MATTERS ARISING

Periarticular bone mineral density at the knee joint

Recently, dual energy x-ray absorptiometry (DXA) was presented by Murphy et al as a new method for assessing periarticular bone mineral density (BMD) at the knee joint. 

Precision errors for BMD measured at the patella, tibia, and femoral neck were examined by Bohr and Lauritzen. 

Petersen et al measured subchondral bone mineral density at the proximal tibia. 

We acknowledge that subchondral bone mineral density has previously been assessed by dual photon absorptiometry. However, we do not feel that this is particularly relevant to our paper. The purpose of our study was to develop and validate a method for measurement of periarticular bone mineral density at the knee joint using the technique now recognised as the gold standard for the assessment of bone mineral density—that is, dual energy x-ray absorptiometry (DXA). With the exception of one study, the studies referred to by Dr Marsden used only dual photon absorptiometry.

As mentioned by Dr Marsden, Petersen et al examined changes in BMD at the proximal tibia after knee arthroplasty. 

Petersen et al examined subchondral BMD after meniscectomy, and Madsen et al reported data for subchondral BMD measured in several subregions of the proximal tibia in healthy subjects and patients with osteoarthritis of the knee. Moreover, Petersen et al studied relationships between bone strength and bone mineral density assessed by DPA and DXA in the proximal tibia.

Related studies could be mentioned. Unfortunately, none of these studies was referred to by Murphy et al.

Author’s reply

Can rheumatologists agree on a diagnosis of inflammatory arthritis in an early synovitis clinic?

Irreversible joint damage can occur within months rather than years of the onset of rheumatoid arthritis. It is therefore important that these patients are diagnosed and treated as early as possible. To facilitate the early introduction of effective treatment, a rapid referral system is important. Throughout Europe, a number of centres have developed early synovitis clinics (ESCs) for this purpose. However, the diagnosis of early inflammatory arthritis (IA) is often difficult and confusing for the primary care doctor. It suggests that the efficiency of ESCs is impaired by inappropriate referrals. Is this criticism justified? If general practitioners find it difficult to diagnose early IA, what about hospital specialists? In this short study we posed the question “Can rheumatologists agree on a diagnosis of IA in an ESC?”

Patients were recruited from primary care in the greater Belfast area (population ca 400 000). We randomly selected 24 patients who had been referred to an ESC in a Belfast teaching hospital and invited them to attend for outpatient assessment. Informed written consent was obtained from each patient before they took part in the study. Six hospital rheumatologists (two specialist registrars and four consultants) independently assessed 20 patients referred to an ESC by their primary care doctor. Patients were randomly assigned to each rheumatologist, who was asked to judge whether or not the patient currently had any type of IA. Before the study, the assessing rheumatologists had agreed on a definition of IA. Each assessment was conducted in a maximum of 15 minutes, but patients were not informed of their diagnosis until the final consultation, which included an additional 15 minutes to provide time to arrange a management plan for their problems.

A mnemonic for SLE diagnostic criteria

Like many rheumatological diseases, systemic lupus erythematosus (SLE) is difficult to diagnose owing to the constellation of findings required. I offer a mnemonic that contains the 11 categories used by the American College of Rheumatology, from which four or more must be present to diagnose SLE: A RASH PONs MAD.

1. M: Malar rash
2. A: Arthritis
3. R: Rheumatoid nodules
4. S: Serositis
5. H: Hematological findings
6. S: Photosensitivity
7. E: Renal disease
8. L: Neurological disease
9. T: Oral ulcers
10. A: Antinuclear antibody
11. I: Immunological disorder (serological tests)
Twenty four patients were invited to participate in the study and 20 consented to take part. Three patients failed to turn up for their outpatient appointment and one patient who did attend declined to take part in the study. There was complete agreement in the assessment of 14/20 patients (70%), 11 (55%) of whom were deemed to have IA (including RA, psoriatic arthritis, and reactive arthritis) and three (15%) who were not. In two cases (10%), only one rheumatologist diagnosed IA. In a further two cases (10%), only two specialists diagnosed IA and in the final two patients (10%), four of the six specialists diagnosed IA. In all cases where there was disagreement, the final assessor shared the majority opinion as to the correct diagnosis. The level of agreement between assessors was calculated using the κ statistic, where a value of 1.0 represents total agreement. The overall κ value for the six assessors was 0.68. Interestingly, the registrars had a higher level of agreement (κ 0.9) than the consultant rheumatologists (κ 0.6), though the difference was not statistically significant. These results show that IA can be a difficult diagnosis to make in the setting of an ESC, even among experienced rheumatologists. Nevertheless, the level of agreement in this study compares favourably with that in other specialties such as radiology and ophthalmology.1 Given these findings, it is clearly important to keep an open mind about the diagnosis of IA in its early stages, especially where the clinical findings are equivocal. Careful follow up of such patients should be an important part of the work of any ESC.

