Myositis

Laboratory Support for Classification and Diagnosis

CLINICAL BACKGROUND

Myositis is a general inflammation of the muscles that is caused by muscle injury, cancer, drugs, infection, genetic defects, or autoimmune disease. The most severe forms of myositis are autoimmune diseases called the idiopathic inflammatory myopathies (IIMs), which include polymyositis, dermatomyositis, inclusion body myositis (IBM), and immune-mediated necrotizing myopathy (IMNM). Because these are systemic diseases, affected individuals may exhibit extramuscular symptoms, such as skin rashes, lung disease, joint pain, arthritis, Raynaud phenomenon, and "mechanic's hands."[1]

Idiopathic inflammatory myopathies are relatively rare causes of myositis, with a prevalence of fewer than 33 cases per 100,000 individuals in the United States.[2] Polymyositis is the predominant type of IIM in adults, whereas juvenile dermatomyositis (JDM) is the predominant type of IIM in children. Polymyositis, dermatomyositis, and IMNM are more often observed in women, whereas IBM is more often diagnosed in middle-aged men.

Polymyositis and dermatomyositis commonly overlap with other autoimmune connective tissue diseases, such as systemic lupus erythematosus (SLE), Sjögren syndrome, systemic sclerosis, and rheumatoid arthritis.[3] Although generally thought to be less severe in these overlap syndromes, myositis symptoms may be of similar or worse intensity compared to those of primary myositis.[4]

The differential diagnosis of IIMs and overlap myositis begins with the exclusion of muscular dystrophy and myopathies of known cause (eg, infectious, metabolic, drug-induced, or neurologic). Diagnosis is aided by imaging, electromyography, biopsy, testing levels of muscle enzymes in serum, and the detection of myositis-specific and myositis-associated antibodies. In addition, the detection of certain antibodies may have prognostic value.

This Clinical Focus provides information on the available laboratory tests and their use. This information is provided for informational purposes only and is not intended as medical advice. A physician's test selection and interpretation, diagnosis, and patient management decisions should be based on his/her education, clinical expertise, and assessment of the patient.

Owing to overlapping features and phenotypes associated with a given antibody, test results should be interpreted carefully in light of clinical and other laboratory data.

INDIVIDUALS SUITABLE FOR TESTING

- Individuals with symptoms of IIM (eg, unexplained muscle weakness, rash, evidence of systemic disease)

TEST AVAILABILITY

Quest Diagnostics offers tests and panels that may be useful for classifying or diagnosing myositis (**Table 1**).

TEST SELECTION AND INTERPRETATION

Idiopathic Inflammatory Myopathies

The EULAR/ACR classification criteria for the idiopathic inflammatory myopathies (IIMs) include biopsy (if available), clinical, and laboratory evaluation (**Table 2**).[5] The criteria have been incorporated into a web-based calculator (http://www.imm.ki.se/biostatistics/calculators/iim/) that estimates the probability that a patient has IIM and what type.

On initial evaluation, about 80% to 90% of myositis patients have elevated creatine kinase (CK) associated with muscle damage.[6] Using elevated CK to diagnose IIMs has limitations, however. CK levels may be only slightly elevated, or normal, due to lack of muscle mass or the presence of circulating CK inhibitors or CK antibodies.[7] Normal CK levels may also be observed in patients with IBM, as well as those with juvenile or amyopathic dermatomyositis. Another limitation is that CK and other muscle enzymes are not specific markers of polymyositis/dermatomyositis. Serum elevations may be due to other types of muscle disease (muscular dystrophies, rhabdomyolysis), hypothyroidism, cardiac, or liver disease. Consequently, tests employing antibody markers, rather than muscle enzymes, are used to specifically diagnose and classify IIMs.

The classical myositis-specific antibodies include Jo-1, EJ, OJ, PL-7, and PL-12 synthetase antibodies, which define antisynthetase syndrome, as well as Mi-2 and SRP antibodies. Of these, only Jo-1 antibody is currently included in the EULAR/ACR criteria.[5] The European Neuromuscular Centre (ENMC) 239th Workshop Study Group uses presence of Mi-2 to classify dermatomyositis and presence of SRP to classify a subgroup of IMNM defined as having "anti-SRP myopathy".[8,9] The myositis-specific antibodies are mostly mutually exclusive (**Figures 1** and **2**).[1]

