Pseudotumours associated with metal-on-metal hip resurfacing


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We report 17 patients (20 hips) in whom metal-on-metal resurfacing had been performed and who presented with various symptoms and a soft-tissue mass which we termed a pseudotumour. Each patient underwent plain radiography and in some, CT, MRI and ultrasonography were also performed. In addition, histological examination of available samples was undertaken.

All the patients were women and their presentation was variable. The most common symptom was discomfort in the region of the hip. Other symptoms included spontaneous dislocation, nerve palsy, a noticeable mass or a rash. The common histological features were extensive necrosis and lymphocytic infiltration. To date, 13 of the 20 hips have required revision to a conventional hip replacement. Two are awaiting revision.

We estimate that approximately 1% of patients who have a metal-on-metal resurfacing develop a pseudotumour within five years. The cause is unknown and is probably multifactorial. There may be a toxic reaction to an excess of particulate metal wear debris or a hypersensitivity reaction to a normal amount of metal debris. We are concerned that with time the incidence of these pseudotumours may increase. Further investigation is required to define their cause.

With the introduction of a metal-on-metal bearing there has been a recent and rapid increase in hip resurfacing. Many major manufacturers are now actively promoting hip resurfacing and tens of thousands are being carried out each year, particularly so in younger, more active patients because of the perceived limitations of conventional hip replacement. Metal-on-metal bearings have better wear properties than conventional metal-on-polyethylene bearings. Although there is no good evidence to support it, many surgeons believe that resurfacing gives a better functional result than a conventional THR. A significant disadvantage of resurfacing is the risk of fracture of the femoral neck. A further problem which is not confined to resurfacing but is also seen with other metal-on-metal hip replacements, is aseptic lymphocytic vasculitic associated lesions. Willert et al\(^5\) studied the histology of peri-prosthetic tissues in patients with a failed second-generation metal-on-metal articulation. They found a diffuse and perivascular infiltrate of T- and B-lymphocytes and plasma cells, high endothelial venules, massive fibrin exudation, accumulation of macrophages with droplike inclusions and infiltrates of eosinophils and necrosis. This response was termed a lymphocyte-dominated immunological response. Their study did not identify any formation of granulomata.

Between 1999 and 2007 we performed more than 1300 metal-on-metal hip resurfacings at our hospital (Nuffield Orthopaedic Centre, Oxford, United Kingdom), which is also a tertiary referral centre. Recently, we have seen a number of patients with varied symptoms after hip resurfacing, but with a common feature of a soft-tissue mass associated with the implant. This mass is neither malignant nor infective in nature. We have therefore described it as a ‘pseudotumour’. We now present the clinical details of a group of patients who presented with these pseudotumours.

Patients and Methods
We identified a heterogeneous group of 17 patients who were experiencing problems after their hip resurfacing. Three had undergone bilateral procedures, thus giving a total of 20 hips in the series. The patients presented at varying intervals post-operatively. The common finding was the presence of a soft-tissue mass.

All the patients were women with a mean age of 53 years (33 to 73) at the time of operation; 12 (12 hips) had undergone a unilateral
primary metal-on-metal resurfacing at our hospital and five (eight hips) had been referred for further management from elsewhere. Of the 20 hips, 14 had a Birmingham Hip Resurfacing (Smith and Nephew, Memphis, Tennessee), four had a Conserve Plus (Wright Medical, Memphis, Tennessee), and two a Cormet (Corin Group PLC, Cirencester, United Kingdom) prosthesis (Table I).

The indication for resurfacing was primary osteoarthritis in 12 and secondary osteoarthritis in five patients. The osteoarthritis was secondary to dysplasia in four and to trauma in one. Three patients suffered from various skin problems (eczema, urticarial vasculitis and psoriasis) and two were known to be allergic to nickel.

Plain radiographs were obtained in each case and the abduction angle of the acetabular component was measured (Fig. 1) using ImageJ software (National Institutes of Health, Bethesda, Maryland). Some of the patients underwent further imaging and needle biopsies were undertaken in three cases and formal biopsies in ten. These were fixed in formalin and processed routinely. Sections (5 mm) were stained with haematoxylin and eosin and other standard stains (Gram, Ziehl-Nielsen, periodic acid Schiff, Grocott and Giemsa staining).

