Clinical applications of Dixon chemical shift MR imaging: Morbus Gaucher, Morbus Hansen
Maas, M.

Citation for published version (APA):
Ridderkerk: M. Maas

General rights
It is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), other than for strictly personal, individual use, unless the work is under an open content license (like Creative Commons).

Disclaimer/Complaints regulations
If you believe that digital publication of certain material infringes any of your rights or (privacy) interests, please let the Library know, stating your reasons. In case of a legitimate complaint, the Library will make the material inaccessible and/or remove it from the website. Please Ask the Library: http://uba.uva.nl/en/contact, or a letter to: Library of the University of Amsterdam, Secretariat, Singel 425, 1012 WP Amsterdam, The Netherlands. You will be contacted as soon as possible.
MR Imaging of neuropathic feet in leprosy patients with suspected osteomyelitis

Mario Maas¹, Erik J. Slim¹,⁴, Agnes F. Hoeksma⁴, Ad J. van der Kleij³, Erik M. Akkerman¹, Gerard J. den Heeten¹, William R. Faber²

Department of Radiology¹, Dermatology² and Surgery³, Academic Medical Center and the department of Rehabilitation, Jan van Breemen Institute⁴, Amsterdam, the Netherlands

Submitted
INTRODUCTION

The invasion by *Mycobacterium leprae* of Schwann cells with the resulting peripheral nerve damage can lead to a so-called neuropathic foot. Ulceration and infection (cellulitis or osteomyelitis) are important complications. Repeated injury secondary to the neuropathy may lead to tarsal disintegration with osteolysis, fragmentation and progressive bone resorption. In extreme cases dissolution of the mid-foot results in separation of the forefoot and the hindfoot, changing all biomechanics and weight bearing areas [1,11,12,22]. The neuro-osteoarthropathy in the foot is a cause of considerable morbidity in leprosy [9,12,22,26]. Therefore, when a patient with a neuropathic foot presents himself with a warm foot, it is a clinical challenge to discriminate between neuro-osteoarthropathy and an ongoing osteomyelitis. Especially, this is difficult in the presence of an ulcer, because an ulcer itself leads to increased local temperature [10,22].

Various diagnostic modalities have been investigated in the analysis of osteomyelitis in neuropathic feet [5,13,24,28]. Magnetic Resonance Imaging (MRI) has been described as an important modality to assess osteomyelitis in the neuropathic foot of diabetic patients [16,18-20,27]. Tissue characterisation and spatial resolution facilitate identification of associated soft tissue pathology [2-4,16,30]. To detect subtle bone marrow pathology, such as a low-grade chronic infection, it is mandatory to use fat-suppression sequences with the use of contrast administration [19-21]. A homogeneous fat-suppression in the entire field of view both before and after intravenous contrast material (Gadolinium-chelate (Gd)) is required, to avoid artefacts and misreading [23]. This can adequately be achieved by the use of two-point Dixon chemical shift imaging (TPDCSI) [14,19].

The radiological literature available on MRI and osteomyelitis in neuropathic feet nearly exclusively concerns diabetic foot pathology, being the most frequent cause of neuropathic feet in the western world. However, leprosy is an important cause of neuropathic feet worldwide. According to the latest World Health Organization (WHO) information at the end of the year 2000 597,232 cases are on treatment, and 719,330 new cases are reported [29].

- 44 -
Literature concerning MRI and leprosy is scarce. Recently, an MRI study of neuropathic leprosy feet without clinical signs of inflammation was published [15]. As far as we know, no papers concerning the use of MRI in neuropathic leprosy feet, clinically suspected of osteomyelitis exist. In this paper we present our results with MRI in leprosy patients with neuropathic feet clinically suspected for osteomyelitis. The purpose of this study was to analyze the value of MRI in diagnosing osteomyelitis as a single diagnostic procedure. The MRI findings are compared to the signs described in literature for evaluating osteomyelitis. These MRI results were compared to the gold standard (bone biopsy or bone culture) or when no gold standard was available the MRI results were compared to the clinical outcome after six months.

**Material & Methods**

**Patients**

We retrospectively evaluated all consecutive MRI studies, following the Dixon protocol (see later) of the foot in leprosy patients performed in the period 1994-2000. All patients had longstanding neuropathic foot pathology and were clinically suspected for inflammation; they had a neuropathic warm swollen foot that did not respond to conservative weight reduction therapy. A neuropathic foot was defined as a foot in which one or more of the neuronal functions i.e. sensory, motor function or autonomic function was disturbed (consensus of the Dutch Neuropathic Foot Society) [7]. Furthermore, the clinical follow-up had to cover a period of six months.