Table 1. Laboratory Tests for Classification and Diagnosis of Myositis

Test code	Test name	Clinical use
823	Alanine Aminotransferase (ALT)	Diagnose PM/DM
227	Aldolase	Diagnose PM/DM
39044	3-Hydroxy-3-Methylglutaryl-Coenzyme A Reductase (HMGCR) Antibody (IgG)	Diagnose statin-induced myopathy
94054	Anti-cN-1A (NT5c1A) IBM[a]	Diagnose sporadic inclusion body myositis
38075	Anti-Synthetase Panel 1[b] Includes Jo-1, EJ, OJ, PL-7,and PL-12 antibodies.	Diagnose antisynthetase syndrome in a symptomatic patient
822	Aspartate Aminotransferase (AST)	Diagnose PM/DM
374	Creatine Kinase (CK), Total	Diagnose PM/DM
39149	Interstitial Lung Disease (ILD) Panel[b,c] Includes Jo-1, EJ, OJ, PL-7, PL-12, MDA-5, SS-A, Th/To, fibrillarin, centromere A and B, PM/Scl-100, PM/Scl-75, Scl-70 antibodies, 14.3.3 eta protein (test code 91455), cyclic citrullinated peptide IgG (test code 11173), rheumatoid factor (test code 4418), RNA polymerase III antibody (test code 19899) and RNP antibody (test code 19887).	Identify connective tissue disease (myositis, rheumatoid arthritis, systemic sclerosis, Sjögren syndrome, or overlap myositis [mixed connective tissue disease]) as a possible cause of interstitial lung disease
5810(X)	Jo-1 Antibody	Diagnose PM/DM
593	Lactate Dehydrogenase (LD)	Diagnose PM/DM
90995	Myositis AssessR™[c] Includes EJ (test code 90998), OJ (test code 90999), PL-7 (test code 90996), PL-12 (test code 90997), Mi-2 (test code 17172), Ku (test code 18855), and SRP (test code 16318) antibodies.	Diagnose PM/DM
10185(X)	Myositis AssessR™ plus Jo-1 Antibodies[c] Includes Myositis AssessR™ (test code 90995) and Jo-1 (test code 5810[X]) antibodies	Diagnose PM/DM (Jo-1 provides a more definitive diagnosis)
94777	Myositis Specific 11 Antibodies Panel[b] Includes Jo-1, EJ, OJ, PL-7, PL-12, SRP, Mi-2α, Mi-2β, MDA-5, NXP-2, and TIF1-γ antibodies.	Diagnose PM/DM (Jo-1 provides a more definitive diagnosis) Diagnose IMNM Diagnose cancer-associated DM Diagnose juvenile DM Diagnose amyopathic DM
94646	Anti-PM/Scl-100 Antibody, EIA	Diagnose overlap of PM/DM with systemic sclerosis
91292	Anti-U3 RNP (Fibrillarin)	Diagnose overlap of PM/DM with systemic sclerosis
18855	Ku Autoantibodies	Diagnose overlap of PM with SLE or systemic sclerosis
38568	Sjögren's Antibody (SS-A)	Diagnose overlap of PM/DM with Sjögren syndrome, SLE, or systemic sclerosis
38567	Sm/RNP Antibody	Diagnose overlap of PM with SLE or systemic sclerosis

DM, dermatomyositis; IMNM, immune-mediated necrotizing myopathy; PM, polymyositis; SLE, systemic lupus erythematosus.

[a] This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the US Food and Drug Administration.

[b] This test was developed and its analytical performance characteristics have been determined by Quest Diagnostics. It has not been cleared or approved by the US Food and Drug Administration. This assay has been validated pursuant to the CLIA regulations and is used for clinical purposes.

[c] Panel components may be ordered separately.

Table 2. IIM Diagnostic Criteria[5]

If no other cause is present, sum of points is ≥5.5 (≥6.7 with biopsy), and age of onset is

- ≥18 years, then classify patient as having
  - DM if rash[a] is present with muscle weakness[b]
  - PM (or IMNM) if rash[a] is absent with muscle weakness[b]
  - IBM if rash[a] is absent with muscle weakness[b], as well as clinical[c] or biopsy[d] features
  - ADM if rash[a] is present without muscle weakness[b]
- <18 years, then classify patient as having
  - JDM if rash[a] is present with muscle weakness[b]
  - Juvenile IIM (not JDM) if rash[a] is absent with muscle weakness[b]

