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A LARGE INCREASE IN ANTI-MELANOMA-DIFFERENTIATION-ASSOCIATED-GENE-5 (MDA5) ANTIBODY POSITIVITY AND ASSOCIATED DISEASE IN YORKSHIRE SINCE 2020

POS1218

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Background

Melanoma differentiation-associated protein 5 (MDA5) is an intracellular detector of viral RNA. It is considered that viral infections are involved in the aetiology of autoimmune diseases, including autoimmune myositis. Previously we reported on a post-COVID-19 pandemic cluster of myositis occurring in the Yorkshire region (De Marco, 2022),

Noting that MDA5 is a critical Pattern Recognition Receptor for SARS-CoV-2, and noting a dramatic increased rate of anti-MDA5 positivity on Myositis Immunoblot testing, we set out to determine patterns of disease associated with MDA5 positivity.

Objective

- To appraise the significance of the observed increased anti-MDA5 positivity recognized at our tertiary centre.

Methods

The Leeds Teaching Hospitals NHS Trust serves as an immunology laboratory reference for the wider Yorkshire region (3.6 million residents).
We audited the increased anti-MDA5 positivity in relationship to other muscle-specific autoantibodies (Euroimmun immunoblot©) analysing retrospectively all tests performed between January 2018 and December 2022.
Clinical notes review focused on: MDA5 positivity without disease; patterns of symptomatic MDA5 disease (including degree of interstitial lung disease); muscle or other organs involvement; response to therapy.

We also appraised the temporal associations between recent COVID-19 infection and SARS-CoV-2 vaccination.

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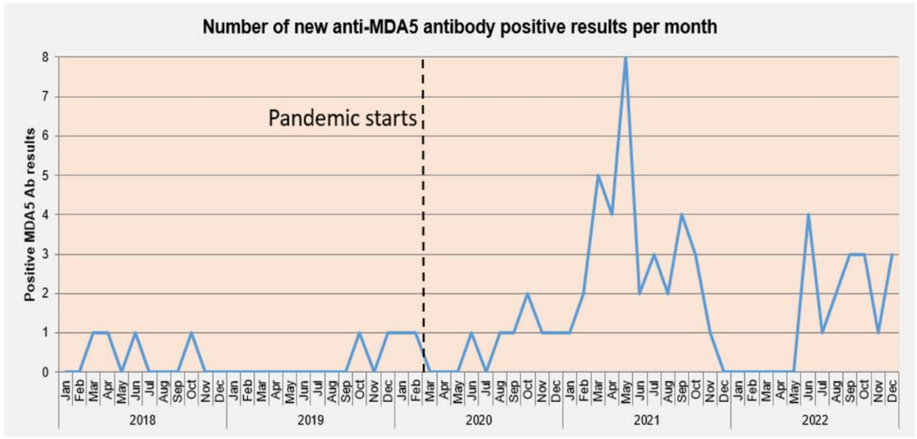
Results

Figure 1



Summary per year	2018	2019	2020	2021	2022
Number of requests	364	535	459	812	1011
Number of patients	339	505	425	726	947
Total MDA5 Ab positive	4	3	10	40	22
New MDA5 Ab positive	4	2	9	35	17
Percentage positive (of total requests)	**1.1**	**0.6**	**2.2**	**4.9**	**2.2**

Table 1

	Anti-MDA5 positive with ILD	Anti- MDA5 positive without ILD
Number of cases (females, males)	18 (11, 7)	32 (21, 11)
Age in years (mean)	54.72	44.06
Indication for antibody testing		
Dyspnoea (isolated)	9	0
Dyspnoea clinically predominant, with associated myositis features	7	0
Myositis features clinically predominant, with dyspnoea	2	0
Dermato-myositis-type clinical features, without dyspnoea	0	15
Scleroderma-type clinical features, without dyspnoea	0	8
Mixed/non-specific clinical features	0	9
Autoimmune serology		
ANA IIF positive	8	10
ANA IIF negative	10	20
ANA IIF not available	NA	2
Myositis-associated autoantibodies	17	20
Anti-SAE1	8	14
Anti-Ro52	6	7
Anti-PMScl100	2	3
Others	2	6
Clinical Features (other than ILD)		
Cutaneous	5	8
Cardiac	0	1
Mechanic's hands	5	6
Synovitis	5	NA
Raynaud's phenomenon	6	6
Proximal myopathy	3	6
Treatment Outcomes		
Response to treatment	4	25
Mortality	6*	0
Progressive lung involvement	6	0
Relationship between MDA5 and COVID-19 Infection/Vaccination		
Infection preceding MDA5 positivity	2	7
Vaccination preceding MDA5 positivity	6	32

MDA5 = Melanoma Differentiation-Associated protein 5; ILD = Interstitial Lung Disease; ANA = Anti-Nuclear Autoantibodies; IIF = Indirect Immmuno-fluorescence; COVID-19 = Coronavirus disease 2019 (COVID-19), a contagious disease caused by the Severe Acute Respiratory Syndrome CoronaVirus 2 (SARS-CoV-2).* 3 cases positive for Anti-SAE1; 1 case positive for Anti-Fibrillarin; 1 case positive for Anti-Ro; 1 case positive for Anti-MDA5

Requests for anti-MDA5 were stable between 2018 and 2020, but doubled thereafter. Anti-MDA5 positivity went from 0.6% to 4.9% in that period, dropping to 2.2% at the end of 2022 (Figure 1). Out of 66 individuals testing positive for anti-MDA5, clinical notes were available in 50 cases. Eleven had myositis without ILD (6 had dermatomyositis/"mechanic" hands rash). 18/50 cases developed ILD (12 with associated myositis, including 5 dermatomyositis rash and 5 "mechanic" hands). No cases of carditis were recorded.

After treatment, outcome was stable/improved in 29 cases (4 ILD cases). 6 died despite therapy (all ILD cases). Twenty cases had signs described as within the connective tissues diseases spectrum (without any lung involvement), though no formal diagnosis.
A minority of cases were associated with evidence of SARS-CoV-2 infection.
14/50 cases had SARS-CoV-2 vaccination documented prior anti-MDA5 positivity.

Conclusions

Our data show an increased rate of anti-MDA5 positivity in the latter stages of the COVID-19 pandemic, as previously noted in the UK (Hannah J, ACR 2022). Most cases had MDA5 positivity without confirmed autoimmune disease and despite the MDA5 positivity occurrence in the face of the COVID-19 pandemic further longitudinal observation is needed to ascertain any potential links with either infection, vaccination or both.

References

1) De Marco G, et al Vaccines (Basel) 2022; 10: 1184.
2) Hannah J, et al. ACR Convergence Meeting 2022; Abstract Number: 1857

Institutions

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7) 7) Airedale NHS Foundation Trust, UK
8) 8) Calderdale and Huddersfield NHS Foundation Trust, UK