**Clinical criteria**

Patient charts were reviewed for clinical information concerning leprosy classification [25], presence and location of an ulcer and clinical signs of inflammation. Twelve patients with neuropathic feet clinically suspected for osteomyelitis were investigated, in which 18 MRI studies were performed. The patients were classified as borderline lepromatous (n=3), borderline tuberculoid (n=1), and at the lepromatous side of the spectrum (n=8).

The gold standard for the diagnosis of osteomyelitis was a positive culture and/or histopathology taken from bone material.
Chapter 4

Clinical outcome after 6 months follow-up was retrospectively evaluated in cases where histopathology or culture was not available or not conclusive. A combination of clinical criteria was evaluated in a consensus reading by a dermatologist (WRF), a physiatrist (AFH) and a surgeon (AJvdK). The clinical criteria that were evaluated were response on antibiotic treatment, nature of surgical treatment when performed, persistent signs of inflammation, status of the ulcer, change in deformity.

**Diagnostic criteria (MRI)**

A total number of 24 MR studies in 12 adult leprosy patients (9 male, 3 female; mean age 63 years; age range 45-81 years) were included for evaluation. Of these 24 MR studies 18 were performed because of clinical suspicion of osteomyelitis. Follow-up MRI was performed in 6 patients (6 MRI studies).

**MRI**

MRI examination was performed using a 1.5 Tesla Vision (Siemens, Erlangen, Germany). All MRI studies were performed following the Dixon protocol [6,14,15]. This protocol consisted of: sagittal turbo-STIR (short tau inversion recovery) (3mm), T1-weighted Dixon sequence with in- and opposed-phase images, sagittal dual echo T2-weighted FSE (Fast Spin Echo) (3mm); after the intravenous administration of Gadolinium chelate (0.1 millimol per kilogram of body weight) T1-weighted Dixon sequence with in- and opposed phase images [6,14,15].

To evaluate the MRI studies signs were used as described in literature concerning diabetic neuropathic feet [16,19,20,27]. Typical, primary MRI signs are decreased marrow signal intensity on T1-weighted images, increased signal intensity on fat suppressed T2-weighted and/or fast STIR images, and focal marrow enhancement after Gadolinium-enhanced fat-suppressed T1-weighted images [14,17,20,21,28]. Secondary MRI signs are: the presence of a cutaneous ulcer, cellulitis, a soft tissue mass, a soft tissue abscess, a sinus tract, and cortical interruption [21,30]. One musculoskeletal radiologist (MM) retrospectively evaluated the images blinded to all clinical information except the knowledge of clinical suspicion for osteomyelitis. The signal intensity of the bone marrow on T1-weighted in and out of phase Dixon images, fast STIR images and Gadolinium enhanced T1-weighted in and out of phase Dixon images (primary signs) was classified as normal or abnormal on a data
collecting form. The secondary signs were classified as present or absent. Furthermore, the site of involvement was noted (medial arch, central compartment or lateral arch) [8,12].

**RESULTS**

*Clinical findings*

In 8 patients there was one event of suspected osteomyelitis. In 4 patients there were multiple events of suspected osteomyelitis; in 3 patients there were 2 events of suspected osteomyelitis, and in 1 patient there were 4 events of suspected osteomyelitis. The foot of involvement was 6 times right and 12 times left. The location of the ulcer was 2 times at the medial side, 14 times at the lateral side, and 2 times an ulcer was present at the medial and lateral side.

The results of the gold standard are listed in table 1. When evaluating results from bone biopsy or bone culture and/or preset clinical criteria, without detailed knowledge of the MRI results, the diagnosis osteomyelitis was made in 16 of 18 events (88.9%).