Criteria	Points without biopsy	Points with biopsy
Biopsy		
Endomysial infiltration of mononuclear cells surrounding, but not invading, myofibers		1.7
Perimysial or perivascular infiltration or both of mononuclear cells		1.2
Perifascicular atrophy		1.9
Rimmed vacuoles		3.1
Clinical		
Age of onset of first symptom assumed to be related to the disease		
≥18 years and <40 years	1.3	1.5
≥40 years	2.1	2.2
Objective symmetric weakness, usually progressive, of the		
proximal upper extremities	0.7	0.7
proximal lower extremities	0.8	0.5
Neck flexors are relatively weaker than neck extensors	1.9	1.6
Proximal muscles are relatively weaker than distal muscles in the legs	0.9	1.2
Heliotrope rash	3.1	3.2
Göttron papules	2.1	2.7
Göttron sign	3.3	3.7
Dysphagia or oesophageal dysmotility	0.7	0.6
Laboratory		
Jo-1 (anti-histidyl-tRNA synthetase) autoantibody present	3.9	3.8
Elevated serum levels of creatine kinase (CK)[e] or lactate dehydrogenase (LD)[e] or aspartate aminotransferase (ASAT/AST/SGOT)[e] or alanine aminotransferase (ALAT/ALT/SGPT)[e]	1.3	1.4

ADM, amyopathic DM; DM, dermatomyositis; IBM, inclusion body myositis; IIM, idiopathic inflammatory myopathy; IMNM, immune-mediated necrotizing myopathy; JDM, juvenile DM; PM, polymyositis.

[a] Heliotrope rash, Göttron sign, or Göttron papules.

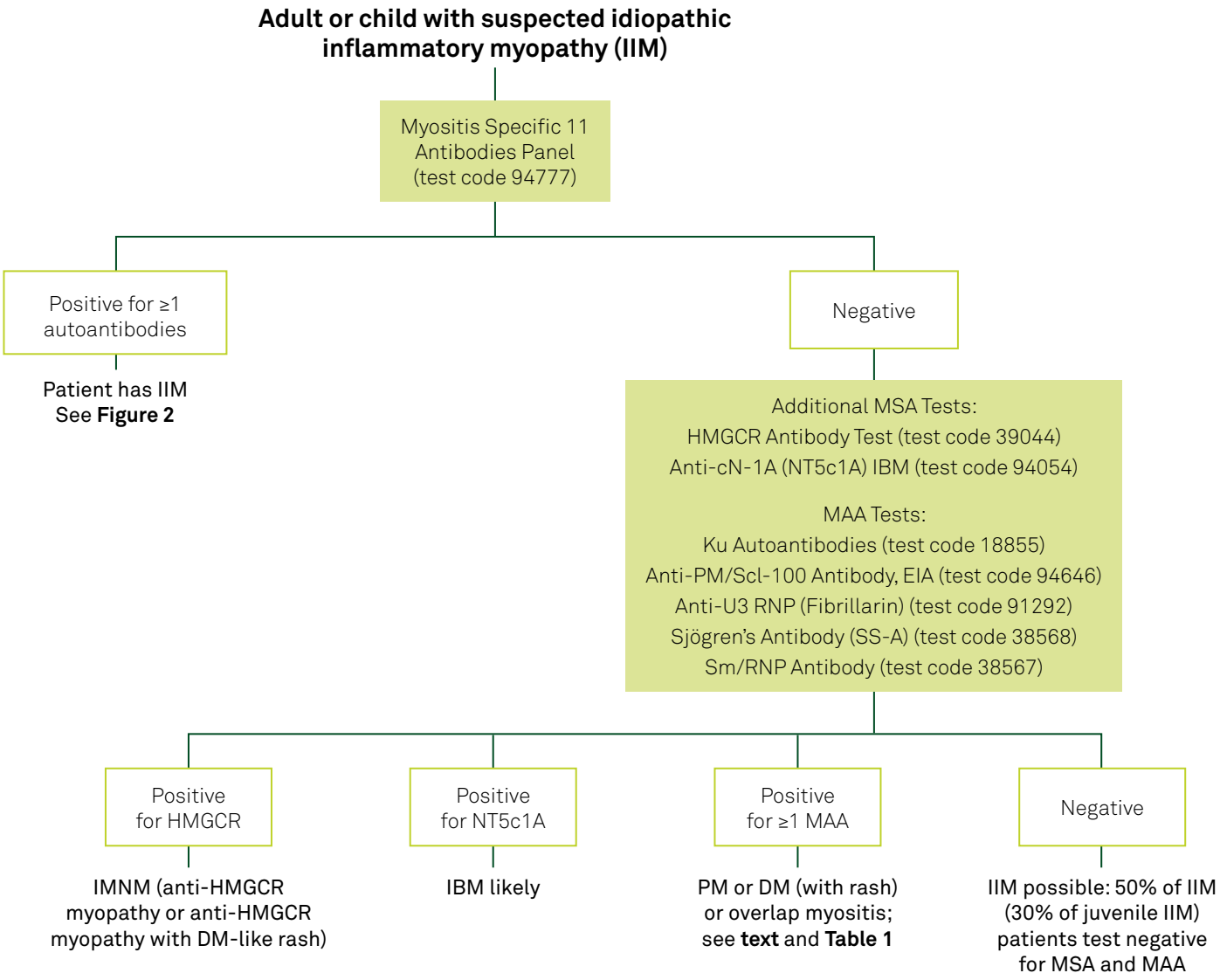
[b] Objective symmetric weakness, usually progressive of the upper or lower extremities; neck flexors weaker than extensors; or proximal leg muscles weaker than distal.

