A clinical and radiological follow-up study in leprosy patients with asymptomatic neuropathic feet

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Summary

Objectives An MRI study done in 2000 on 10 leprosy patients with neuropathic feet, without clinical complications such as ulcerations, osteomyelitis or Charcot deformities revealed abnormalities in nine patients, with degradation, interruption of subcutaneous fat and effusion/synovitis, all located in the first metatarsophalangeal (MTP) region. Since these MRI abnormalities may precede clinical complications of the foot, a follow-up study was performed.

Design A new evaluation was based on a clinical examination and an MRI of the same patients who participated in the initial study.

Results Four patients were lost to follow-up. Average follow-up period was 4.6 years. MRI abnormalities in the MTP 1 region in the first study were no longer visible in three patients, but were still present in two patients. In six patients new MRI findings were found, without clinical evidence of ulceration, osteomyelitis or Charcot deformity. No relationship was found between MRI findings in the MTP 1 region at the start of the study and the development of foot ulcers, callus or skin fissures in the MTP 1 region during follow-up.

Conclusion MRI findings of interruption and infiltration of the subcutaneous fat in leprosy patients with uncomplicated neuropathic feet do not necessarily have any clinical implication for the development of future foot problems.

Introduction

Infection with the Mycobacterium leprae causing infiltration of the skin and Schwann cell may result in nerve function impairment (NFI). In the lower extremities, nerve impairment can lead to a so-called ‘neuropathic foot’ in which there is loss of at least one of the three primary nerve functions. Impaired motor function can result in muscle atrophy and subsequently changes in the shape of the foot and claw toes. Secondly, through loss of protective sensibility patients do not feel increased pressure, pain or heat, and this can result in blisters, burns...
and ulcers. Thirdly, loss of autonomic function causes dryness of the skin and hyperkeratosis, in which fissures occur. Altered biomechanical forces, which often occurs in combination with osteoporosis, can cause damage to the skeleton, and can eventually result in neuro-osteoarthropathy (Charcot deformity) of the foot.\textsuperscript{1–5} the bone prominences and the plantar surface of the foot are vulnerable for repeated trauma, resulting in callus and ulceration.\textsuperscript{6} Foot ulcers are a major problem in leprosy patients, and can lead to complications such as osteomyelitis and cellulitis.\textsuperscript{3} Osteomyelitis is often related to ulceration and may lead to amputation.\textsuperscript{7} Appropriate footwear and good foot management can prevent the development of foot ulcers, and the development of ulcer-related complications.\textsuperscript{3} Little is known about the exact mechanism of the first complications that develop in the neuropathic foot.

Magnetic Resonance Imaging is an useful imaging technique in assessing the neuropathic foot in patients with leprosy and diabetes.\textsuperscript{8,9} It has the capacity to detect subtle bone changes and soft-tissue abnormalities in the neuropathic feet of leprosy patients.\textsuperscript{8,10,11} In a previous study of neuropathic feet in leprosy patients, but with no clinical complications such as ulceration, osteomyelitis or neuro-osteo-arthropathy, MRI revealed abnormalities in nine out of ten feet, showing degradation and interruption of the subcutaneous fat and effusion/synovitis, all located in the first metatarsophalangeal (MTP) region.\textsuperscript{11}

Although the clinical significance of these MRI findings was not yet clear at the time of that first study, these MRI abnormalities may provide more insight into the way in which early complications, such as foot ulcers or callus formation, may develop. The MTP 1 region is known as a foot area at risk for developing complications in leprosy patients and may be related to a limited MTP 1 joint mobility causing shearing stress under the metatarsal head.\textsuperscript{3,12} We therefore performed a clinical and radiological follow-up study of the leprosy patients with neuropathic feet who participated in our first study.

The aim of the present study was to answer the following questions:

1. Did clinically relevant pathology, located in the MTP 1 region of the neuropathic foot, develop over time?
2. Did the MRI findings located in the MTP 1 region change over time, and what are the radiological findings on a follow-up MRI?
3. Is there a relationship between the MRI findings in the former study and the clinical findings after a follow-up period?

Answering these questions would indicate the clinical significance of MRI abnormalities findings in the MTP 1 region, and may also improve our current ulcer prevention programme.

