



Anti-Isoleucyl-tRNA synthetase autoantibodies (OJ)

Synonyms	anti-OJ (the antibodies were also called NJ according to the initials of another patient).
Indications	<ul style="list-style-type: none">▶ Dermatomyositis▶ Polymyositis▶ PM/DM-overlap syndromes with other connective tissue diseases▶ Antisynthetase syndrome▶ Interstitial lung disease▶ Raynaud's phenomenon (active stage, before starting therapy)
see also	▶ Autoantibodies in idiopathic inflammatory myopathies
Antigens	The isoleucyl-tRNA synthetase (EC 6.1.1.5; M _r 145 kDa; chromosome 9q22.31) belongs to the family of aminoacyl tRNA synthetases, which catalyze the ester bond of amino acids to their specific transport RNA (tRNA). The latter ones are engaged in the transport of amino acids for their assembly into the nascent polypeptide chain within the ribosomes.
Autoantibodies	<p>The indirect immunofluorescence test (HEp-2-cells) of sera containing anti-tRNA synthetase antibodies reveals an exclusive cytoplasmic fluorescence pattern. The anti-OJ antibodies react with multiple conformational and conformation independent epitopes of the antigen. Some antibodies also recognize the catalytic domain of the synthetase and inhibit its catalytic activity <i>in vitro</i>. The antibodies largely belong to the immunoglobulin isotype IgG.</p> <p>Aminoacyl-tRNA synthetases can assemble with each other and with other proteins forming macromolecular complexes. In mammalian cells nine of these tRNA synthetases (arginyl-, asparaginyl-, glutaminy-, α-glutaminy-, isoleucyl-, leucyl-, lysyl-, methionyl- and prolyl-tRNA synthetase) associate with three protein factors (AIMP/p18, AIMP2/p38, and AIMP1/p43) to form a large multi-aminoacyl-tRNA synthetase complex. The three accessory proteins are important for its the formation, stability, RNA-binding and other non-translation associated processes (Quevillon und Mirande 1996; Ibbas und Soll 2000; Kim et al. 2013). In some patients harboring antibodies against isoleucyl-tRNA synthetase (with the capability of precipitation of isoleucyl-tRNA) simultaneously were present antibodies reacting with leucyl-tRNA synthetase (4 of 11), lysyl-tRNA synthetase (2 of 11) and potentially with glutaminyl-tRNA synthetase (3 of 11). These additional anti-synthetase antibodies were able to inhibit the catalytic activity of the corresponding enzymes, but did not precipitate the tRNA. Probably the additional antibodies were caused by immunological processes like epitope spreading (Targoff et al. 1993). Since these additional antibodies were always found to be associated with precipitating antibodies against isoleucyl-tRNA-synthetase, their separate determination seems not to bear an additional diagnostic significance.</p>
Prevalence	Antibodies against the alanyl-tRNA synthetase can be detected in up to 3 % of adult patients manifesting polymyositis/dermatomyositis and/or particularly in cases of myositis associated interstitial lung disease. In adults the antibodies can be detected early in the beginning of the disease and sometimes also prior to the onset of the clinical manifestations.
Clinic	Patients exhibiting antibodies against isoleucyl-tRNA synthetase may develop an antisynthetase syndrome, which presents itself with varying symptoms of myositis, interstitial lung disease, arthritis, so called "mechanic hands" (rough, cracked skin at the tips and lateral aspects of the fingers forming irregular dirty-appearing fissures because of hyperkeratosis), Raynaud's phenomenon, sclerodactyly, calcinosis cutis and sicca-syndrome. The clinical manifestations of the antisynthetase syndromes may vary according to the antigen specificity of the respective anti-synthetase antibodies (table 1).



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Table 1 Clinical manifestations in anti-OJ positive patients (Hamaguchi et al. 2013).

DM	CADM	PM	DM/PM-OM	SSc	ILD	LES
13 %	-	25 %	-	-	63 %	
DM	dermatomyositis					
CADM	clinically amyopathic dermatomyositis					
DM/PM-OM	DM/PM-overlap					
PM	polymyositis					
SSc	systemic sclerosis					
ILD	interstitial lung disease					
SLE	systemic lupus erythematosus					

Autoantibodies against tRNA synthetases are mutually exclusive. The simultaneous occurrence of two anti-tRNA-synthetase antibodies of different antigen specificities is, apart from the findings mentioned above, extremely rare. But their association with antibodies not specific for myositis, so called myositis-associated antibodies (MAA), directed against topoisomerase, centromeres, U1snRNP, Th/To, U3snRNP, Sm, SS-A/Ro 52 or SS-A/La may be seen quite often.

Literature

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