[c] Finger flexor weakness that does not improve in response to treatment.

[d] Rimmed vacuoles present.

[e] Serum levels above the upper limit of normal.

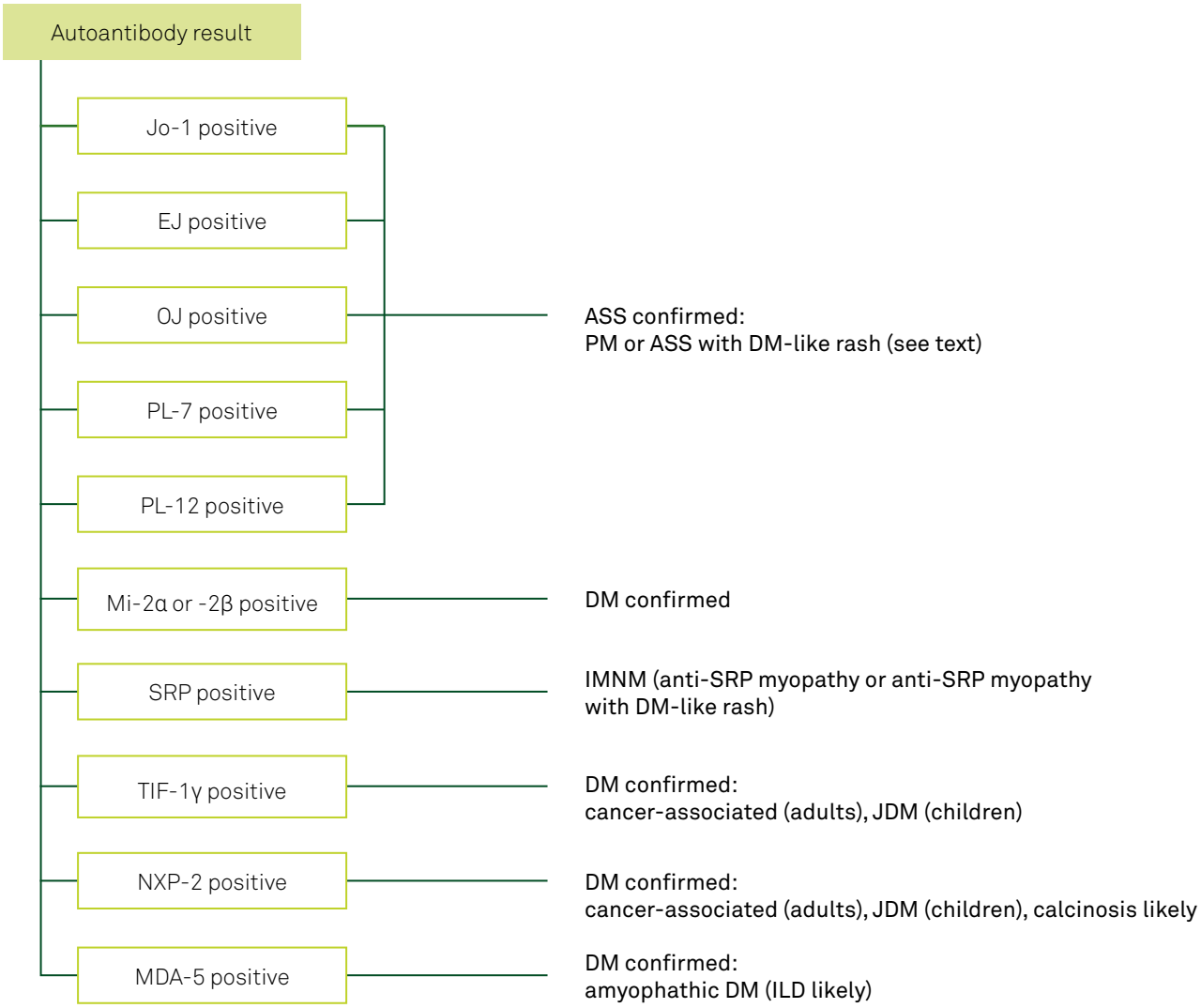
Figure 1. Idiopathic Inflammatory Myopathy: Selecting the Appropriate Laboratory Tests



