



15. The anti-MDA5 autoantibody phenotype: Defining clinical, biochemical and radiological features suggestive of anti-MDA5-associated rapidly progressive interstitial lung disease.

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Background: Anti-MDA5 antibody is a novel autoantibody associated with characteristic cutaneous manifestations, and whose clinical phenotype has been reported to be a mimicker of the anti-synthetase syndrome. Unlike anti-synthetase syndrome, anti-MDA5 has often been associated with rapidly progressive interstitial lung disease (RPILD) with a poor prognosis, especially with elevated serum ferritin.

Objective: The primary goal of our study was to define clinical, biochemical, and radiological features predictive of MDA5-associated RPILD that would justify empirical treatment, pending MDA5 autoantibody confirmation.

Methods: We retrospectively analyzed the clinical features of 7 patients who presented in an inpatient setting and were subsequently confirmed to have MDA5-associated RPILD, using a novel line immunoassay in 3 patients.

Results: Six of the 7 patients were men. Six patients presented with dyspnea, and RPILD developed in all (100%) patients. MDA5-associated cutaneous symptoms appeared within one month of respiratory symptoms in 6 (86%) patients, but were recognized at initial presentation in 2 patients. These included palmar papules and/or erythema (n=4 patients), lateral papules of the fingers (n=3), skin ulcerations (n=2), and mechanic's hands (n=4). Gottron papules and sign were sometimes psoriasiform. Shawl and V-signs were not seen, whereas periungueal erythema was always present. Profound weight loss ranging from 14 to 37 lbs (mean 21.9 lbs) occurred in all (100%) patients over 1 to 2 months before presentation. All patients had articular symptoms. One patient had Raynaud phenomenon. Four patients were clinically amyopathic; only 1 patient had CK levels >500 U/L. AST/ALT were elevated in 6 (86%) patients. Nuclear and cytoplasmic fluorescence on ANA testing on HEp-2 substrate were absent. Imaging at initial presentation showed ground glass opacities with consolidation in 6 (86%) patients, isolated ground glass opacities in 1 patient, and reticulations in 4 patients, in a bibasilar peripheral distribution in 6 patients. Four (57%) patients died. Time from hospitalization to death ranged from 6 to 31 days. Survivors received mycophenolate mofetil and/or tacrolimus, concomitantly with corticosteroids. Hyperferritinemia (>1000 ng/ml, n=4 patients) upon admission was associated with a fatal outcome (n=4 deaths).

Conclusion: In an inpatient setting, anti-MDA5-associated ILD was a severe, rapidly progressive condition with a high mortality. Cutaneous findings were subtle and often followed the respiratory symptoms. Dyspnea, anti-MDA5-associated cutaneous findings, profound weight loss, articular symptoms, normal or low CKs with elevated AST/ALT, and absence of nuclear and cytoplasmic fluorescence on ANA testing should alert the clinician to the possibility of anti-MDA5-associated RPILD. Hyperferritinemia was associated with a poor outcome. Early institution of combination immunosuppressive therapy may prove lifesaving.