rapid response within the first month of RTX treatment has been observed in other diseases, such as relapsing remitting multiple sclerosis [6] and refractory ITP [7]. These observations, coupled with our own, provide important insights into the mechanism of action of B-cell depletion. RTX does not target mature plasma cells, therefore it is unlikely that a reduction in the number of pathological autoantibodies—which may take several weeks or months to become apparent—can explain these rapid treatment effects. Given that circulating B-cell depletion normally occurs within 48 h of administration of RTX [8], it is likely that loss of B-cell-mediated antigen presentation, cytokine production or T-cell regulation is the therapeutic target leading to the early improvement observed post-RTX [9].

Detailed pharmacokinetic studies are required to delineate the mechanism of response to RTX in patients with autoimmune diseases and its precise role in SLE-related PH. We believe that such studies are warranted given the successful outcome reported in our case.

Rheumatology key message

- Rapid improvement of SLE-PH treated with early CYC/RTX suggests additional mechanisms of action of BCDT.

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References


HLA-B51-related seronegative spondyloarthopathy associated with membranous nephropathy

Sir, SpA is defined as the entity that has seronegative, inflammatory arthritis characterized by involvement of the spine, peripheral arthritis and enthesitis. SpAs represent a variety of diagnoses, including AS, PsA, reactive arthritis, enteropathic and uSpA. HLA-B51-related seronegative SpA (SNSpA), first reported by Matsumoto et al. [1], is the SpA presenting with positive HLA-B51 and negative RF.

A 48-year-old Japanese man with proteinuria, lumbago and arthralgia of the bilateral shoulders and hip joints was admitted to our hospital. Two months before admission, lumbago, arthralgia and leg oedema suddenly occurred and progressed. He visited another hospital and his laboratory data showed massive proteinuria (10 g/day). Therefore, he was transferred to our hospital.

On admission, physical examination showed leg oedema. Laboratory data revealed that white blood cell counts, red blood cell counts, haemoglobin and platelet counts were 13.1 × 1012/l (with 81% neutrophils), 37.4 × 1012/l, 108 g/l and 5500 × 1012/l, respectively. Serum creatinine, bloodurea nitrogen and uric acid were 66.3 μmol/l, 5.0 mmol/l and 303 μmol/l, respectively. Liver function and electrolytes were within normal ranges. Total protein and albumin were 60 and 28 g/l, respectively. CRP was 40 mg/l. IgG, IgA, IgM and IgE were 11.1 g/l, 4.36 g/l, 1.24 g/l and 88.4 × 109 IU/l, respectively. IgD was 331 mg/l (138). Urinalysis showed that protein was 3.0 g/l.
(4.2 g/day) and occult blood was ≥ 2. Creatinine clearance rate was 2.157 ml/s. Serological tests revealed that ANAs, RF, anti-RNP antibodies, anti-Sm antibodies, anti-dsDNA antibodies, anti-ssDNA antibodies, anti-Jo-1 antibodies, MPO-, PR3-ANCA, anti-SS-A and -SS-B antibodies were all negative. HCV antibody and HBs antigen were negative. CH50, C3 and C4 were 48.4 x 10^2 CH50/l, 1.8 g/l and 0.446 g/l, respectively. HLA typing was A24, A26, B48 and B51.

Imaging tests such as X-rays, echographies, etc. showed no remarkable findings. [18F]fluorodeoxyglucose (18F-FDG) PET–CT demonstrated a short segment of increased FDG activity corresponding to the ligaments within the bilateral shoulder joints, the bilateral hip joints and the interspinal ligament between L2, L3 and L4, compatible with enthesitis (Fig. 1). Renal biopsy specimen included 24 glomeruli with two global scleroses. LM revealed the thickness of basement membrane without mesangial proliferation and interstitial damage. IF showed the deposits of IgG (granular pattern) and C3 without IgA, IgM, C4, C1q and fibrinogen. EM showed subendothelial electron-dense deposits. He was diagnosed as having membranous nephropathy (MN) with SNSpA.

He was treated with 200 mg/day of celecoxib and 1000 mg/day of salazosulphapyridine, 40 mg/day of prednisolone and 150 mg/day of cyclosporin. His clinical features gradually improved without relapse.

Fig. 1 The findings of PET–CT. (A) PET–CT demonstrated the enthesitis of the ligaments within the bilateral shoulder joints, the bilateral hip joints and the interspinal ligament between L2, L3 and L4. (B) Right shoulder joint, (C) interspinal ligament between L3 and L4 and (D) left hip joint.

HLA-B51, which is strongly associated with Behçet’s disease (BD), have been recently described to be involved in the pathogenesis of SpA in Japanese and Tunisian populations and the new entity called HLA-B51-related SNSpA is proposed [1–3]. Patients with HLA-B51-related SNSpA have been described to have no other clinical manifestations of BD, such as recurrent oral and genital ulcers, skin lesions and uveitis [1]. In the present case, the clinical manifestations are compatible with HLA-B51-related SNSpA, and PET–CT is useful to detect enthesitis, leading to diagnosis of SpA.

The association with SpA and MN has been rarely reported [4]. Since HLA-B51-related SNSpA is not widely well known [1, 2, 5–7], the association with HLA-B51-related SNSpA and renal involvements including MN has not been previously reported. On the other hand, amyloidosis (AA type), GN (proliferative GN) and macroscopic/microscopic vascular disease are the main causes of renal BD [8]. Therefore, it is suggested that renal involvements in HLA-B51-related SNSpA might be different from those in BD. The combination of arthritisc- causing micro-organisms, such as Shigella, Salmonella, Chlamydia and Klebsiella, and host factors, such as HLA-B27 and HLA-B51, is considered to play an important role in the pathogenesis of SpA [2, 4]. Furthermore, CD4^+ and CD8^+ T cells could be activated by specific bacterial antigens in HLA-B27-positive SpA [9]. HLA-B51-related SNSpA might also result from T-cell
activation by an infectious event. On the other hand, T-cell dysfunction had been reported to play a role in the pathogenesis of MN [10]. Though the association between HLA-B51-related SNSpA and MN could be by chance, there might be a common pathogenic mechanism caused by T-cell function in both SpA and MN. In the present case, the combination therapy including CSA was very efficient to improve proteinuria and arthralgia. We suspect that this could support our hypothesis.

We report the first case of HLA-B51-related SNSpA associated with MN. HLA-B51 is much more common in the Japanese population than HLA-B27 [5]. HLA-B51-related SNSpA might be included in uSpA and there might be more frequent cases with this condition than we thought, especially in the Asian region. We propose that one should consider HLA-B51-related SNSpA as one of the differential diagnoses in Japanese patients with SpA and/or MN.

Rheumatology key message

- HLA-B51-related SpA should be considered as one of the differential diagnoses in Japanese patients with SpA and/or MN.

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