DM, dermatomyositis; HMGCR, 3-hydroxy-3-methylglutaryl-coenzyme A reductase; IBM, inclusion body myositis; IIM, idiopathic inflammatory myopathy; IMNM, immune-mediated necrotizing myopathy; MAA, myositis-associated antibody; MSA, myositis-specific antibody; PM, polymyositis.

This algorithm is intended as a guide for using Quest Diagnostics laboratory tests to diagnose IIM. It is based on references 1, 8-22, and 27. The algorithm is provided for informational purposes only and is not intended as medical advice. A physician's test selection and interpretation, diagnosis, and patient management decisions should be based on his/her education, clinical expertise, and assessment of the patient.

Figure 2. Interpretation of Myositis Specific 11 Antibodies Panel (Test Code 94777) and Antisynthetase Panel 1 (Test Code 38075)



ASS, antisynthetase syndrome; DM, dermatomyositis; IIM, idiopathic inflammatory myopathy; ILD, interstitial lung disease; IMNM, immune-mediated necrotizing myopathy; JDM, juvenile DM; PM, polymyositis.

Positivity for 1 or more myositis-specific antibodies confirms a diagnosis of IIM. This algorithm is intended as a guide for using Quest Diagnostics laboratory tests to diagnose IIM. It is based on references 1 and 8-22. The algorithm is provided for informational purposes only and is not intended as medical advice. A physician's test selection and interpretation, diagnosis, and patient management decisions should be based on his/her education, clinical expertise, and assessment of the patient.

Jo-1 antibody is observed in 21% of patients with polymyositis and in 11% of those with antisynthetase syndrome with dermatomyositis-like rash.[1] Because it is 100% specific for IIM,[10,11] Jo-1 positivity is a major contributor to a definitive IIM diagnosis.[5] The remaining classical myositis-specific antibodies occur less frequently than Jo-1[1] but are also highly specific (97% to 100%) for IIM.[10,13,14] Accordingly, a positive test result for any of the classical myositis-specific antibodies is highly suggestive of IIM (**Table 2**). A negative test result does not rule out IIM; classical myositis-specific antibodies are not detected in 50% of affected patients.[1]

The type of myositis-specific antibody detected correlates with clinical phenotype, disease severity, and treatment response:

- Mi-2 antibodies are associated with dermatomyositis rash with few other extramuscular signs.[1] Detection of Mi-2 antibodies suggests that the patient may respond well to standard immunosuppressive therapy.[23]
- Although SRP antibody is associated with few extramuscular signs in IMNM,[1] it is associated with severe disease onset and a poor response to standard immunosuppressive therapy.[13,18,23] Detection of an SRP antibody thus suggests a need for more aggressive treatment than used for patients with the other classical myositis-specific antibodies.[8,13,18,23]
- Synthetase antibodies are associated with antisynthetase syndrome in IIM patients. In IIM patients with antisynthetase syndrome, arthralgia and interstitial lung disease are the most prevalent extramuscular symptoms.[1] Patients with antisynthetase syndrome typically have a moderate response to standard immunosuppressive therapy.[23] Depending on the type of synthetase antibody, symptoms vary. A meta-analysis of 3,487 patients (27 studies) indicated that[1]
  - Jo-1 antibody is associated with a significantly higher risk of myositis, arthralgia, and mechanic's hands compared with non-Jo-1 antibodies.
  - Non–Jo-1 antibodies are associated with a significantly higher risk of fever and interstitial lung disease compared with Jo-1 antibody.
  - The risk of Raynaud phenomenon does not differ significantly between patients with Jo-1 antibodies and those with non-Jo-1 antibodies.

