Human leucocyte antigen typing class I and class II of five patients with rheumatoid arthritis/ polymyositis overlap syndrome

<table>
<thead>
<tr>
<th>Patient</th>
<th>A locus</th>
<th>B locus</th>
<th>DRB1</th>
<th>DQA1</th>
<th>DQB1</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>101,11</td>
<td>0101,0407</td>
<td>101,301</td>
<td>501,301</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>29,31</td>
<td>1302,0701</td>
<td>102,201</td>
<td>502,303</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>1,11</td>
<td>0301,0301</td>
<td>501,501</td>
<td>201,201</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>2,68</td>
<td>0901,0802</td>
<td>201,401</td>
<td>301,201</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>2,74</td>
<td>0302,1304</td>
<td>401,501</td>
<td>301,402</td>
<td></td>
</tr>
</tbody>
</table>

Five patients seen at The University of Texas Medical Branch at Galveston satisfied the American Rheumatism Association criteria for RA and Bohan criteria for PM. Two white and two black women (mean age 54 years, range 48–57) had disease ranging in duration from three to nine years. Clinical evaluation included medical histories, physical examinations, serum creatine phosphokinase levels, antinuclear antibodies (ANA) by indirect immunofluorescence on HEp-2 cells, antibodies to double stranded DNA using *Citrullus luciliae*, antinucleoprotein, and anti-Sm antibodies by immunoaffraction, latex fixation test for rheumatoid factor, HLA class I and class II typing, and radiographs of hands, wrists, feet, and ankles. Electrocardiography was performed and muscle biopsy specimens examined in all patients.

All the patients had RA, were older than 40 and were receiving disease modifying drugs and prednisone <7.5 mg/day before onset of PM. Nodules were present in four of the five. None had lung involvement. Two patients had positive ANA results, and skin biopsy proven dermatomyositis. One patient was previously exposed to penicillamine.

The table shows HLA typing results. A single patient had HLA DRB*0407, an allele not usually associated with RA, and DRB*0101, the only RA susceptibility gene found. HLA-B8, seen in patients with myositis, was present in three of the five patients, DRB1*03 in two of the five, and DQB1*03 in four.

Patients 5 and anti-Jo-1 and Pt-7 antibodies. Both of these antisynthetases are associated with HLA-DR3, HLA-DQA1*0401, and *0501 alleles, all present in this patient. Patient 3 was positive for anti-Pm-Scl, SS-A, and homoygous for DRB1*0301.

There were no serological markers unique to the patients. Although the population was small, the phenotypes and autoantibodies resembled more closely those found in idiopathic PM than those in RA.

ARUN SHARMA
BRUCE A BAETTGE
JEFFREY R LILLIS
Division of Rheumatology,
The University of Texas Medical Branch of Galveston,
Texas, USA

SMITA VADYA
Division of Rheumatology,
University of Texas Medical Center,
Houston, Texas, USA

Letters to the editor

Cytidine deaminase is not released from degranulating polymorphonuclear neutrophils

Cytidine deaminase (CD) is an enzyme involved in DNA metabolism which is particularly abundant in cytoplasm of polymorphonuclear neutrophils (PMN) and may be useful as a marker of granulocyte mediated inflammation. In the inflamed joints of rheumatoid arthritis, PMN are the predominant cells in synovial fluid and release CD which diffuses into the blood and provides an important measure of overall synovitis. Current theories argue that CD is released by cell lysis, by cell activation and degranulation, or by a combination of the two. We therefore examined these two possible mechanisms of CD release from normal PMN.

PMN were obtained from the peripheral blood of eight normal volunteers by a one step sodium metrizoate-Dextran 500 separation and used at concentrations of 2.5–9×10⁶ cells/ml. Cell suspensions were subjected either to freeze-thawing in liquid nitrogen for varying times (0–50 seconds) to disrupt cell membranes and cause lysis of different proportions of cells, or to stimulation with formyl methylionyl leucyl phenylalanine (FMLP) in varying concentrations (10⁻⁶–10⁻⁷ M) to cause degranulation of different proportions of cells. Cells were spun down and supernatants collected for the assays shown below. After each procedure cells were resuspended, lysed by sustained freezing (which does not interfere with the assay for CD and lactate dehydrogenase (LDH) and spun down.

In the case of the degranulation experiments, cells were resuspended, divided into two aliquots, lysed either by sustained freezing or by adding Triton X-100 (which ensures complete disruption of granules), and spun down. These supernatants also were collected for assay.

The amount of cell lysis was assessed by measuring LDH released into the supernatant and comparing the (after freeze-thawing) with the total LDH release after complete disruption of the cells and was expressed as a percentage of the total amount of LDH. The extent of PMN degranulation after stimulation was assessed by measuring myeloperoxidase (MPO) release from primary granules using standard methods and expressing it as a percentage of the total MPO released after lysis of all cells and granules by Triton X-100. CD concentrations were measured by standard methods.

