Reumatologia 2022; 60, 5: 361–362
DOI: https://doi.org/10.5114/reum.2022.120762

Mixed connective tissue disease and severe renal disease – an apparent misconception?

Filipe Oliveira Pinheiro, Pedro Madureira, Maria Seabra Rato, Lúcia Costa

Department of Rheumatology, Centro Hospitalar Universitário de São João, Porto, Portugal

Dear Editor,

Mixed connective tissue disease (MCTD) is a connective tissue disease characterized by the presence of anti-RNP (anti-U1 ribonucleoprotein) antibodies, and by a set of signs and symptoms that it shares with other connective tissue diseases, such as systemic lupus erythematosus (SLE) [1]. Because of this clinical overlap of syndromes, the presence of high titer anti-RNP antibodies is a central feature of the diagnosis of MCTD [2]. Importantly, one of the most distinctive features of MCTD is the absence of severe renal or central nervous system involvement, which may be present in other connective tissue diseases, such as SLE, and this is a focal and key point of MCTD [3].

In fact, high anti-RNP titers appear to be protective against renal involvement, particularly diffuse proliferative glomerulonephritis, even when they occur at lower titers, in other connective tissue diseases [4]. Renal involvement mandating intense immunosuppressive therapy has been reported seldomly [3].

Mixed connective tissue disease treatment is largely empirical, since there have been no randomized controlled trials on the treatment of MCTD and no specific guidelines exist either [5].

We report a case of a female patient, 32 years old, who presented with a 2-month history of polyarthritis. Laboratory tests showed a high erythrocyte sedimentation rate (ESR, 69 mm/h), antinuclear antibodies (ANA) with a 1 : 1280 titer, speckled pattern, and strongly positive anti-U1 RNP antibodies. There was no complement decrease, and the results of other immunological testing, comprising anti-double stranded DNA (anti-dsDNA), rheumatoid factor, antineutrophil cytoplasmic antibodies (ANCA), and other autoantibodies to extractable nuclear antigens (ENAs), were normal.

The diagnosis of MCTD was made and the patient was started on hydroxychloroquine 400 mg/day and a short course of low-dose steroids. The patient then missed follow-up appointments due to being pregnant. When the patient presented again, she had abandoned all her medications due to pregnancy-related concerns, and had fatigue, new onset of Raynaud phenomenon and puffy hands. Blood tests revealed anemia (hemoglobin 10.3 g/dl) high ESR (97 mm/h), and hypoalbuminemia (32 g/l), and repeated immunological testing was remarkable only for high ANA and anti-RNP antibodies. Urine studies showed proteinuria of 2.5 g/24 h and microscopic hematuria (142/µl).

The patient underwent renal biopsy, which showed "segmental sclerosis lesions and presence of mesangial and membrane immune-type deposits by immunofluorescence", with a full-house pattern on immunofluorescence but absence of mesangial or endocapillary proliferation. Therapy with prednisolone 1 mg/kg/day (60 mg/day) in a progressive dose reduction regimen, hydroxychloroquine 400 mg/day, mycophenolate mofetil (titrating dose up to 3000 mg/day), and captopril was started. At 6 months, prednisolone was reduced to 7.5 mg/day, and she was in renal remission, as renal function was normal, proteinuria had decreased to 370 mg/24 h, serum albumin was normal, and hematuria had resolved. At 24 months after this admission, prednisolone was suspended, and the patient remains in remission.

Anti-RNP antibodies are associated with a protective role in MCTD and in other systemic connective tissue diseases where they are present, namely regarding severe renal or central nervous system involvement [4]. Renal disease in MCTD has been described, but is usually in the form of low grade proteinuria or hematuria; in fact,

Address for correspondence:
Filipe Oliveira Pinheiro, Department of Rheumatology, Centro Hospitalar Universitário de São João, Alameda Professor Hernâni Monteiro, 4200-319 Porto, Portugal, e-mail: filipe.pinheiro92@gmail.com

Submitted: 24.08.2021; **Accepted:** 23.09.2022

more severe forms of presentation have been seldomly reported, and intensive immunosuppressive therapy is exceptional in MCTD [3].

The need for immunosuppressive therapy in renal disease has mostly been reported in MCTD and accompanying histopathological features, such as ANCA-mediated glomerulonephritis, or SLE-associated glomerulonephritis [6, 7].

In that sense, being an exceptional feature, and since no specific guidance exists for patients with MCTD [5], data are scarce to guide physicians in the use of immunosuppressive regimens in renal involvement in MCTD, and there is a need for more studies in this field.

The authors declare no conflict of interest.

References

1. Sharp GC, Irvin WS, Tan EM, et al. Mixed connective tissue disease – an apparently distinct rheumatic disease syndrome associated with a specific antibody to an extractable nuclear antigen (ENA). Am J Med 1972; 52: 148–159, DOI: 10.1016/0002-9343(72)90064-2.
2. Jonsson J, Norberg R. Symptomatology and diagnosis in connective tissue disease. II. Evaluations and follow-up examinations in consequence of a speckled antinuclear immunofluorescence pattern. Scand J Rheumatol 1978; 7: 229–236, DOI: 10.3109/03009747809095661.
3. Lundberg IE. The prognosis of mixed connective tissue disease. Rheum Dis Clin North Am 2005; 31: 535–547, vii-viii, DOI: 10.1016/j.rdc.2005.04.005.
4. Kitridou RC, Akmal M, Turkel SB, et al. Renal involvement in mixed connective tissue disease: a longitudinal clinicopathologic study. Semin Arthritis Rheum 1986; 16: 135–145, DOI: 10.1016/0049-0172(86)90047-8.
5. Chaigne B, Scirè CA, Talarico R, et al. Mixed connective tissue disease: state of the art on clinical practice guidelines. RMD Open 2018; 4 (Suppl 1): e000783, DOI: 10.1136/rmdopen-2018-000783.
6. Konstantinov KN, Harris AA, Barry M, et al. Sustained remission of antineutrophil cytoplasmic antibody-mediated glomerulonephritis and nephrotic syndrome in mixed connective tissue disease. J Clin Med Res 2013; 5: 316–321, DOI: 10.4021/jocmr1391w.
7. Kuroda H, Ishii K, Negoro Y, et al. A case of mixed connective tissue disease presenting with nephrotic syndrome. Mod Rheumatol 2004; 14: 236–240, DOI: 10.1007/s10165-004-0298-1.