Results
The mean time to presentation was 17 months (0 to 60). The most common presenting symptom was discomfort, either in the groin, on the lateral aspect of the hip or in the buttock. Two patients (two hips) had late dislocation and two others (two hips) complained of symptoms of instability which they described as clicking, clunking or giving way. A lump was present either under the scar on the lateral side

### Table I. Clinical details of the 17 patients

<table>
<thead>
<tr>
<th>Case</th>
<th>Age (yrs)</th>
<th>Implant*</th>
<th>Diagnosis of OA†</th>
<th>Past medical history‡</th>
<th>Presenting symptoms</th>
<th>Onset (mths)</th>
<th>ESR/CRP§</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>53</td>
<td>Cormet</td>
<td>Primary</td>
<td>None</td>
<td>Pain in the groin and buttock</td>
<td>30</td>
<td>Normal</td>
</tr>
<tr>
<td>2</td>
<td>55</td>
<td>BHR</td>
<td>Primary</td>
<td>None</td>
<td>Pain and locking</td>
<td>3</td>
<td>Normal</td>
</tr>
<tr>
<td>3</td>
<td>52</td>
<td>BHR</td>
<td>Primary</td>
<td>Fibrosarcoma opposite thigh needing amputation</td>
<td>Pain on the lateral aspect and groin, click and clunk</td>
<td>12</td>
<td>Normal</td>
</tr>
<tr>
<td>4</td>
<td>37</td>
<td>BHR</td>
<td>Primary</td>
<td>None</td>
<td>Pain on the lateral aspect</td>
<td>Since surgery</td>
<td>Normal</td>
</tr>
<tr>
<td>5</td>
<td>73</td>
<td>BHR</td>
<td>Primary</td>
<td>Psoriasis, DM, HT, eczema</td>
<td>Cystic lump, bloated feeling, flank pain</td>
<td>30</td>
<td>Normal</td>
</tr>
<tr>
<td>6</td>
<td>56</td>
<td>Conserve+</td>
<td>Primary</td>
<td>Glandular fever, eczema</td>
<td>Pain on the lateral aspect, partial femoral nerve injury at surgery</td>
<td>Since surgery</td>
<td>Normal</td>
</tr>
<tr>
<td>7</td>
<td>67</td>
<td>BHR</td>
<td>Primary</td>
<td>None</td>
<td>Pain in the groin and buttock</td>
<td>24</td>
<td>Normal</td>
</tr>
<tr>
<td>8</td>
<td>48</td>
<td>Cormet</td>
<td>Primary</td>
<td>Allergic to penicillin and NSAIDs</td>
<td>Instability, crepitus, recurrent spontaneous dislocation</td>
<td>66</td>
<td>Normal</td>
</tr>
<tr>
<td>9R</td>
<td>55</td>
<td>BHR</td>
<td>Primary</td>
<td>None</td>
<td>Pain in the groin and buttock, cystic lump</td>
<td>60</td>
<td>Normal</td>
</tr>
<tr>
<td>L</td>
<td>55</td>
<td>BHR</td>
<td>Primary</td>
<td>None</td>
<td>None</td>
<td>Not applicable</td>
<td>Normal</td>
</tr>
<tr>
<td>10</td>
<td>35</td>
<td>BHR</td>
<td>Secondary</td>
<td>Dysplastic hip; allergic to ampicillin and penicillin</td>
<td>None</td>
<td>36</td>
<td>Normal</td>
</tr>
<tr>
<td>11</td>
<td>44</td>
<td>Conserve+</td>
<td>Primary</td>
<td>Allergy to penicillin</td>
<td>Burning pain over thigh, cystic lump, signs of femoral nerve irritation</td>
<td>Since surgery</td>
<td>Normal</td>
</tr>
<tr>
<td>12R</td>
<td>45</td>
<td>BHR</td>
<td>Secondary</td>
<td>Fractured pelvis</td>
<td>None</td>
<td>Not applicable</td>
<td>Elevated</td>
</tr>
<tr>
<td>L</td>
<td>45</td>
<td>BHR</td>
<td>Secondary</td>
<td>Fractured pelvis</td>
<td>Pain in the groin and buttock, cystic lump</td>
<td>12</td>
<td>Elevated</td>
</tr>
<tr>
<td>13R</td>
<td>64</td>
<td>BHR</td>
<td>Secondary</td>
<td>Dysplastic hips, allergy to antibiotics and anaphylactic shock</td>
<td>Pain in the groin and buttock, femoral nerve palsy</td>
<td>8</td>
<td>Normal</td>
</tr>
<tr>
<td>L</td>
<td>64</td>
<td>BHR</td>
<td>Secondary</td>
<td>Dysplastic hips, allergy to antibiotics and anaphylactic shock</td>
<td>Pain in the groin and buttock</td>
<td>12</td>
<td>Normal</td>
</tr>
<tr>
<td>14</td>
<td>40</td>
<td>Conserve+</td>
<td>Secondary</td>
<td>Dysplastic hip; allergy to antibiotics and nickel</td>
<td>Pain on the lateral aspect and groin, skin rash over scar</td>
<td>12</td>
<td>Normal</td>
</tr>
<tr>
<td>15</td>
<td>62</td>
<td>BHR</td>
<td>Primary</td>
<td>None</td>
<td>Femoral nerve palsy, clunk</td>
<td>3</td>
<td>Normal</td>
</tr>
<tr>
<td>16</td>
<td>62</td>
<td>BHR</td>
<td>Secondary</td>
<td>Polymyalgia, allergy to dust, wool, waps and nickel; urticarial vasculitis</td>
<td>Pain on the lateral aspect and groin, recurrent spontaneous dislocation</td>
<td>36</td>
<td>Elevated</td>
</tr>
<tr>
<td>17</td>
<td>63</td>
<td>Conserve+</td>
<td>Primary</td>
<td>Herpes zoster, allergy to antibiotics</td>
<td>Pain on the lateral aspect, cystic lump</td>
<td>Since surgery</td>
<td>Normal</td>
</tr>
</tbody>
</table>

