb; SSA/SSB, anti-Sjögren's syndrome A/syndrome B antibodies

Definition of positive findings are as follows: abnormal Schirmer's I test (≤5 mm in 5 min), decreased whole salivary flow (≤1.5 ml in 15 min), focal lymphocytic sialoadenitis [evaluated by an expert histopathologist, with a focus score ≥1, defined as a number of lymphocytic foci (which are adjacent to normal-appearing mucous acini and contain more than 50 lymphocytes)] per 4 mm^2 of glandular tissue.

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