Letters to the Editor

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Clinical, serological and HLA profiles in non-Caucasian UK idiopathic inflammatory myopathy

Sir, Since 2000, the UK Adult Onset Myositis Immunogenetic Collaboration (AOMIC) has recruited idiopathic inflammatory myopathy (IIM) cases across the UK. In this brief report, we summarize the clinical, serological and HLA Class II status of non-Caucasian IIM cases, to ascertain whether differences are observed among UK IIM ethnic populations.

DNA was available from 28 UK non-Caucasian IIM cases. Adult IIM patients, aged ≥18 years of age at disease onset, with probable or definite myositis [1] were recruited through AOMIC [2]. Data were also available from 303 UK Caucasian IIM cases previously described [2, 3]. The collaborating AOMIC physicians confirmed interstitial lung disease (ILD) and cancer-associated myositis (CAM) [4] by relevant investigations. Radio-immunoprecipitation was used for determination of myositis-specific antibodies (anti-synthetases: Jo-1, PL-7, PL-12, EJ, OJ, KS; anti-Mi-2, anti-SRP and anti-155/140) and myositis-associated antibodies [anti-polymyositis (PM)-Scl, anti-Ku, anti-U1-RNP, anti-U3-RNP], as previously described [2, 4]. This study was approved by the local research ethics committee and informed consent was obtained according to the Declaration of Helsinki. A Wilcoxon–Mann–Whitney test was used to compare the age of onset between Caucasians and non-Caucasians. Associations were calculated from 2 x 2 contingency tables using the chi-squared test.

Of the 28 non-Caucasian IIM cases, 14 were Asian, 12 African/Afro-Caribbean and 2 of mixed-race origin (Table 1). Sixty-four percent of the non-Caucasian cohort was significantly lower than 64% in Caucasian cohort [non-Caucasians, 37 years (inter-quartile range 27, 45) vs Caucasians, 49 years (38, 60), P = 0.0001].

After stratification by gender, this observation was only significantly lower in non-Caucasian females [non-Caucasians females, 33 years (27, 41) vs Caucasian females, 49 years (38, 60), P = 0.0001]. No significant difference for age of onset was noted between African/Afro-Caribbean or Asian cases.

CAM was not detected in the non-Caucasian cohort, but was present in 6% of the Caucasian IIM cohort, and in 15% of the DM cases [4]. With respect to ILD, there were eight (29%) non-Caucasian IIM cases and six of seven (86%) anti-synthetase antibody-positive cases. Although a higher frequency of ILD was observed in African/Afro-Caribbean (35%) compared with Asian (18%) cases, due to the small sample size this was not statistically significant (P = 0.24). This difference was not attributable to differences in anti-synthetase antibody frequency. In comparison, the overall frequency of ILD in the Caucasian cohort was 20%, and 44% in anti-synthetase positive cases. Within the non-Caucasian cohort, only PM cases possessed anti-Jo-1 antibody (n = 3) and anti-Mi-2 antibody (n = 2). Two additional DM cases (PL-12, OJ) and none of the overlap cases possessed anti-synthetase antibodies other than anti-Jo-1. The only myositis-specific antibodies recorded in the Asian cases were two cases with anti-Jo-1 antibodies. Three PM cases possessed multiple antibodies (one with Jo-1 and U1-RNP, one with Mi-2 and U1-RNP; one with EJ, Ku and U1-RNP). No cases with anti-SRP, -KS or -155/140 antibodies were noted.

All anti-Pm-Scl, anti-Mi-2, two of three anti-Jo-1 and the single anti-PL-12 antibody-positive positive case possessed a copy of HLA-DRB1*03. Six of 10 anti-U1-RNP antibody-positive patients possessed a copy of HLA-DR2 (DRB1*15/16). None of the anti-U-RNP antibody-positive patients was HLA-DRB1*04 positive and neither of the anti-Mi-2 antibody-positive patients was HLA-DRB1*07 positive.

We have presented the first correlation of phenotype/serotype-HLA Class II genotype in non-Caucasian UK IIM cases. Although this is a small study, it has provided a useful opportunity to compare these data with existing UK Caucasian data [2]. A lower median age of onset in non-Caucasian females has also been observed in SLE [5]. There is a high frequency of ILD in non-Caucasians possessing anti-synthetase antibody. Notably, ILD is also increased in African–American compared with Caucasian anti-topoisomerase I antibody-positive SSc cases [6]. The absence of CAM in the non-Caucasian cohort could be due to lack of statistical power. A low CAM frequency (2.7%) was noted in a recent larger study of 262 African–American IIM cases [7].

The known HLA-DRB1*03 association in anti-PM-Scl and anti-synthetase positive cases is apparent across ethnic groups, but the U1-RNP/DRB1*04 and Mi-2/DRB1*07 associations described in UK IIM Caucasians [2] are not observed. The Mi-2/DRB1*03 association in UK African cases may relate to the Mi-2/DRB1*0302 association observed in African–Australians, where a shared amino acid sequence motif has been described between DRB1*0701 and DRB1*0302 [7]. However, an anti-RNP/DRB1*08 association described in the same US study was not observed in our data. We acknowledge that the low patient numbers in our study make it difficult to conduct a meaningful comparison.

Despite our data possessing comparatively small numbers, consistencies are observed with other published data [7], emphasizing the importance of case stratification by ethnicity and serotype. Larger-scale analyses of non-Caucasian IIM cases may yield further useful information to investigate similarities and differences between different IIM ethnic groups.

*Results expressed as median (interquartile range). DM: dermatomyositis.

