Synovitis, Acne, Pustulosis, Hyperostosis, Osteitis (SAPHO) syndrome: is PTPN22 involved?

Sirs,

The aetiology of Synovitis, Acne, Pustulosis, Hyperostosis, Osteitis (SAPHO) syndrome has been debated since its first description in 1987 (1-4) and controversy has existed as to whether the categorisation of SAPHO syndrome as a distinct disease is appropriate (2, 3). To date, there is increasing evidence that SAPHO syndrome may be a multifactorial auto-inflammatory disorder, resulting from complex interactions between a number of predisposing factors and a variety of exogenous factors that trigger, accelerate or exacerbate the disease (5). Studies of class II HLA antigens have revealed no role for HLA-B27, Cw6 and other psoriatic or psoriatic arthritis susceptibility genes (1, 2, 6).

We report the results of a case control analysis aiming to investigate whether the genetic component of SAPHO syndrome could be disclosed by PSTPIP2, LPIN2, NOD2 as well as PSTPIP1 or PTPN22 single nucleotide polymorphisms (SNPs). This study was approved by the Human Studies Committee of the Azienda Ospedaliera-Universitaria Sant’Anna (Ferrara). Informed written consent was obtained from all the participants. In the 5 abovementioned genes, we interrogated 22 SNPs possibly associated to SAPHO syndrome and further studies may attempt to replicate our findings in another population of similar genetic background. Our restricted cases/controls cohort did not allow for a significant statistical achievement. No independent sample was available to replicate our findings. PTPN22 allele frequencies are known to vary widely across different Italian regions, and recent migratory events might have contributed to introduce stratification in the Italian population. For this reason we recruited controls born in the same region of origin of patients, in an attempt to avoid stratification.

Our results, which reflect differences in frequency profiles associated with different Italian regions, and recent migratory events might have contributed to introduce stratification in the Italian population. For this reason we recruited controls born in the same region of origin of patients, in an attempt to avoid stratification. Thus, no SNP was found in association to SAPHO syndrome, as well as in 2 genes (PSTPIP1 and PTPN22) which we looked at for the first time. The same as for the French cohort, no SNP was found in association to SAPHO syndrome in our Italian cohort of 53 patients.

The highest divergence in frequency between cases and controls was observed for SNP rs3811021, which is suspected to predispose to rheumatoid arthritis (RA) (9). PTPN22 is a reasonable candidate for SAPHO syndrome and further studies may attempt to replicate our findings in another population of similar genetic background. Our restricted cases/controls cohort did not allow for a significant statistical achievement. No independent sample was available to replicate our findings. PTPN22 allele frequencies are known to vary widely across different Italian regions, and recent migratory events might have contributed to introduce stratification in the Italian population. For this reason we recruited controls born in the same region of origin of patients, in an attempt to avoid stratification.

Our results, which reflect differences in frequency profiles in controls/alleles frequencies in a small cohort of cases affected with a very rare multi-factorial syndrome, may deserve attention even if not statistically significant.

Table I. Results of the SNP association analysis.

<table>
<thead>
<tr>
<th>GENE</th>
<th>CHR</th>
<th>SNP</th>
<th>Variant</th>
<th>Allele frequency</th>
<th>p-value</th>
<th>p-value (corrected)</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTPN22</td>
<td>1</td>
<td>rs3811021</td>
<td>c.*864T&gt;c</td>
<td>C</td>
<td>0.201</td>
<td>0.097</td>
<td>0.0060(0.132)</td>
</tr>
<tr>
<td>PTPN22</td>
<td>1</td>
<td>rs2476601</td>
<td>c.1858C&gt;T</td>
<td>C</td>
<td>0.982</td>
<td>0.927</td>
<td>0.043(0.946)</td>
</tr>
</tbody>
</table>

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References