The General Practice Guide to Autoimmune Diseases

Edited by Y. Shoenfeld and P. L. Meroni

EASi™
European Autoimmunity
Standardisation Initiative


ThermoFisher
SCIENTIFIC

The General Practice Guide to Autoimmune Diseases

Edited by Y. Shoenfeld and P. L. Meroni

Pabst Science Publishers
Lengerich, Berlin, Bremen, Miami,
Riga, Viernheim, Wien, Zagreb

Bibliographic information published by Deutsche Nationalbibliothek
The Deutsche Nationalbibliothek lists this publication in the Deutsche Nationalbibliografie; detailed bibliographic data is available in the Internet at <http://dnb.ddb.de>.

http://www.pabst-publishers.de

Printing: MercedesDruck, Berlin
Typesetting: Hilmar Schlegel, Berlin
Cover: Agentur für zeitgemäße Kommunikation Kaner Thompson
www.kanerthompson.de

ISBN 978-3-89967-770-6

Undifferentiated connective tissue diseases (UCTD)

Falk Hiepe

1 Definition

UCTD is an oligosymptomatic connective tissue disease with a limited autoantibody repertoire that does not meet the classification criteria of any specific connective tissue disease such as systemic lupus erythematosus (SLE), Sjögren's syndrome (SS), systemic sclerosis (SSc), autoimmune myositis or mixed connective tissue disease (MCTD). Only a minority of patients with UCTD will develop a defined connective tissue disease.

2 Epidemiology

Data regarding prevalence and incidence of UCTD are not available although Mosca et al noted that 20 %–52 % of patients in rheumatology clinics with a CTD may have UCTD. Mainly women suffer from this disease (female : male ratio is 20 : 1). The mean age at disease onset is 32 years (range 7–72 years).

3 Clinical manifestations

The course of the disease is mild. Each patient exhibits few clinical manifestations, mainly arthralgia (66 %), arthritis (32 %), Sicca symptoms (30 %), Raynaud's phenomenon (30 %), leukopenia (19 %), photosensitivity (17 %), anaemia (15 %), oral ulcerations (14 %) and alopecia (13 %). Severe organ manifestations e. g. of CNS or kidneys are uncommon. Most patients present manifestations similar to SLE, SSc or SS with a related ANA profile but do not meet the corresponding classification criteria.

4 Laboratory

Inflammatory parameters (ESR, gamma globulins) may be slightly or moderate increased. CRP levels are often normal. Anaemia, leukopenia and thrombocytopenia may occur. Some patients have low C3 and/or C4 levels.

Autoantibody profile: Antinuclear antibodies (ANA) detected by indirect immunofluorescence on HEp2 cells are positive in all patients. The ANA titre is usually low. Detailed analysis of the ANA antibodies usually identifies Anti-Ro/SSA, anti-La/SSB, anti-centromere or anti-U1-RNP antibodies. A patient will usually present with only one specificity of ANA antibody. Anti-dsDNA antibodies are rarely detectable. Some patients show ANA positivity without any specific antibodies able to be identified.

Table 1. Preliminary Classification Criteria for Undifferentiated Connective-Tissue Disease.

Inclusion Criteria	Clinical manifestations which may be considered specific to a defined CTD and are thus excluders of UCTD*	Laboratory markers which may be considered specific to a defined CTD and are thus excluders of UCTD*
1. Signs and symptoms suggestive of a CTD but not fulfilling the diagnostic or classification criteria for any of the defined CTDs** for at least 3 years*** 2. Presence of antinuclear antibodies determined on two different occasions	Malar rash Subacute cutaneous lupus Discoid lupus Cutaneous sclerosis Heliotrope rash Gottron's papules Erosive arthritis	Anti-dsDNA Anti-Smith Anti-Scl70

* Applicable to patients at disease onset

** Using established classification criteria for PM/DM,CTD, SLE SSc, RA and SS (see relevant chapters)

*** If the disease duration is less than 3 years, patients may be defined as having an early UCTD.

Adapted from Mosca et al. and Doria et al.

5 Classification criteria

Preliminary classification criteria were proposed by Mosca at al in 1990.

1. Signs and symptoms suggestive of a connective tissue disease, but not sufficient to meet the criteria for a defined connective tissue disease,
2. Positive ANA,
3. Disease duration of at least 3 years. Patients with shorter disease duration (< 3 years) are considered as early UCTD. During these 3 years, some of the so-called "early UCTD" patients develop a defined connective tissue disease.

An amendment has since been suggested to avoid the misdiagnosis of transitory or early, defined CTD (Table 1).

Differential diagnosis: defined connective tissue disease (SLE, primary Sjögren's syndrome, SSc, dermatomyositis, polymyositis, MCTD, scleroderma/myositis overlap), ANA-positive rheumatoid arthritis.

Treatment: In accordance with the mild clinical manifestations, UCTD patients require symptomatic therapy and sometimes no treatment at all. The therapy includes NSAID, low-dose glucocorticoids and antimalarials. Immunosuppressive drugs are not indicated.

References

[1] Mosca M, Neri R, Bombardieri S. Undifferentiated connective tissue diseases (UCTD): a review of the literature and a proposal for preliminary classification criteria. Clin Exp Rheumatol 1999; 17: 615–20.
[2] Mosca M, Tani C, Bombardieri S. Undifferentiated connective tissue diseases (UCTD): a new frontier for rheumatology. Best practice & research. Clin Rheumatol 2007; 21: 1011–23.
[3] Mosca M, Tani C, Neri C, et al. Undifferentiated connective tissue diseases (UCTD). Autoimmun Rev 2006; 6: 1–4.
[4] Mosca M, Tani C, Talarico R, Bombardieri S. Undifferentiated connective tissue diseases (UCTD): simplified systemic autoimmune diseases. Autoimmun Rev 2011; 10: 256–8.
[5] Vaz CC, Couto M, Medeiros D, et al. Undifferentiated connective tissue disease: a seven-center cross-sectional study of 184 patients. Clin Rheumatol 2009; 28: 915–21.
[6] Doria A, Mosca M, Gambari PF, Bombardieri S. Defining unclassifiable connective tissue diseases: incomplete, undifferentiated, or both? J Rheumatol 2005; 32: 213–5.