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**Table 1. Patient details and antibody frequencies in non-Caucasian IIM**

<table>
<thead>
<tr>
<th></th>
<th>PM (n = 14)</th>
<th>DM (n = 6)</th>
<th>Overlap (n = 8)</th>
<th>Combined (n = 28)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Females</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median age of onset*</td>
<td>39 (34, 57)</td>
<td>44 (29, 46)</td>
<td>27 (26, 33)</td>
<td>37 (27, 45)</td>
</tr>
<tr>
<td><strong>Myositis-specific antibodies</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jo-1</td>
<td>3 (21)</td>
<td>0</td>
<td>0</td>
<td>3 (11)</td>
</tr>
<tr>
<td>PL-7</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1 (4)</td>
</tr>
<tr>
<td>PL-12</td>
<td>0</td>
<td>1 (17)</td>
<td>0</td>
<td>1 (4)</td>
</tr>
<tr>
<td>EJ</td>
<td>1 (7)</td>
<td>0</td>
<td>0</td>
<td>1 (4)</td>
</tr>
<tr>
<td>OJ</td>
<td>0</td>
<td>1 (17)</td>
<td>0</td>
<td>1 (4)</td>
</tr>
<tr>
<td>Any of the above</td>
<td>2 (14)</td>
<td>2 (33)</td>
<td>0</td>
<td>7 (25)</td>
</tr>
<tr>
<td><strong>Myositis-associated antibodies</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>U1-RNP</td>
<td>4 (29)</td>
<td>0</td>
<td>6 (75)</td>
<td>10 (36)</td>
</tr>
<tr>
<td>US-RNP</td>
<td>0</td>
<td>0</td>
<td>1 (13)</td>
<td>1 (4)</td>
</tr>
<tr>
<td>Ku</td>
<td>1 (7)</td>
<td>0</td>
<td>1 (13)</td>
<td>2 (7)</td>
</tr>
<tr>
<td>PM-Scl</td>
<td>1 (7)</td>
<td>0</td>
<td>1 (13)</td>
<td>2 (7)</td>
</tr>
<tr>
<td>None of the above autoantibodies</td>
<td>5 (36)</td>
<td>3 (50)</td>
<td>0</td>
<td>8 (29)</td>
</tr>
</tbody>
</table>
**Rheumatology key message**

- A lower age at onset and cancer frequency is observed in non-Caucasian IIM.

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**Non-infectious endocarditis in a patient with cANCA-associated small vessel vasculitis**

Sir, ANCs are frequently associated with a limited group of small vessel vasculitic syndromes, referred to as ANCA-associated small vessel vasculitis (ANCA-associated SVV) [1]. ANCA-associated SVV is the most common primary systemic small vessel vasculitis in adults and includes three categories: WG, microscopic polyangiitis and Churg-Strauss syndrome [1].

Non-infectious cardiac involvement in ANCA-associated SVV is more frequent than it is thought [2]. However, both ANCA-associated SVV with endocardial compromise and subacute bacterial endocarditis (SBE) have the many overlapped clinical manifestations including detectable vegetations by cardioechography, inflammatory signs, renal involvement and constitutional symptoms. In addition, streptococcal SBE sometimes shows positive cANCA testing [3]. Here we report a case of non-infectious endocarditis with ANCA-associated SVV, which could be diagnosed in early stage by careful clinical observation as well as laboratory findings.

A 67-year-old woman presented a 1-month history of fever, polymyalgia and anorexia. Two weeks before admission, she visited the former hospital and subsequently received antibiotic therapies. As her symptoms continued, she was admitted to our hospital. On admission, her temperature was 38.5°C. Heart rate was 80/min and blood pressure was 130/80 mmHg. Lungs were normal. Auscultation of the heart revealed a systolic murmur over the aortic area. On laboratory data, white blood cell counts were 16400/mm³, with 84% neutrophils. Red blood cell count was 329 x 10⁹/mm³ and haemoglobin was 9.5 g/dl. Platelet count was 21.3 x 10⁹/mm³. CRP was 5.2 mg/dl. ESR was 121 mm/h. Blood cultures were performed four times and were all negative. Plasma glucose was 103 mg/dl. Electrolytes, proteinogram, renal function and liver enzymes were all within the normal range. Urinalysis revealed that glucose was 100 mg/dl, proteinuria 30 mg/dl, microhaematuria 3+ [20–29 red blood cells/high-power field (HPF)]. Complements were all within the normal range. ANA was negative. RF was 38.7 IU/ml (<19). The cANCA and pANCA by ELISA were 8.9 U/ml (<3.5) and <1.3 U/ml (<9.0), respectively. Anti-SS-A antibody was positive. Other serological tests including anti-SS-B antibody, anti-ds-DNA antibody, anti-Sm antibody, anti-RNP antibody, anti-cardiolipin β2GPI antibody, LAC, hepatitis B virus antigen and hepatitis C virus antibody were all negative. Electrocardiography showed inverted T wave in III, aVF and V3–V6. Echocardiography revealed the vegetation on the aortic valve, consistent with endocarditis (Fig. 1), with moderate AR. Chest X-rays showed cardiomegaly and pleuritis with bilateral pleural effusion. Chest CT revealed the infiltration of the left upper lobe, the pleuritis with bilateral pleural effusion and pericardial effusion. Abdominal CT detected no remarkable findings including mass, ascites and splenomegaly.

The administration of 30 mg daily of oral prednisolone (PSL) was started. Her clinical manifestations, such as fever, polymyalgia and anorexia, were improved within 8 days. Fourteen days after the administration of steroid therapy, all laboratory data, including CRP (0.1 mg/dl), ESR (24 mm/h), cANCA (3.7 U/ml) and findings of imaging tests, including electrocardiography, X-rays and CT, were almost normalized. The dosage of PSL was tapered gradually, and finally decreased to 12.5 mg daily at discharge. Though the laboratory data concerning inflammation improved, she complained of acute onset dyspnoea and oedema at...