Lymphocutaneous fistulas: pre-therapeutic evaluation by magnetic resonance lymphangiography

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Objective: Lymphocutaneous fistulas with intractable lymphatic leakage represent a serious clinical condition leading to a severe impairment of quality of life for the affected patients. To date, no adequate diagnostic imaging modality is in existence to allow selection of the correct treatment option. The aim of this study was to perform a pre-therapeutic evaluation of the lymphatic system in patients with lymphocutaneous fistulas by magnetic resonance lymphangiography (MRL).

Methods: Eight lower extremities in four patients with lymphocutaneous fistulas were examined by MRL. Three locations were examined: first, the lower leg and foot regions; second, the upper leg and the knee region; and third, the pelvic and retroperitoneal regions. A T_1 weighted three-dimensional (3D) spoiled gradient echo and a heavily T_2 weighted 3D turbo spin echo (3D-TSE) sequence were utilised to undertake MRL.

Results: In all four patients (100%), the clinically suspected lymphocutaneous fistulas (groin and forefoot) were exactly delineated by MRL. In two patients (50%) adjacent diffuse lymphangiomatous changes were detected, extending into the upper leg, pelvis, retroperitoneum, abdomen and abdominal walls. In one patient (25%) with primary lymphoedema of the right lower extremity, MRL revealed an aplasia of the lymphatic collectors at the levels of the lower and upper leg. All patients (100%) suffered from an ipsilateral lymphoedema of the lower extremity, whereby in two patients with diffuse lymphangiomatosis the lymphatic vessels were consecutively enlarged up to a diameter of 6 mm.

Conclusion: MRL is a safe and accurate imaging modality for a comprehensive evaluation of the lymphatic system in patients suffering from lymphocutaneous fistulas.

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Lymphocutaneous fistulas are rare clinical phenomena and represent a challenging diagnostic and therapeutic complication for the attending physician. On the basis of their origin, lymphocutaneous fistulas can be divided into primary, *e.g.* patients with congenital lymphoedema and diffuse lymphangiomatosis, or secondary, which are often caused by interventional procedures and surgery [1–4]. The incidence has been reported to be between 0.5% and 6% [1–3, 5]. Additionally, various reports exist in the medical literature describing the occurrence of secondary lymphocutaneous fistulas in patients with malignancy and during the treatment of venous leg ulcer [6]. Persistent, inadequately treated lymphocutaneous fistulas considerably decrease the patient's quality of life with an increased risk of infection.

Because the exact delineation and extent of the lymphocutaneous fistulas with adjacent lymphatic pathologies are important prognostic factors, performing a radiological evaluation with a high resolution is crucial for the patient's optimal therapeutic planning, which is used to describe the lymphatic anatomy in patients

suffering from lymphocutaneous fistulas [7–10]. Magnetic resonance lymphangiography (MRL) with intracutaneous injection of an extracellular paramagnetic contrast agent is an innovative diagnostic imaging method for the evaluation of the lymphatic system. This method has proved to be feasible in patients with primary or secondary lymphoedema [11–13].

The intention of this study was to perform a comprehensive evaluation of the lymphatic system in patients suffering from lymphocutaneous fistulas using the MRL technique. To our knowledge, to date the patient series presented here concerning the examination of primary and secondary lymphocutaneous fistulas by means of MRL is the first medical publication on this topic.

Methods and materials

Between January 2006 and April 2007, 8 lower extremities in 4 patients (aged 17–64 years; mean age 40 years; 1 female, 3 males) with lymphocutaneous fistulas were examined by MRL. All patients had given their informed consent prior to MRI and were identified retrospectively.

A total amount of 18 ml of contrast material (Gadoteridol, Prohance, Bracco-Byk Gulden, Konstanz, Germany) and 2 ml of mepivacainhydrochloride 1% was subdivided into

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10 portions and injected intracutaneously into the dorsal aspect of each foot in the region of the 4 interdigital webs and medial to both first proximal phalanges. The injection process per patient took approximately 10 min. MRL was conducted using a 1.5T system (Avanto; Siemens Medical Systems, Erlangen, Germany); three locations were examined: the lower leg and foot region; the upper leg and the knee region; and the pelvic and retroperitoneal regions. A phased array body coil was used to image the pelvic region, and a dedicated peripheral surface coil was used to examine the upper and lower leg. To minimise leg movements, foam pillows were placed between the legs of the patients and the dedicated peripheral surface coil.