Myositis-specific antibodies for IBM and IMNM have been more recently described:

- cN-1a antibodies target cytosolic 5'-nucleotidase and are highly predictive for IBM; a positive result correctly identifies 90% to 95% IBM of patients compared to 5% to 10% of patients with other IIMs or immune neuromuscular disease.[24] However, sensitivity estimates vary widely, ranging from 37% to 76%.[24]
- HMGCR antibodies target 3-hydroxy-3-methylglutaryl-coenzyme A reductase (HMGCR); positive results correctly identify nearly 100% of patients with IMNM. However, sensitivity for IMNM is about 45%.[25] Presence of HMGCR antibodies defines the "anti-HMGCR myopathy" IMNM subgroup and is mostly associated with statin exposure. It is also observed in "statin-naive" patients, although some of these patients may have been exposed to natural statins in foods.[8] Compared to statin-exposed IMNM patients, statin-naive patients tend to be younger and their symptoms more severe and refractory to immunosuppressive drugs.[26]
- IMNM patients with anti-HMGCR myopathy are distinguished from those with anti-SRP myopathy and "antibody-negative" IMNM patients (the third IMNM subgroup) in other ways:
  - IMNM patients with anti-HMGCR myopathy may be at elevated risk for cancer compared to those with anti-SRP myopathy and the general population, but lower risk than antibody-negative IMNM patients.[8]
  - For cases of severe anti-HMGCR myopathy, the IMNM Working Group recommends intravenous immunoglobulins be considered earlier in the initial treatment regimen than for anti-SRP myopathy. Treatment recommendations for antibody-negative IMNM are similar to those for anti-HMGCR myopathy.[8]

Myositis-associated antibodies, Ku, PM/Scl, Sjögren's antibody [SS-A], and Smith [Sm]/U1-RNP antibody, are less specific for polymyositis and dermatomyositis and are found in 1% to 13% of these patients.[1] Ku and SS-A are found in 9% to 14% of IBM patients.[1] In one study, myositis-associated antibodies were found in several statin-naïve patients with anti-HMGCR myopathy.[26] In another study involving patients with systemic sclerosis, presence of U3-RNP (fibrillarin) antibody was highly indicative of overlap with myositis (31% of patients with myositis were fibrillarin-antibody positive compared with 12% with myositis who were fibrillarin-antibody negative).[27] Thus, a positive test result for a myositis-associated antibody in a symptomatic patient suggests the presence of either

polymyositis, dermatomyositis (with rash), IMNM, or IBM; overlap myositis is also a possibility (discussed below).

Cancer- and Juvenile-associated Dermatomyositis

Additional myositis-specific antibodies include TIF1-γ (p155) and NXP-2 (p140) antibodies, which are prevalent in adults with cancer-associated dermatomyositis and children with juvenile dermatomyositis.

In adults with dermatomyositis, TIF1-γ antibody has a sensitivity of 78% and a specificity of 89% for cancer.[15] NXP-2 is detected in 31% of adults with cancer-associated adult dermatomyositis and, when combined with TIF1-γ measurement, improves the sensitivity for detecting cancer.[16] Positive test results for either TIF1-γ or NXP-2 antibodies identify cancer in 83% of adults with dermatomyositis and are thus highly suggestive of malignancy.[16]

TIF1-γ can be detected in 35% of children with juvenile dermatomyositis, making it the most prevalent myositis-specific antibody among this group.[17] NXP-2 is also prevalent, detected in 22% of these patients.[17] Classical myositis-specific antibodies are generally far less prevalent in children, so including both TIF1-γ and NXP-2 in the panel improves sensitivity for juvenile dermatomyositis over the classical myositis-specific antibodies alone.[17]

Unlike in adults, TIF1-γ antibody is not associated with cancer in children.[18] However, the presence of NXP-2 is highly associated with disease severity and calcinosis, which affects nearly one-third of patients with juvenile dermatomyositis and is a major cause of morbidity in this group.[18]