Correspondence to: Dr Gormley

GORMLEY
K STEELE
D GILLILAND
Department of General Practice,
Queen’s University of Belfast,
Belfast, N Ireland

M STEVENSON
D O’REILLY
Department of Epidemiology,
Queen’s University of Belfast

R MCKANE
Department of Rheumatology,
Ulster Hospital,
Belfast, N Ireland

G WRIGHT
A L BELL
C MATTHEWS
G MEENAGH
A J TAGGART
Department of Rheumatology,
Musgrave Park Hospital,
Belfast, N Ireland

Figure 1 Ultrasound, transverse sections, showing (A) a thickened plantar fascia and (B) fluid dispersal superficial to the plantar fascia.

Two patients with a clinical diagnosis of idiopathic plantar fasciitis, unresponsive to an initial palpation guided injection with 10 mg of triamcinolone acetonide, underwent ultrasound examination of the heel. Increased thickness of the plantar fascia near the calcaneal insertion was noted with both plantar fasciae measuring 7.5 mm in depth. Under real time ultrasound guidance, using a medial approach, the tip of a 21 gauge needle was positioned in the centre of the plantar fascia. However, on both occasions, considerable resistance was experienced on attempting to inject triamcinolone and lidocaine mixture into the centre of the plantar fascia. Injection was possible only by withdrawing the needle, under ultrasound guidance, to the edge of the plantar fascia where the injected solution was seen to disperse around the edge of the plantar fascia as shown in figs 1A and 1B. Both patients responded well to this treatment, being symptomatic free on review one month later.

Kane et al described injection directly into the substance of the plantar fascia with dispersal of the injection mixture into the substance of the fascia. Our experience suggests that it is difficult to inject into the substance of the plantar fascia. Rather, one may inject at the edge of the plantarfasciawith perifascial dispersal of steroid. This still appears to result in satisfactory alleviation of symptoms.

Correspondence to: Dr Gormley

gerry@teamgormley.fsfree.co.uk


3 Sackett D L, Haynes RB, Guyatt GH. Clinical epidemiology—a basic science for clinical medicine. London: Little.

Ultrasound guided injection of plantar fasciitis

Kane et al reported four cases of ultrasound guided injection in recalcitrant idiopathic plantar fasciitis.1 We would like to report a different experience using a similar method.

HLA-DRB1 and DQB1 genes in anticientromere antibody positive patients with SSc and primary biliary cirrhosis

The frequency of certain HLA class II alleles has been reported to be high in patients with systemic sclerosis (SSc), especially in the clinical subsets defined by SSc related antinuclear antibodies and ethnicity.7 In anticientromere antibody (ACA) positive SSc, a high frequency of HLA-DQB1*0501 has been reported.8 In the present study, we examined the frequency of HLA-DRB1 and DQB1 alleles in ACA positive patients with systemic sclerosis.

Table 1 Gene frequency of selected HLA-DRB1 and DQB1 alleles in anticientromere antibody (ACA) positive patients