* BHR, Birmingham Hip Resurfacing
† OA, osteoarthritis
‡ DM, diabetes mellitus; HT, hypertension; NSAIDs, non-steroidal anti-inflammatory drugs
§ ESR, erythrocyte sedimentation rate; CRP, C-reactive protein
or over the front of the hip in six patients (six hips). One patient presented with a rash over the hip and one with tenderness in the flanks and a bloated feeling. This patient was initially referred to a general surgeon and underwent a laparotomy and biopsy to exclude an abdominal or pelvic tumour. Five patients (six hips) presented with symptoms of nerve irritation or a frank nerve palsy. One had sustained a palsy of the femoral nerve during the primary procedure. The remaining four did not have any nerve symptoms either before or immediately after their first operation, but three subsequently developed symptoms of irritation of the femoral nerve and one of irritation of the lateral cutaneous nerve of the thigh possibly because of pressure by a soft-tissue mass. The white cell count was normal in each case as were the erythrocyte sedimentation rate and the level of C-reactive protein in 15 patients.

Radiological and imaging findings. The abduction angle of the acetabular component varied between 22° and 75°. Those patients with steep components developed symptoms within a year of their resurfacing (Pearson correlation coefficient with \( t \)-test, \( r = -0.41; p = 0.095; \) Fig. 2).

Plain radiographs showed no radiolucency around either of the components. Ten patients (13 hips) underwent further imaging including ultrasonography, MRI and CT and two had arthrography. Three of these had bilateral abnormalities. There were two main types of imaging abnormality, namely, a predominantly cystic mass lateral to or behind the joint, or a mainly solid mass, lying anteriorly and involving psoas and its bursa. The most common finding, seen in ten hips (eight patients) was a mainly cystic mass lying posterolaterally to the joint (Fig. 3). It varied in size, the largest being 200 mm in diameter. In five hips, the abnormality involved the psoas and its bursa. In four of these the mass was mainly solid and in one it was mainly cystic. In one case there was also a mass involving the adductor muscles, and extensive oedema in all the periartricular muscles and surrounding subcutaneous tissues. Histological examination. This was available for 13 of the 20 hips. In three cases, infection had been suspected intra-operatively, but no organisms were cultured and therefore they were treated empirically as culture-negative infections.

A number of histological features were common to all the pseudotumours. These included extensive necrosis of dense connective tissue within the pseudotumour. In several cases, this was associated with marked cystic degeneration. Most, although not all, pseudotumours contained metal wear particles. They also had a scattered, focally heavy macrophage and lymphocytic infiltrate including lymphoid aggregates, some of which were found around small vessels. Plasma cells and eosinophil or neutrophil polymorphs were noted in some cases. The presence of plasma cells, polymorphs and a heavy lymphocytic infiltrate including lymphoid aggregates was difficult to distinguish histologically from the changes of low-grade infection, but in no case were organisms identified on Gram, Ziehl-Nielsen, periodic acid Schiff, Grocott or Giemsa staining. Three pseudotumours were distinguished by the presence of extensive coagulation necrosis of connective tissue, around which there was a pseudotuberculoid macrophage and giant-cell granulomatosus reaction (Fig. 4) and a diffuse inflammatory cell infiltrate of lymphocytes, plasma cells and eosinophil polymorphs.

To date, there have been 13 revisions of a resurfacing arthroplasty to a conventional THR. The revision surgery was staged in two patients because the presence of thick fluid in the hip raised the suspicion of infection.

After revision all the symptoms improved in eight patients (nine hips) and settled completely in four (four hips). Two further patients are awaiting revision. The remaining three patients are currently coping well. They are aware of the abnormal soft-tissue reaction to
the metal-on-metal bearing and are kept under regular review.