\textbf{Study Population and Methodology}

\textbf{PATIENTS}

A follow-up study was performed among the patients who participated in our former study.\textsuperscript{11} Inclusion criteria were: nerve function impairment, normal foot shape with no clinical signs of inflammation, ulcers or neuro-osteo-arthropathy. The study was performed in the Academic Medical Centre in Amsterdam, and was approved by the Medical Ethical Committee of this institute. In the present study a new evaluation was based on a clinical examination and an MRI. Of the 10 original patients, four were lost to follow-up (one patient died, one could not be traced, one refused informed consent and one had emigrated). Therefore, six patients
were included in the study. Informed consent was obtained from all participating patients. The follow-up period was between October 1997 and June 2004 and ranged from 3·2 to 6·2 years (average 4·6 years). Data on hospital admissions, complications, and treatment with regard to the neuropathic foot and leprosy during the follow-up period, were collected from the patient files.

The age of the six patients at the time of follow-up ranged from 52–70 years (average 61·5 years; three males and three females). According to the Ridley–Jopling classification system, patients were classified as: Borderline Lepromatous (BL; three patients), Borderline Tuberculoid (BT; one patient) and Lepromatous (LL; two patients).13

CLINICAL ASSESSMENT

In our first study, physical examination was performed by a dermatologist who specialised in neuropathic foot pathology (WRF). Findings that were described in 2000 were signs of nerve function impairment, especially sensory malfunction, and also signs of ulceration, osteomyelitis or acute neuro-osteo-arthropathy. The physical examination in our follow-up study was performed by the same dermatologist (WRF) and by a rehabilitation medicine resident (FJS). The clinical assessment of the foot deformities was based on consensus. Nerve function impairment was diagnosed as an impaired 10-gram force filament test (Semmes-Weinstein filament).14 Signs of inflammation in the foot were evaluated by palpation of the skin on the forefoot of both feet.15

For both feet, detailed information was recorded with regard to ulcer size and aspect, dryness of the skin, foot and toe deformities, callus formation, fissures, edema, redness and increased temperature. Types of footwear (off-the-shelf or (semi-)custom-made), inlays and any technical adjustments of the shoe (rocker-bar) were described. Patient files were used to record information on all foot problems and treatment during the follow-up period.

RADIOLOGICAL ASSESSMENT

State of the art MRI examinations were performed for this follow-up study and consisted of: sagittal T-STIR (4 mm) T1-W, T2-W images and coronal T1 FATSAT imaging before and after intravenous contrast administration (Gadolinium®).9 The MRI readings were performed by a radiologist who specialised in skeletal radiology (MM), and who was blinded for all the clinical data and the previous MRI results.

Results

The information is described per patient because of the importance of every (minor) clinical and radiological change. Tables 1 and 2 present the findings that are described more in detail below.

PATIENT 1

Clinical findings in the first study: The right foot was studied. Dryness of the skin with callus located at the top of digit 1 was found and claw toes. Clinical findings in the
Table 1. Clinical findings at the start of the study (I) and after follow-up (II)

<table>
<thead>
<tr>
<th>Patient</th>
<th>Class†</th>
<th>Footwear</th>
<th>Ulcer I</th>
<th>Callus I</th>
<th>Deformities I</th>
<th>Ulcer II</th>
<th>Callus II</th>
<th>Deformities II</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>LL</td>
<td>Custom-made</td>
<td>–</td>
<td>Top digit 1</td>
<td>Clawtoes</td>
<td>Dorsal PIP 2,3</td>
<td>Top digit 1–5, MT 5</td>
<td>Clawtoes 2–5, varus hindfoot, hallux limitus</td>
</tr>
<tr>
<td>2</td>
<td>BL</td>
<td>Custom-made</td>
<td>–</td>
<td>MTP 1</td>
<td>–</td>
<td>–</td>
<td>MTP 1</td>
<td>Clawtoes 2–5, pes planovalgus, hallux valgus</td>
</tr>
<tr>
<td>3</td>
<td>BL</td>
<td>Semi-custom-made</td>
<td>–</td>
<td>MTP 5</td>
<td>–</td>
<td>–</td>
<td>Dorsal digit 5</td>
<td>Clawtoes 2–4, pes planovalgus, hallux valgus</td>
</tr>
<tr>
<td>4</td>
<td>BT</td>
<td>Custom-made</td>
<td>–</td>
<td>–</td>
<td>Shortened digit 1</td>
<td>–</td>
<td>–</td>
<td>Clawtoes 2–5, pes planovalgus, shortened digit 1</td>
</tr>
<tr>
<td>5</td>
<td>LL</td>
<td>Off the shelf</td>
<td>Digit 1‡</td>
<td>Fissure MTP 1</td>
<td>–</td>
<td>–</td>
<td>MT 5, dorsal digit 1,5</td>
<td>Clawtoes 2–5, pes planus</td>
</tr>
<tr>
<td>6</td>
<td>BL</td>
<td>Semi-custom-made</td>
<td>–</td>
<td>Top digit 1,2 and heel</td>
<td>Clawtoes 3–5</td>
<td>Digit 1§</td>
<td>MTP 1</td>
<td>Clawtoes 3–5, pes planovalgus, hammer toe digit 1</td>
</tr>
</tbody>
</table>

