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Letter to the Editor (Other)

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 × 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 IIM cases were females, compared with 71% female Caucasian cases (P = 0.46). The median age of onset of the non-Caucasian IIM cohort was significantly lower than that of the Caucasian cohort [non-Caucasians, 37 years (interquartile 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].

<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*, years</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>1 (14)</td>
<td>3 (11)</td>
</tr>
<tr>
<td>PL-7</td>
<td>1 (7)</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>1 (14)</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>5 (36)</td>
<td>2 (33)</td>
<td>0</td>
<td>7 (25)</td>
</tr>
<tr>
<td>Mi-2</td>
<td>2 (14)</td>
<td>0</td>
<td>0</td>
<td>2 (7)</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>U3-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>1 (17)</td>
<td>0</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>

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

No significant difference for age of onset was noted between African/Afro-Caribbean or Asian cases.

CAM was not observed 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 U3-RNP were noted.

All anti-PM-Scl, anti-Mi-2, two of three anti-Jo-1 and the single anti-PL-12 antibody-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-U1-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 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-Americans, 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.
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