Amyopathic Dermatomyositis

MDA-5 antibody, another myositis-specific antibody, is prevalent in patients with clinically amyopathic dermatomyositis. These patients have rashes in the absence of clinical myositis. The unique cutaneous phenotype includes cutaneous and oral ulcerations, painful palmar papules, alopecia, and panniculitis.[28] The presence of MDA-5 antibody is associated with a high likelihood of interstitial lung disease (9% to 75% of IIM patients, highest in Asian cohorts).[19] Dermatomyositis patients with interstitial lung disease typically have a poorer prognosis because of rapid disease progression. A meta-analysis indicated that the odds of interstitial lung disease is substantially increased in patients who test positive for MDA-5 antibody results than in those who test negative (odds ratio 18.3; 95% CI, 9.7-24.5, $P<.00001$).[19] Early detection of interstitial lung disease by identifying the MDA-5 antibody may improve prognosis by prompting intensive immunosuppressive therapy early in the disease.[20]

Overlap Myositis

Myositis-associated autoantibodies are most often detected in patients with overlap myositis syndromes. Ku, PM/Scl, Sm/RNP, and SS-A antibodies are found in 13% to 32% of these patients.[1] A positive result for PM/Scl or U3-RNP antibodies suggests overlap of polymyositis (or dermatomyositis with rash) with systemic sclerosis. Ku or Sm/RNP antibodies suggest overlap with SLE or systemic sclerosis. The presence of Sjögren's antibody suggests overlap with SLE, Sjögren syndrome, or systemic sclerosis (**Table 1**).[21]

References

1. Lega JC, Fabien N, Reynaud Q, et al. The clinical phenotype associated with myositis-specific and associated autoantibodies: a meta-analysis revisiting the so-called antisynthetase syndrome. *Autoimmun Rev*. 2014;13(9):883-891. doi:10.1016/j.autrev.2014.03.004
2. Meyer A, Meyer N, Schaeffer M, et al. Incidence and prevalence of inflammatory myopathies: a systematic review. *Rheumatology (Oxford)*. 2015;54(1):50-63. doi:10.1093/rheumatology/keu289
3. Iaccarino L, Gatto M, Bettio S, et al. Overlap connective tissue disease syndromes. *Autoimmun Rev*. 2013;12(3):363-373. doi:10.1016/j.autrev.2012.06.004
4. Garton MJ, Isenberg DA. Clinical features of lupus myositis versus idiopathic myositis: a review of 30 cases. *Br J Rheumatol*. 1997;36(10):1067-1074. doi:10.1093/rheumatology/36.10.1067
5. Lundberg IE, Tjärnlund A, Bottai M, et al. 2017 European League Against Rheumatism/American College of Rheumatology classification criteria for adult and juvenile idiopathic inflammatory myopathies and their major subgroups. *Ann Rheum Dis*. 2017;76(12):1955-1964. doi:10.1136/annrheumdis-2017-211468
6. Nagaraju K, Lundberg IE. Inflammatory diseases of muscle and other myopathies. In: Firestein GS, Budd RC, Gabriel SE, et al, eds. *Kelley's Textbook of Rheumatology*. Elsevier/Saunders; 2013:1404-1430.
7. Volochayev R, Csako G, Wesley R, et al. Laboratory test abnormalities are common in polymyositis and dermatomyositis and differ among clinical and demographic groups. *Open Rheumatol J*. 2012;6:54-63. doi:10.2174/1874312901206010054
8. Allenbach Y, Mammen AL, Benveniste O, et al. 224th ENMC International Workshop: clinico-sero-pathological classification of immune-mediated necrotizing myopathies Zandvoort, The Netherlands, 14-16 October 2016. *Neuromuscul Disord*. 2018;28(1):87-99. doi:10.1016/j.nmd.2017.09.016
9. Mammen AL, Allenbach Y, Stenzel W, et al. 239th ENMC International Workshop: classification of dermatomyositis, Amsterdam, the Netherlands, 14-16 December 2018. *Neuromuscul Disord*. 2020;30(1):70-92. doi:10.1016/j.nmd.2019.10.005