<table>
<thead>
<tr>
<th>DNA alleles</th>
<th>SSc‡ (%)(n=20)</th>
<th>PBC‡ (%)(n=13)</th>
<th>Healthy control (%)(n=215)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DRB1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0101</td>
<td>20 (8/40)*</td>
<td>8 (2/26)</td>
<td>5</td>
</tr>
<tr>
<td>0102</td>
<td>15 (6/40)</td>
<td>12 (3/26)</td>
<td>11</td>
</tr>
<tr>
<td>0401</td>
<td>0 (0/40)</td>
<td>0 (0/26)</td>
<td>1</td>
</tr>
<tr>
<td>0403</td>
<td>8 (3/40)</td>
<td>0 (0/26)</td>
<td>1</td>
</tr>
<tr>
<td>0405</td>
<td>8 (3/40)</td>
<td>8 (2/26)</td>
<td>11</td>
</tr>
<tr>
<td>0406</td>
<td>5 (2/40)</td>
<td>12 (3/26)</td>
<td>4</td>
</tr>
<tr>
<td>0802</td>
<td>3 (1/40)</td>
<td>0 (0/26)</td>
<td>4</td>
</tr>
<tr>
<td>0803</td>
<td>8 (3/40)</td>
<td>23 (6/26)†</td>
<td>7</td>
</tr>
<tr>
<td>0901</td>
<td>18 (7/40)</td>
<td>8 (2/26)</td>
<td>14</td>
</tr>
<tr>
<td>DQB1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0301</td>
<td>0 (0/40)</td>
<td>4 (1/26)</td>
<td>13</td>
</tr>
<tr>
<td>0302</td>
<td>20 (8/40)</td>
<td>12 (3/26)</td>
<td>10</td>
</tr>
<tr>
<td>0303</td>
<td>18 (3/40)</td>
<td>15 (4/26)</td>
<td>16</td>
</tr>
<tr>
<td>0401</td>
<td>8 (2/26)</td>
<td>8 (2/26)</td>
<td>11</td>
</tr>
<tr>
<td>0402</td>
<td>0 (0/40)</td>
<td>4 (1/26)</td>
<td>4</td>
</tr>
<tr>
<td>0501</td>
<td>20 (8/40)*‡</td>
<td>8 (2/26)</td>
<td>7</td>
</tr>
<tr>
<td>0502</td>
<td>5 (2/40)</td>
<td>0 (0/26)</td>
<td>2</td>
</tr>
<tr>
<td>0601</td>
<td>20 (8/40)</td>
<td>35 (9/26)</td>
<td>18</td>
</tr>
<tr>
<td>0602</td>
<td>8 (3/40)</td>
<td>8 (2/26)</td>
<td>8</td>
</tr>
</tbody>
</table>

*p<0.0005, †p<0.01, ‡p<0.005, OR=3.5. Differences in alleles was analysed by χ2 test or Fisher’s exact test.

When the association with a particular specificity had not been reported previously, p values were corrected (pcorr) for the number of alleles tested for each locus (28 in DRB1 and 18 in DQB1). SSc = systemic sclerosis; PBC = primary biliary cirrhosis.

Seven patients with SSc-PBC overlap were included both in the 20 patients with SSc and the 13 with PBC.

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been reported by some investigators. In addition, we found a high frequency of DRB1*0101 in ACA positive Japanese patients with SS (J Rheumatol, in press).

ACA is also found in patients with primary biliary cirrhosis (PBC), and patients with SS and ACA commonly overlap PBC or Sjögren’s syndrome (SS), or both. Some studies on HLA class II alleles in Japanese patients with PBC showed high frequencies of DRB1*0803 and DRB1*0501. However, we found no reports which analysed HLA class II alleles in patients with PBC with respect to the relation with ACA or SS.

To clarify the relation of HLA class II alleles with ACA, SS, and PBC we carried out molecular genetic analyses of HLA-DQB1 and DRB1 alleles in 86 Japanese patients with PBC or ACA positive SSc and ACA negative SSc and DRB1*0803 was frequently found in PBC patients frequently overlapped SS compared with DRB1*0803 negative ones, and one of the five patients with DRB1*0803 overlapped SSc. DRB1*0803 may be a candidate allele to determine the susceptibility to SS and PBC in patients with SS with no relation to the presence of ACA, and the existence of common candidate alleles in PBC and SS may explain the high frequency of overlap of both the diseases. There was no significant difference in skin sclerosis or organ involvement in patients with ACA classified by the presence of DRB1*0803 (data not shown).

Our report describes the variation of HLA class II alleles among ACA positive patients according to their clinical features; high frequency of HLA-DQB1*0101/DRB1*0501 and DRB1*0803 are restrictively found in SSc and PBC, respectively. Although DRB1*0803 is not related to the production of ACA, this allele may be related to the susceptibility not only to PBC but also to SS in patients with SS.

We thank Dr Takehiko Abe and Dr Akira Kojima, The First Department of Internal Medicine, for their help in collecting blood samples from patients with PBC.

This study was partly supported by grants from Kanzawa Medical Research Foundation (1999) and a Scleroderma Grant for Intractable Disease from the Ministry of Health and Welfare (1999).

