Human leucocyte antigen in a Chinese family with thyrotoxic periodic paralysis in Singapore

C F Sum, A C K Fok, K T Tan, S H Chan, J S Cheah

Periodic paralysis is a dramatic complication in some patients who have thyrotoxicosis (Graves' disease). It occurs more commonly in thyrotoxic men of Mongoloid descent.

The familial occurrence of thyrotoxic periodic paralysis is, however, infrequent. To date there have been only a few reports of familial thyrotoxic periodic paralysis. Most reports have been based on a positive family history elicited during questioning of the patient. We report the first, to our knowledge, documented occurrence of familial thyrotoxic periodic paralysis in a Chinese family in Singapore together with the human leucocyte antigen genotypes of the family members.

Case report

A 31 year old Chinese man was admitted with characteristic clinical and biochemical features of hypokalaemic thyrotoxic periodic paralysis. His thyrotrophin receptor antibody concentration was 195 IU/l (normal <10 IU/l). He was treated with oral potassium supplements together with propranolol and carbimazole. The next day he had completely regained his muscular power. The case records of all his immediate family members who had thyrotoxicosis or thyrotoxic periodic paralysis, including a thyrotoxic maternal uncle, were recalled and studied. Subsequently the human leucocyte antigen type of all the immediate family members and maternal uncle was tested with the National Institutes of Health lymphocyte microcytotoxicity method.1 The figure shows the pedigree and human leucocyte antigen genotypes of the family.

Comment

Lately there has been much interest in the genetics of thyrotoxicosis and thyrotoxic periodic paralysis. Chan et al reported an association between human leucocyte antigen Bw46 and DR9 and thyrotoxicosis in Chinese patients.2 Those members of the family whom we studied who had documented thyrotoxicosis (with or without periodic paralysis) were haplotype A or B, each of which contains the alleles DR9, DRw53, and DQw3.

In addition, Yeo et al showed that the haplotypes A2 Bw22 and Aw19 B17 were associated with thyrotoxic periodic paralysis among Chinese patients in Singapore.3 It was reported that Bw22 and B17 were in linkage disequilibrium with A2 and Aw19, respectively. In another study Cheah concluded that it was the alleles Bw22 and B17 that carried an increased relative risk for thyrotoxic periodic paralysis.4 He also observed that the haplotype A2 Bw22 occurred in Chinese thyrotoxic patients who had periodic paralysis and was absent in Chinese thyrotoxic patients who did not have periodic paralysis.

In the family that we studied, besides the two siblings who had thyrotoxic periodic paralysis, three other siblings were haplotype A thus carrying the allele Bw22. It is tempting to speculate that thyrotoxic periodic paralysis may occur in these three siblings should they develop thyrotoxic state recur.

Familial thyrotoxicosis occurs more commonly than familial thyrotoxic periodic paralysis. Several studies of human leucocyte antigen have been performed in such families. On reviewing the cumulative results of studies of white and Chinese subjects Tian et al noted that of 36 different families that had multiple cases of

Human leucocyte antigen haplotypes:

A= A9 Bw22 DR9 DRw53 DQw3
B= A2 DR9 DRw53 DQw3
C= A11 B16 DR2 DRw52 DQw1
D= A26 B15 DR5 DRw52 DQw1
E= A13 Bw46 DR2 DQw1

Human leucocyte antigen haplotypes:
Notification of tuberculosis: Can the pathologist help?

B L Bradley, K M Kerr, A G Leitch, D Lamb

The incidence of tuberculosis in Great Britain has declined steadily over recent decades, the trend being confirmed by statutory notification data.¹ In 1986 over 6000 cases of tuberculosis were notified but this figure may be too low, for ambiguities and inaccuracies are recognised to exist in the notification system in England and Wales.¹ Data for the United States show that 37% of cases go unreported.¹

For many years in Scotland it has been the practice to notify all positive bacteriological results to cover possible failures in notification by clinicians. We wondered whether a similar procedure of notification for positive pathological biopsy specimens would further improve notification practices. We therefore identified pathological diagnoses of tuberculosis over four years, examined their characteristics, and related the findings to notification data.