10. Hengstman GJ, van Brenk L, Vree Egberts WT, et al. High specificity of myositis specific autoantibodies for myositis compared with other neuromuscular disorders. *J Neurol*. 2005;252(5):534-537. doi:10.1007/s00415-005-0683-5
11. Vázquez-Abad D, Rothfield NF. Sensitivity and specificity of anti-Jo-1 antibodies in autoimmune diseases with myositis. *Arthritis Rheum*. 1996;39(2):292-296. doi:10.1002/art.1780390218
12. Pilkington C, Tjärnlund A, Bottai M, et al. A47: progress report on the development of new classification criteria for adult and juvenile idiopathic inflammatory myopathies. *Arthritis Rheumatol*. 2014;66:S70-S71. doi:10.1002/ART.38463
13. Aggarwal R, Oddis CV, Goudeau D, et al. Anti-signal recognition particle autoantibody ELISA validation and clinical associations. *Rheumatology (Oxford)*. 2015;54(7):1194-1199. doi:10.1093/rheumatology/keu436
14. Nakashima R, Imura Y, Hosono Y, et al. The multicenter study of a new assay for simultaneous detection of multiple anti-aminoacyl-tRNA synthetases in myositis and interstitial pneumonia. *PLoS One*. 2014;9(1):e85062. doi:10.1371/journal.pone.0085062
15. Trallero-Araguás E, Rodrigo-Pendás JÁ, Selva-O'Callaghan A, et al. Usefulness of anti-p155 autoantibody for diagnosing cancer-associated dermatomyositis: a systematic review and meta-analysis. *Arthritis Rheum*. 2012;64(2):523-532. doi:10.1002/art.33379
16. Fiorentino DF, Chung LS, Christopher-Stine L, et al. Most patients with cancer-associated dermatomyositis have antibodies to nuclear matrix protein NXP-2 or transcription intermediary factor 1γ. *Arthritis Rheum*. 2013;65(11):2954-2962. doi:10.1002/art.38093
17. Shah M, Mamyrova G, Targoff IN, et al. The clinical phenotypes of the juvenile idiopathic inflammatory myopathies. *Medicine (Baltimore)*. 2013;92(1):25-41. doi:10.1097/MD.0b013e31827f264d
18. Tansley S, Wedderburn LR. Comparing and contrasting clinical and serological features of juvenile and adult-onset myositis: implications for pathogenesis and outcomes. *Curr Opin Rheumatol*. 2015;27(6):601-607. doi:10.1097/BOR.0000000000000224
19. Zhang L, Wu G, Gao D, et al. Factors associated with interstitial lung disease in patients with polymyositis and dermatomyositis: a systematic review and meta-analysis. *PLoS One*. 2016;11(5):e0155381. doi:10.1371/journal.pone.0155381
20. Nakashima R, Hosono Y, Mimori T. Clinical significance and new detection system of autoantibodies in myositis with interstitial lung disease. *Lupus*. 2016;25(8):925-933. doi:10.1177/0961203316651748
21. Peng SL, Craft JE. Antinuclear antibodies. In: Firestein GS, Budd RC, Gabriel SE, et al, eds. *Kelley's Textbook of Rheumatology*. Elsevier/Saunders; 2013:789-803.
22. Bohan A, Peter JB. Polymyositis and dermatomyositis (first of two parts). *N Engl J Med*. 1975;292(7):344-347. doi:10.1056/NEJM197502132920706
23. Love LA, Leff RL, Fraser DD, et al. A new approach to the classification of idiopathic inflammatory myopathy: myositis-specific autoantibodies define useful homogeneous patient groups. *Medicine (Baltimore)*. 1991;70(6):360-374. doi:10.1097/00005792-199111000-00002
24. Greenberg SA. Inclusion body myositis: clinical features and pathogenesis. *Nat Rev Rheumatol*. 2019;15(5):257-272. doi:10.1038/s41584-019-0186-x
25. Musset L, Allenbach Y, Benveniste O, et al. Anti-HMGCR antibodies as a biomarker for immune-mediated necrotizing myopathies: a history of statins and experience from a large international multi-center study. *Autoimmun Rev*. 2016;15(10):983-993. doi:10.1016/j.autrev.2016.07.023
26. Jiao Y, Cai S, Lin J, et al. Statin-naive anti-HMGCR antibody-mediated necrotizing myopathy in China. *J Clin Neurosci*. 2018;57:13-19. doi:10.1016/j.jocn.2018.08.010
27. Tall F, Dechomet M, Riviere S, et al. The clinical relevance of antifibrillarin (anti-U3-RNP) autoantibodies in systemic sclerosis. *Scand J Immunol*. 2017;85(1):73-79. doi:10.1111/sji.12510
28. Kurtzman DJB, Vleugels RA. Anti-melanoma differentiation-associated gene 5 (MDA5) dermatomyositis: a concise review with an emphasis on distinctive clinical features. *J Am Acad Dermatol*. 2018;78(4):776-785. doi:10.1016/j.jaad.2017.12.010