The proportion of cells lysed by freeze-thawing varied between 0 (controls) and 98%, and this was mirrored by a similar range for CD release. The correlation between LDH release (cell lysis) and CD release was *r* = 0.975 (*p* < 0.001) (fig 1). The proportion of degranulation achieved varied between 0 and 35%, but in these experiments the maximum CD release was only 2.4% and release of CD did not correlate significantly with that of MPO (*r* = 0.367, *p* > 0.05) (fig 2).

These results confirm previous reports that PMN lysis causes CD release, but also show that FMLP stimulated degranulation does not cause CD release. It seems unlikely that other stimuli to degranulation would cause CD release, although it might be valuable to confirm that immune complexes or aggregated IgG do not have this effect. Our findings support the notion that increased synovial fluid and serum concentrations of CD reflect intra-articular PMN lysis. It is possible that CD release might be caused by other stimuli to PMN activation within inflammatory synovial fluid which do not lead to degranulation. There also remains the possibility that PMN from synovial fluid in...
inflammatory arthritis may behave differently from normal peripheral blood PMN, either because of changes in responsiveness to stimuli, or because PMN apoptosis may alter the pattern of enzyme release.

MONIQUE HOEKSTRA
JOHN KIRWAN
Rheumatology Unit,
University Department of Medicine,
Bristol Royal Infirmary, Bristol BS2 8HW,
United Kingdom

Correspondence to: Dr J R Kirwan.


Carpal tunnel syndrome as initial manifestation of inflammatory connective tissue diseases

Carpal tunnel syndrome (CTS) is the most common entrapment neuropathy presented at rheumatology consultation. Most CTS are considered idiopathic or related to activities that require repetitive flexor handwork. However, it is well known that CTS may also occur in the context of inflammatory connective tissue diseases (ICTD), and may precede other manifestations of these associated inflammatory disorders by weeks or months. In order to determine how frequently CTS appears as the first manifestation of ICTD, we undertook a prospective study of patients referred to our unit with suspected CTS.

From January 1983 to December 1992, 324 consecutive patients were evaluated and included in the study. CTS was defined by the presence of a suggestive clinical picture together with a positive Tinel or Phalen sign, or characteristic electrodagnostic findings. Patients with previous or concomitant inflammatory rheumatic disease were excluded. All patients underwent anamnesis, physical examination, blood cell count, urine analysis, elemental biochemistry, proteinogram, serum rheumatoid factor assay and electrodagnosis. Thyroid hormones were determined only if hypothyroidism was suspected clinically or by typical laboratory findings (hypercholesterolaemia or increased creatine phosphokinase). Of the 324 patients initially studied, 201 fulfilled the inclusion criteria and were followed during a mean period of 13.6 months (range 6–24).

The mean age of the population was 52.8 (SD 10–3) years; 92% were women. Patients had suffered symptoms of CTS for a mean period of 38 (22) weeks before their first consultation in our clinic. The table summarizes the different aetiologies. In 18 patients CTS was the first manifestation of ICTD, with a mean period of 10–4 months (range 1–34) between the onset of CTS symptoms and the definitive diagnosis of related ICTD. Rheumatoid arthritis was the related inflammatory disease most commonly in the follow up of CTS patients. It was initially defined following the 1958 American Rheumatism Association (ARA) criteria. During the last four years of the study, the 1987 ARA criteria were used and previous rheumatoid arthrits diagnoses were reviewed.

Of the different parameters tested, only serum rheumatoid factor and period of evolution before diagnosis were significantly different between the ICTD and non-ICTD groups. Serum rheumatoid factor was detected in 50% of the ICTD group, compared with 3.2% of the non-ICTD group (p < 0.001, Fisher test). Symptoms before diagnosis were present for 23.1 (21.4) weeks and 39.4 (21.8) weeks in the ICTD and non-ICTD groups, respectively (p < 0.01, Student’s t test), probably reflecting a more severe clinical picture in ICTD patients.

In conclusion, our study found CTS to be the first manifestation of ICTD in 9% of cases (95% confidence interval 5 to 13.2%). In addition, serum rheumatoid factor could be a marker of those patients with CTS who may progress to ICTD, having a positive predictive value of 69.1% and negative predictive value of 96.9%. Thus we propose that seropositive CTS patients should be followed for a period of 10–12 months because of their high risk of developing an inflammatory rheumatic disease.

SISIDORO GONZÁLEZ-ALVARO
INMACULADA CARVAJAL
MIGUEL ESTEVEZ
JUAN PEDRO LÓPEZ-BOTE
ALBERTO GARCÍA-VADVILLO
Rheumatology Section,
Hospital de la Princesa,
Madrid, Spain

Correspondence to: Dr Isidoro González-Alvaro, Sección de Reumatología, Hospital de la Princesa, c/ Diego de Leon 62, 28006 Madrid, Spain.

Cytidine deaminase is not released from degranulating polymorphonuclear neutrophils.

M Hoekstra and J Kirwan

doi: 10.1136/ard.54.9.781

Updated information and services can be found at:
http://ard.bmj.com/content/54/9/781.citation

These include:

**Email alerting service**
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/