<table>
<thead>
<tr>
<th>Event</th>
<th>Gold standard</th>
<th>Clinical outcome</th>
<th>Event</th>
<th>Gold standard</th>
<th>Clinical outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Pos</td>
<td></td>
<td>10</td>
<td>Pos</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Pos</td>
<td></td>
<td>11</td>
<td>Pos</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Pos</td>
<td></td>
<td>12</td>
<td>Pos</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Pos</td>
<td></td>
<td>13</td>
<td>Neg</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Pos</td>
<td></td>
<td>14</td>
<td>Pos</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Pos</td>
<td></td>
<td>15</td>
<td>Neg</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Pos</td>
<td></td>
<td>16</td>
<td>Pos</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>Pos</td>
<td></td>
<td>17</td>
<td>Pos</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Pos</td>
<td></td>
<td>18</td>
<td>Pos</td>
<td></td>
</tr>
</tbody>
</table>

Table 1. Results of clinical follow-up in diagnosing osteomyelitis
**Diagnostic findings (MRI)**

In a total number of 18 events of suspected osteomyelitis we encountered 17 MRI examinations positive for primary MR signs for osteomyelitis (94.4%). Decreased signal on T1 in and out of phase on 16 MRI (88.9%), increased signal on T2 on 13 MRI (72.2%), fast SE STIR on 13 MRI (72.2%), and focally marrow enhancement after gadolinium-enhanced fat suppressed T1 on 17 MRI (94.4%) (Table 2).

<table>
<thead>
<tr>
<th>Positive primary sign</th>
<th>T1</th>
<th>T2</th>
<th>STIR</th>
<th>Contrast</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of MRI (%)</td>
<td>16 (88.9%)</td>
<td>13 (72.2%)</td>
<td>13 (72.2%)</td>
<td>17 (94.4%)</td>
</tr>
</tbody>
</table>

The secondary signs were positive in all MRI examinations (100%). Cellulitis was present in all cases (100%). A cutaneous ulcer in the region of the suspected osteomyelitis was also present in all cases (100%). Cortical interruption was found in 16 investigations (88.9%). A sinus tract was present in 5 cases (27.7%). A soft tissue abscess was present in 3 cases (16.6%). A soft tissue mass was found on two occasions (11.1%) (Table 3).

<table>
<thead>
<tr>
<th>Positive secondary sign</th>
<th>Cellulitis</th>
<th>Ulcer</th>
<th>Cortical interruption</th>
<th>Sinus tract</th>
<th>Soft tissue abscess</th>
<th>Soft tissue mass</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of MRI (%)</td>
<td>18 (100%)</td>
<td>18 (100%)</td>
<td>17 (88.9%)</td>
<td>5 (27.7%)</td>
<td>3 (16.6%)</td>
<td>2 (11.1%)</td>
</tr>
</tbody>
</table>

Table 2. Primary MRI signs: number of positive findings on various MRI sequences

Table 3. Presence of positive secondary MRI signs
An example of positive primary signs and secondary signs at the lateral side of the foot is shown in figure 1.

**Figure 1a.** Two-point Dixon fat suppression image of the right foot of a 79-year-old female patient. Note the degradation of the plantar fat with the presence of soft tissue edema (interrupted arrow) and the high signal intensity in the partly destroyed cuboid bone (non-interrupted arrow).

**Figure 1b.** Same patient after intravenous gadolinium chelate administration. Note the marked enhancement at the lateral side of the foot both in the soft tissue (cellulitis) (interrupted arrow) and in the cuboid bone (osteomyelitis) (non-interrupted arrow).

The sites of involvement (MRI)
The sites of involvement: medial-central-lateral, on MRI were analysed. The areas of osteomyelitis were located at the medial site (MTP1 joint, os metatarsal 1, cuneiform 1, navicular bone) in 3 events, medial/central in 2 events, central (MTP 2-3, os metatarsal 2-4) in 3 events, lateral (MTP 4-5 joint, os metatarsal 4-5, cuboid, calcaneus) in 9 events. In 1 patient all three areas were involved.

Follow-up (MRI)
Six follow-up MRI were made after antibiotic treatment. Mean time of follow-up was 5 months. A complete healing of the ulcer occurred in two patients with a normal follow-up MRI.
Chapter 4

Two patients had an improved but still abnormal MRI; the MRI changes that were seen were a reduction but still present zone of enhancement of the bone marrow. Both patients eventually showed a complete clinical remission. The foot of the patient that showed an unchanged follow-up MRI despite continued antibiotics eventually was amputated.

**DISCUSSION**

Osteomyelitis is a well-known complication in patients with neuropathic foot pathology [4,13,16,19,20,24,26,28,30]. These patients may develop ulcers that persist over a long period of time. In this way spread of infection *per continuitatem* can cause an infection of the osseous structures in the foot. Clinical examination lacks specificity in this patient group, since by clinical examination alone it is difficult to differentiate between cellulitis, osteomyelitis and neuro-osteoarthropathy [22,26]. MR imaging is potential powerful in the evaluation of the neuropathic foot; it is useful for the evaluation of presence and extent of osteomyelitis, as well as for the identification of the presence and extent of associated soft tissue abnormalities that may have clinical importance, such as cellulitis, abscess, and sinus tract [4,16,18-21,27,30]. Nearly all data available on MRI and neuropathic feet concern patients suffering from diabetes. As far as we know this is the first report on the use of MRI as a diagnostic procedure in neuropathic leprosy feet suspected for osteomyelitis.