† Class = classification of leprosy into LL = Lepromatous Leprosy, BL = Borderline Lepromatous, BT = Borderline Tuberculoid.
‡ History of ulcer.
§ Haematoma.
MTP = metatarsophalangeal joint; MT = metatarsal; PIP = proximal interphalangeal joint.
Table 2. MRI findings at the start of the study (I) and after follow-up (II)

<table>
<thead>
<tr>
<th>Patient</th>
<th>Eff I</th>
<th>Edema I</th>
<th>Enhanc I</th>
<th>Interrup subcut fat I</th>
<th>Muscle atrophy I</th>
<th>Others I</th>
<th>Eff II</th>
<th>Edema II</th>
<th>Enhanc II</th>
<th>Interrup subcut fat II</th>
<th>Muscle atrophy II</th>
<th>Others II</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>MTP 1</td>
<td>–</td>
<td>–</td>
<td>MTP 1</td>
<td>Intrinsics</td>
<td></td>
<td>MTP 1</td>
<td>–</td>
<td>–</td>
<td>MTP 1–5</td>
<td>Intrinsics</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>MTP 1</td>
<td>MTP 1</td>
<td>MTP 1</td>
<td>MTP 1</td>
<td>Intrinsics</td>
<td>Tophi1*, OA</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>MTP 1</td>
<td>Intrinsics</td>
<td>Tophi1,3,4*, OA midfoot</td>
</tr>
<tr>
<td>3</td>
<td>MTP 1</td>
<td>–</td>
<td>–</td>
<td>MTP 1</td>
<td>Intrinsics</td>
<td></td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>PIP1</td>
<td>Intrinsics</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>MTP 1</td>
<td>Intrinsics</td>
<td>Stress-induced injury navicular</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>MTP 2,3</td>
<td>Intrinsics</td>
<td>Stress-induced injury navicular</td>
</tr>
<tr>
<td>5</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>Intrinsics</td>
<td>Stress-induced injury navicular</td>
<td></td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>MTP 5, MT 5</td>
<td>Intrinsics</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>MTP 1</td>
<td>–</td>
<td>–</td>
<td>MTP 1–4</td>
<td>Intrinsics</td>
<td></td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>MTP 4,5</td>
<td>Intrinsics</td>
<td></td>
</tr>
</tbody>
</table>

Eff = effusion; Enhanc = enhancement; interrup subcut fat = interruption of subcutaneous fat; Intrinsics = intrinsic foot muscles. MTP = metatarsophalangeal joint; MT = metatarsal; PIP = proximal interphalangeal joint. OA = osteoarthritis midfoot. * Gout.
follow-up study: Dryness of the skin was found with callus on top of digits 1–5 and at the base and lateral part of the fifth metatarsal (MT 5). A superficial wound was found dorsal to the proximal interphalangeal (PIP) joints of digits 2 and 3. No other signs of inflammation were found during the follow-up period. A varus position of the hindfoot was found and claw toes on digits 2–5. Limited mobility was found in digit 1. This patient wore custom-made shoes with a rocker-bar and total contact inlays.

MRI findings in the first study: Effusion was seen in the MTP 1 region, with interruption and infiltration of the subcutaneous fat plantar to the MTP 1 region. Fatty muscle atrophy in the intrinsic foot muscles was found.

MRI findings in the follow-up study: Interruption and infiltration of the subcutaneous fat was seen plantar to MTP 1–5, and effusion was seen in the MTP 1 region. Fatty muscle atrophy in the intrinsic muscles was found.

Conclusion after follow-up:
Clinical: no ulcer, more callus, minor changes in foot posture.
MRI: MTP 1 abnormalities still present, more MRI abnormalities at different locations.

PATIENT 2

Clinical findings in the first study: The right foot was studied. Dry skin was found with callus located plantar to MTP 1. No foot or toe deformities were found. Clinical findings in the follow-up study: Dry skin was found with callus located medial to MTP 1. No ulcers or signs of inflammation were found during the follow-up period. Pes planovalgus with a hallux valgus and collapsed longitudinal and transversal plantar arch was found with claw toes located on digits 2–5. This patient wore ankle-high, custom-made shoes with semi-stiff outsole with a small rocker-bar, a rounded heel and total contact inlays. On the left leg there was a transtibial amputation with a below knee prosthesis.