Discussion

We have not previously seen this type of pseudotumour after a conventional hip replacement. We therefore believe it is a new type of complication which is directly related to hip resurfacing. We do not know its precise incidence. However, symptoms first occurred up to five years postoperatively and since we have now carried out approximately 1300 metal-on-metal resurfacings, in 12 of which pseudotumours have developed, we estimate the incidence to be approximately 1% at five years. We do not know whether this will increase with time or not. If it does, it may present a major problem. Two of the pseudotumours were asymptomatic and were detected incidentally only because they occurred in patients with bilateral resurfacings who had a symptomatic contralateral pseudotumour. This suggests that there may be an appreciable number of unrecognised asymptomatic pseudotumours and it is of concern that these may become symptomatic. Further study is needed to determine their incidence.

A series of patients with a soft-tissue mass arising from a metal-on-metal resurfacing has not previously been described, but Boardman, Middleton and Kavanagh did report a single case of a benign psoas mass in relation to a metal-on-metal resurfacing. The mass was excised with revision of the resurfacing to a conventional THR. It contained metal wear particles and a lymphocytic infiltration into the fibrous tissue around the psoas.

There are a few reports in the literature of soft-tissue reactions occurring after conventional metal-on-metal THR. Madan, Jowett and Goodwin reported a recurrent intrapelvic cyst which first became symptomatic 14 years after a bilateral McKee-Farrar prosthesis had been implanted. The authors did not report their histological findings and the onset of symptoms was much later than for our cases. Gruber et al reported cystic lesions in two female patients five and six years after primary metal-on-metal total hip replacement. The cysts showed lymphocyte infiltration and were considered to be the result of hypersensitivity. The response in peri-prosthetic tissues described by Willert et al is characterised by the presence of T- and B-lymphocytes and plasma cells. In some cases, small areas of necrosis and eosinophil and polymorph infiltrates were noted. The inflammatory changes found in our patients are in keeping with those previously described as aseptic lymphocyte-laminated vascular-associated lesions, but were characterised by a more diffuse lymphocytic infiltrate as well as extensive connective tissue necrosis. In three cases, the additional presence of a pseudotuberculous granuloma-
tous response around the areas of necrosis was noted. The spectrum of host changes seen in these pseudotumours could represent that of an inflammatory response associated with a delayed hypersensitivity reaction to antigen components such as nickel-chromium or chromium-cobalt. Similar sarcoid-type granulomas and necrosis in response to these components have been found in nodules which form at sites of ear piercing. This could account for the female preponderance of the development of pseudotumours seen in our series. It has been reported previously that greater metal sensitivity is observed in patients with metal-on-metal hip replacement, although this was not found to be associated with symptoms.

The pseudotumours presented in a number of ways, such as the presence of pain, spontaneous dislocation, nerve palsy and a palpable lump. Since there is no typical presentation, we suggest that all patients with unexpected symptoms after a hip resurfacing should be investigated. Ultrasonography, MR and CT scanning may all be used to detect the mass. The former can differentiate solid from cystic lesions and can also be used as a guide for biopsy and aspiration. Metal artefact will obscure the tissues immediately adjacent to the resurfacing, and MRI and standard CT may miss small lesions. Careful attention to CT settings and the use of metal-artefact-reducing software will improve the quality of the image. Arthrography will show the extent of any collection which communicates with the joint. Ultrasonography is probably the best initial examination if a pseudotumour is suspected. All aspects of the joint must be carefully examined. Large masses warrant further imaging with MRI or CT to define accurately the extent of the pseudotumour. Arthrography should not be required routinely, but is the most accurate way of demonstrating communication between any cyst and the joint.

The cause of these pseudotumours is not apparent. Metal wear particles were found in every case which was examined histologically. However, in most cases there was no gross clinical metallosis. There is weak evidence of a relationship between the inclination of the acetabular component and the time of onset of symptoms; steeply positioned cups are more likely to lead to edge loading thereby generating a large amount of metal debris. However, there were also well-positioned implants in this series. We suggest that in some cases the pseudotumour may be the result of a toxic effect on cells of a large amount of particulate wear debris resulting from some problem with the articulation such as edge loading, whereas in other cases it is an idiosyncratic response to a moderate release of cobalt-chrome particles. Detailed further investigation is required. This should include measurement of the ion levels within the joint as well as in the pseudotumours.

All our patients were female, which raises the possibility that pre-operative sensitisation to metal may be a factor. Nickel allergy is predominantly a condition of women and is related to the wearing of jewellery and in particular to ear piercing. It is interesting to note that seven of the patients in our series were allergic to antibiotics.

In all three patients with bilateral replacements, bilateral abnormalities were found on imaging. One patient had bilateral symptomatic disease. In the other two patients asymptomatic cysts were found on MRI around the contralateral hip. This implies either that asymptomatic peri-articular abnormalities are common after metal-on-metal resurfacing or that there is a systemic factor present in these patients, such as a hypersensitivity response to metal. Our series highlights the need for regular clinical follow-up for new devices. This is also the recommendation of The National Institute of Clinical Excellence but is increasingly difficult to undertake in the current NHS climate.

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No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

References