When analyzing the primary MRI signs for osteomyelitis we found in our population that in 17 out of 18 events (94.4%) primary MRI signs were positive. Decreased signal intensity on in and out of phase T1-weighted images and the marrow enhancement after gadolinium administration on fat-suppressed T1 were the most frequent encountered abnormalities. In our retrospective analysis (gold standard and/or clinical outcome) 16 out of 18 events were diagnosed as positive for osteomyelitis. Comparing this evaluation with the primary MRI signs there was agreement in 17 out of 18 events. The disagreement found in one patient was caused by the primary MRI sign focal marrow enhancement after contrast administration. Therefore, we conclude that these primary signs, used in evaluating MRI examinations in diabetics can adequately be used to analyze MRI examinations in leprosy patients with longstanding complicated neuropathic feet.
MRI and osteomyelitis in leprosy patients

Of the secondary MR signs ulcer and cellulitis were present in all cases. The areas on MRI suspected of osteomyelitis were in continuity with the ulcer. The relation between ulcer and osteomyelitis has also been described in diabetes [5]. In contrast to diabetic feet only a minority of examinations revealed a sinus tract or soft tissue abscess in our population [21]; it seems that these latter secondary signs are infrequently found in leprosy. However, the presence of an ulcer and cellulitis is common in leprosy patients with longstanding neuropathic feet suspected for osteomyelitis. Contrary to diabetic foot literature the secondary MRI signs seem of no additional value in diagnosing osteomyelitis in a population of leprosy patients with longstanding neuropathic foot disease. However, the value of these findings in a patient population of leprosy patients with neuropathy and clinical suspicion of inflammation, without longstanding disease was not evaluated in this study. For this purpose a study is currently conducted.

The present study demonstrates in 9 events MRI changes suspected for osteomyelitis at the lateral side only (50%). In a minority of events these changes were found at the medial side only (16.7%). This is in contrast to the results found in a recent study of asymptomatic neuropathic feet in leprosy patients in which 90 percent of the MRI changes were located at the medial site of the foot [15]. Most likely the biomechanics in the two patient groups (clinically unsuspected versus clinically suspected in longstanding neuropathic foot disease) are different. Biomechanical analysis in early tarsal disintegration shows the highest stress to occur during the push off phase in the bones of the lateral foot arch [12]. Perhaps this is caused by inversion due to paralysis of the lateral musculature. An analysis of the walking cycle in two groups of leprosy patients with neuropathic feet with and without clinical abnormalities may be of additional value in order to analyse the stress distribution.

When a leprosy patient with longstanding neuropathic foot disease is suspected of osteomyelitis clinical examination lacks specificity. Contrast enhanced MRI with the use of two-point Dixon chemical shift imaging, as fat-suppression technique is a valuable technique to detect osteomyelitis. The primary MR signs known from literature, concerning diabetic neuropathic foot can adequately be assessed. MRI can serve as a one step diagnostic strategy to diagnose osteomyelitis in leprosy patients with a longstanding neuropathic foot problem.
Summary
This study was undertaken to analyze the MRI findings in leprosy patients with neuropathic feet, suspected for osteomyelitis. As far as we know, no papers concerning osteomyelitis and MRI in neuropathic leprosy feet are present.

We included MRI examination of 18 events of suspected osteomyelitis in 12 leprosy patients. All patients with longstanding neuropathic foot problems were clinically suspected for osteomyelitis. All patients underwent the MRI protocol with the inclusion of two-point Dixon chemical shift imaging as fat-suppression sequence.

For the MRI evaluation we used signs that are described in literature for detecting osteomyelitis in diabetic feet. The primary MRI signs were positive in 17 of 18 patients. The secondary MRI signs were positive in 100% of patients.

Our results show that MRI with the use of two-point Dixon chemical shift imaging is a promising diagnostic modality to detect osteomyelitis in the presence of neuro-osteoarthropathic changes in patients with leprosy. Whenever available MRI could play an important role in detecting osteomyelitis in leprosy patients with longstanding neuropathic feet, suspected for osteomyelitis.

References