MRI findings in the first study: Bone marrow edema was seen in the MTP 1 region, together with effusion and enhancement. Infiltration and interruption of subcutaneous fat was seen located plantar to MTP 1 and gout tophi was found dorsal in the MTP 1 region. Talonavicular, cuneiform and tarsometatarsal osteo-arthritis was found in the midfoot. Fatty atrophy was found in the intrinsic foot muscles.

MRI findings in the follow-up study: Interruption and infiltration of the subcutaneous fat plantar to MTP 1 and gout tophi dorsal to digits 1, 3, 4. Talonavicular, cuneiform and tarsometatarsal osteo-arthritis was seen in the midfoot. Fatty atrophy was found in the intrinsic foot muscles.

Conclusion after follow-up:
Clinical: no ulcer, callus status quo in MTP 1 region, minor changes in footing posture and more claw toes.
MRI: MTP 1 abnormalities still present, more MRI abnormalities at different locations.

PATIENT 3

Clinical findings in the first study: The right foot was studied. Dry skin with callus plantar to MTP 5 was found. No foot or toe deformities were found. Clinical finding in the
follow-up study: Dry skin with callus was found dorsal to digit 5, and there were signs of increased pressure (local redness) dorsal to digit 4. No ulcers or signs of inflammation were found during the follow-up period. Pes planovalgus with a hallux valgus was found and clawtoes located in digits 2–4. This patient wore semi-custom-made shoes with a stiff outsole, a rocker-bar and custom made inlays.

MRI findings in the first study: Effusion was seen in the MTP 1 region with interruption and infiltration of the subcutaneous fat plantar to MTP 1. Fatty muscle atrophy was found in the intrinsic foot muscles. MRI findings in the follow-up study: Infiltration and interruption of the subcutaneous fat was found plantar to the interphalangeal (IP) joint of digit 1, and fatty atrophy in the intrinsic foot muscles.

Conclusion after follow-up:
Clinical: no ulcer, new callus at different location, minor changes in footing posture and more clawtoes.
MRI: different MRI abnormalities located in the same toe.

PATIENT 4

Clinical findings in the first study: The left foot was studied. Dry skin but no callus was found. Shortening of digit 1 was seen (caused by surgery 15 years ago) but no other foot or toe deformities. Clinical findings in the follow-up study: Dry skin but no callus, ulcers or signs of inflammation were found during the follow-up period. Valgus position of the hindfoot was found with a pes planovalgus. Claw toes were located in digits 2–5, and digit 1 was shortened. This patient wore custom-made shoes with a rocker-bar and custom made inlays.

MRI findings in the first study: Infiltration and interruption of the subcutaneous fat was seen located plantar to MTP 1 and fatty atrophy in the intrinsic foot muscles. MRI findings in the follow-up study: Infiltration and interruption of the subcutaneous fat was seen located plantar to MT 2, 3, 5. Fatty atrophy was seen in the intrinsic foot muscles.

Conclusion after follow-up:
Clinical: no callus or ulcer, minor changes in footing posture and more clawtoes.
MRI: no MRI abnormalities in MTP 1 region but more MRI abnormalities at different locations.

PATIENT 5

Clinical findings in the first study: The right foot was studied. Dry skin with a skin fissure was seen plantar to MTP 1. The patient had a history of a foot ulcer at the distal part of the phalanx of digit 1. No foot or toe deformities were found. Clinical findings in the follow-up study: Dry skin with callus was seen at the base of MT 5, lateral to PIP of digit 1 and on top of PIP of digit 5. No ulcers or signs of inflammation were found during the follow-up period. A collapsed transversal plantar-arch was found and claw toes in digits 2–5. This patient wore off-the-shelf footwear with a rocker-bar and custom-made inlays for treating a fasciitis plantaris.

MRI findings in the first study: A stress-induced injury of the navicular bone was found and there was fatty muscle atrophy seen in the intrinsic muscles. MRI findings in the follow-up study: Infiltration and interruption of the subcutaneous fat was seen plantar to
MTP 5 and MT 5 and fatty muscle atrophy in the intrinsic foot muscles. (Figure 1)
A stress-induced injury was found in the navicular bone.