Table 2. Clinical and laboratory findings of patients with systemic sclerosis (SSc) classified by the presence of anticientromere antibody (ACA) and HLA-DRB1*0803 allele

<table>
<thead>
<tr>
<th></th>
<th>SS* (%)</th>
<th>PBC* (%)</th>
<th>Positive for ACA* (%)</th>
<th>Positive for SS-A* (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DRB1*0803</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive (n=3)</td>
<td>9/15 (60)</td>
<td>4/15 (27)</td>
<td>6/17 (35)</td>
<td>0/3 (0)</td>
</tr>
<tr>
<td>Negative (n=17)</td>
<td>11/18 (61)</td>
<td>6/17 (33)</td>
<td>8/20 (40)</td>
<td>2/17 (12)</td>
</tr>
<tr>
<td>Total (n=20)</td>
<td>20/32 (62)</td>
<td>10/32 (31)</td>
<td>14/37 (38)</td>
<td>2/20 (10)</td>
</tr>
</tbody>
</table>

Table 2 shows clinical analyses in patients with SSc classified by the presence of ACA and DRB1*0803. Phenotype frequency of DRB1*0803 was 43% (3/7) in SSc-PBC overlap and 33% (8/24) in PBC without SSc related features. Although DRB1*0803 is not related to the production of ACA, this allele may be related to the susceptibility not only to PBC but also to SS in patients with SS.

*SS = Sjögren’s syndrome; PBC = primary biliary cirrhosis; AMA = antimitochondrial antibody; SS-A = anti-Ro/SS-A antibody.

The p values were calculated by Fisher’s exact test: p<0.005, p<0.01, p<0.05.

Table 1 summarises the gene frequency in ACA positive patients with SSc or PBC. HLA-DRB1*0101 and DQB1*0501 were frequently found in SSc, and HLA-DRB1*0803 was frequently found in PBC compared with the healthy controls. These results were consistent with previous reports analysing HLA-DRB1 and DQB1 in patients with SSc or PBC from different institutions.

In PBC, no difference in phenotype frequency (the number of patients positive for an allele) of DRB1*0803 was found between ACA positive patients and ACA negative ones (6/13 (46%) vs 5/18 (28%)). Patients with PBC who were ACA positive frequently overlapped SSc compared with ACA negative patients (6/13 (46%) vs 1/18 (6%), p<0.05).

On the other hand, DRB1*0803 in PBC showed no association with overlapping SSc; phenotype frequency of DRB1*0803 was 43% (3/7) in SSc-PBC overlap and 33% (8/24) in PBC without SSc related features. In PBC, no significant difference was observed in phenotype frequency of DRB1*0803 between ACA positive and ACA negative patients with PBC.

Table 1. Gene frequency in ACA positive patients with SSc or PBC

Table 1. Gene frequency in ACA positive patients with SSc or PBC

<table>
<thead>
<tr>
<th>DRB1*0803</th>
<th>Positive (n=20)</th>
<th>Negative (n=42)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive (n=3)</td>
<td>9/15 (60)</td>
<td>4/15 (27)</td>
</tr>
<tr>
<td>Negative (n=17)</td>
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<td>6/17 (33)</td>
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</tbody>
</table>

Table 1 shows clinical analyses in patients with SSc classified by the presence of ACA and DRB1*0803. Phenotype frequency of DRB1*0803 was not different between ACA positive SSc and ACA negative SSc. ACA positive SSc frequently overlapped SS and PBC with compared ACA negative SSc. In ACA negative SSc, DRB1*0803 positive patients frequently overlapped SS compared with DRB1*0803 negative ones, and one of the five patients with DRB1*0803 overlapped SSc. Although DRB1*0803 is not related to the production of ACA, this allele may be related to the susceptibility not only to PBC but also to SS in patients with SS.

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S AKIMOTO
M ABE
O ISHIKAWA
Department of Dermatology,
Gunma University School of Medicine,
Japan

The First Department of Internal Medicine,
Gunma University School of Medicine,
Japan

Correspondence to: Dr S Akimoto, Department of Dermatology, Gunma University School of Medicine, 3–39–22 Showa-machi, Maebashi, Gunma 371–8511, Japan

HLA-DRB1 and DQB1 genes in anticentromere antibody positive patients with SSc and primary biliary cirrhosis

S AKIMOTO, M ABE, O ISHIKAWA, H TAKAGI and M MORI

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