Methods and results

All pathology reports issued from the University Department of Pathology, Edinburgh, in which tuberculosis was listed as the primary diagnosis or in the differential diagnosis were examined for the years 1981-4. The slides of all cases were reviewed. Patients’ case notes were scrutinised for details of diagnosis, treatment, and whether a respiratory physician had been consulted. Cases were checked against the local tuberculosis register for the corresponding years to see whether they had been notified.

Pathology reports were coded as follows: (A) a firm pathological diagnosis of tuberculosis in which acid fast organisms were present in the sections; (B) strongly suggestive or firm diagnosis of tuberculosis made on morphological grounds, though acid fast bacilli were not seen; (C) cases in which a firm diagnosis of inactive, calcified, or healed tuberculosis was made; (D) cases in which tuberculosis was mentioned in the differential diagnosis for confirmation or exclusion on clinical grounds.

Eighty two sets of case notes and pathology reports were examined. Eighty sets of case notes could not be traced. Thirty four cases were coded A, 35 B, five C, and eight D.

Codes A and B—The table gives the age and sex characteristics of the 69 patients coded A or B by the pathologist together with information on the number of notifications and number of consultations with a respiratory physician. Of patients in whom acid fast bacilli were identified, 11 (32.4%) were not notified, and of those in whom acid fast bacilli were not seen but a firm pathological diagnosis was made, 15 (42.9%) were not notified. Only eight of the 69 patients were not seen by a respiratory physician. One of the unnotified patients had acid fast bacilli in a sputum smear. Sixty two of the 69 patients were treated for tuberculosis. Of these 62 patients treated, and therefore considered to have active disease, only two thirds were notified. In this group 50 patients (81%) had chemotherapy for the standard six or nine months. Unusual treatment combinations, all based on rifampicin, were employed in 12 patients, on four occasions by chest physicians. Failure to notify was equally common in physicians and surgeons, though the comparatively larger number of pathological diagnoses on material obtained by surgeons (46:21) led to a greater number of failed notifications.

Codes C and D—None of the 13 patients coded C or D was notified or treated as a case of tuberculosis.

<table>
<thead>
<tr>
<th>Code</th>
<th>A</th>
<th>B</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age in years (range)</td>
<td>53 (9-80)</td>
<td>52 (11-87)</td>
<td>53 (9-87)</td>
</tr>
<tr>
<td>No male</td>
<td>21</td>
<td>16</td>
<td>37</td>
</tr>
<tr>
<td>No female</td>
<td>13</td>
<td>19</td>
<td>32</td>
</tr>
<tr>
<td>No notified</td>
<td>23</td>
<td>20</td>
<td>43</td>
</tr>
<tr>
<td>No (%) not notified</td>
<td>11 (32.4)</td>
<td>15 (42.9)</td>
<td>26 (37.7)</td>
</tr>
<tr>
<td>Not seen by respiratory physician</td>
<td>4</td>
<td>4</td>
<td>8</td>
</tr>
<tr>
<td>Notified</td>
<td>2</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Not notified</td>
<td>2</td>
<td>3</td>
<td>5</td>
</tr>
</tbody>
</table>

Comment

This study shows that almost 40% of patients (26/69) with a convincing combined clinical and pathological diagnosis of tuberculosis were not notified, in keeping with findings in the United States.¹ Most failures of notification occurred in surgical wards, though physicians also failed to notify positive pathological diagnoses of tuberculosis. Fortunately, treatment was conventional in most cases and respiratory physicians were consulted in most. Our study suggests that all positive pathological diagnoses of tuberculosis should be notified to the local health board to ensure that notifications reflect the true incidence of disease. This would also ensure that appropriate contact procedures can be instituted.¹