**Conclusion after follow-up:**
Clinical: ulcer in the past, callus in MTP 1 region improved, new callus at different locations, minor changes in footing posture and more clawtoes.
MRI: more MRI abnormalities at different locations.

**PATIENT 6**

**Clinical findings in the first study:** The right foot was studied. Dry skin with callus was found at the top of digit 1, 2 and heel. Claw toes were found on digits 3–5. **Clinical findings in the follow-up study:** Dry skin with callus was found medially to the MTP 1 region. A small haematoma was found on the top of digit 1 and there were signs of increased pressure (local redness) at the dorsal part of digits 2–4. No ulcers or signs of inflammation were found during the follow-up period. Pes planovalgus was found and claw toes on digit 3–5 and a hammertoe located on digit 1. This patient wore semi-custom-made shoes and custom-made inlays with support for the transversal foot arch. **MRI findings in the first study:** Infiltration of subcutaneous fat was found plantar to MTP of digits 1–4 and effusion in the MTP 1 region. Fatty muscle atrophy was found in the intrinsic foot muscles. **MRI findings in the follow-up study:** Interruption and infiltration of subcutaneous fat was found plantar to MTP 4 and 5, with fatty atrophy of intrinsic foot muscles.

**Conclusion after follow-up:**
Clinical: no ulcer, new callus at MTP 1 region and at different locations, minor changes in footing posture, clawtoes status quo.
MRI: fewer MRI abnormalities in MTP 1 and digit 1–4 region, but new MRI abnormalities at different locations.
Discussion

Clinical Findings

In our first study, physical examination of the feet was performed by a dermatologist who specialised in neuropathic foot pathology. In our present follow-up study the physical examinations were performed by both the same dermatologist and a rehabilitation medicine resident. The various foot deformities were described in much more detail in our follow-up study. For the description of changes over time we limited ourselves to comparing only the signs of callus formation, ulceration, osteomyelitis and acute neuro-osteo-arthropathy.

Only one patient (patient 6) developed new callus at the MTP 1 region. The other patients showed a status quo (patient 2) or an improvement in callus at the MTP1 region (patient 5). New callus was found at different locations in three patients (patients 1, 3, and 5).

Apart from a superficial wound on the dorsum of digits 2 and 3 (patient 1) and a small haematoma at the top of digit 1 (patient 6), no ulceration was found. No ulceration at all was found in the MTP 1 region during a follow-up period of 5 years.

Severe foot deformities, such as an active neuro-osteo-arthropathy did not develop during this follow-up period. Only minor foot deformities and claw toes were seen.

MRI Findings

In two patients (patients 1 and 2) interruption and infiltration of the subcutaneous fat plantar to MTP 1 was unchanged at follow-up, in three patients (patients 3, 4 and 6) this had disappeared. In one patient (patient 5) this phenomenon was first seen at follow-up but at the MTP 5 region. All patients had new MRI abnormalities at different locations.

Relationship Between Former MRI Abnormalities and Recent Clinical Findings

No correlation could be found between the MRI abnormalities observed in our former study and the recent clinical observations of the feet, with regard to the development of callus, ulceration or neuro-osteo-arthropathy.

We also looked for a possible relationship between fatty atrophy of the intrinsic foot muscles and the development of claw toes. Therefore, we again compared the MRI results and clinical findings from our former study with the information obtained in the present study. Fatty muscle atrophy was found on the MRI in both studies in all our patients, but could not in all cases be related to the development of claw toes. This is in line with the findings in diabetic neuropathic feet.16

Our study results may be influenced by the use of custom-made shoes, good foot care and regular check-ups at the outpatient clinics. This may have prevented the development of ulcers in our population of leprosy patients. During the follow-up there was no relevant change in footwear or any other form of therapy. In leprosy endemic countries these facilities are often not available to patients and increase the risk of developing foot complications.

The present study shows that an interruption and infiltration of the subcutaneous fat found on MRI does not necessarily have clinical implications for the development of plantar foot ulcers. It has been proposed that the MRI findings may be a haematoma caused by micro trauma in the foot, which may precede a foot ulcer.17 The results of our study with a 5-year follow-up period can not confirm this conclusion. However, several clinical and
radiological changes in the neuropathic foot and toes did appear during a follow-up period of 5 years, despite the use of custom-made shoes, good foot care and regular check-ups. The abnormalities found on MRI seem to change over time and may be caused by a dynamic (biomechanical) process happening within the soft-tissue area of the foot. Therefore, an extension of the follow-up investigation is important to study if complications develop within a longer follow-up period.

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References