In coherence with previous MRL studies, the imaging protocol consisted of a heavily T_2 weighted three-dimensional turbo spin echo (3D-TSE) sequence (repetition time/echo time (TR/TE), 2000/694; flip angle, 180°; matrix, 256 × 256, bandwidth, 247 Hz/pixel; 6/8 rectangular field of view 480 mm; slices, 96; voxel size, 2.0 × 1.9 × 1.7 mm; acquisition time, 4 min 48 s) to evaluate the extent and distribution of the lymphoedema [11,12]. MRL was performed with a T_1 weighted 3D spoiled gradient echo sequence (volumetric interpolated breath-hold examination, VIBE) (TR/TE, 3.58/1.47; flip angle, 35°; matrix, 448 × 448; bandwidth, 490 Hz/pixel; 6/8 rectangular field of view with a maximum dimension of 500 mm; slices, 128; voxel size, 1.2 × 1.1 × 1.2 mm; acquisition time, 1 min 40 s) with image subtraction 15, 25, 35, 45 and 55 min after intracutaneous contrast material injection. The enhancement of gadoteridol in the lymphatic pathways, inguinal lymph nodes and veins was qualitatively and quantitatively assessed by two authors, a diagnosis was reached by consensus.

Results

In all four patients, MRL was able to exactly identify the lymphocutaneous fistulas using either the T_1 weighted 3D spoiled gradient echo sequence after intracutaneous contrast material application or the heavily T_2 weighted 3D-TSE sequence (Tables 1 and 2; Figure 1b). Additionally, in the case of the T_1 weighted 3D spoiled gradient echo sequence after intracutaneous contrast material application, a detailed description of the lymphatic vascular system was performed in the examined eight lower extremities, whereby the findings ranged from an aplasia to an enlargement of 6 mm in the lymphatic vessels (Table 2, Figures 1a and 2). In all four patients, the clinically diagnosed lymphoedema could be consistently

proved by means of high signal intensities on the T_2 weighted 3D-TSE images (Tables 1–3). In two patients with inguinal lymphocutaneous fistulas, adjacent diffuse lymphangiomatous changes extending to the pelvic and retroperitoneal regions were detected (Tables 1 and 2; Figure 1a–c). Owing to the severe network of adjacent lymphangiomatous changes, surgical treatment of the lymphocutaneous fistula was not indicated and a conservative treatment plan was chosen, including complex decongestive therapy (CDT) with a compression stocking covering the inguinal and pelvic regions (Table 4). The remaining two patients received surgery of lymphocutaneous fistulas (Table 4). Up to the present time, the two surgically treated patients have not experienced a recurrence of lymphocutaneous fistulas. In the conservatively treated patients, the lymphorrhoea has slightly decreased.

In three of the four patients, the lymphorrhoea through the lymphocutaneous fistulas was observed to be clear, whereas in one patient an alternating unclear lacteal was present, proving a lymphangiomatous involvement of the visceral lymphatics (Table 1). Consequently, the patient was prescribed a “multichain triglyceride (MCT) diet” (Table 4). Furthermore, all patients were informed about the importance of skin hygiene with a constant disinfection of the cutaneous lymph cysts arising from the lymphocutaneous fistulas (Table 4).

Discussion

To date, lymphoscintigraphy and intra-operative blue dye staining have been used to describe the lymphatic anatomy in patients suffering from lymphocutaneous fistulas [7–10]. Jackson et al [7] presented a patient in whom a lymphatic wound discharge was observed post-operatively after renal transplantation. A lymphoscintigraphy was then capable of revealing the iatrogenic-induced lymphatic interruption, proving the lymphatic origin of the extracorporeal fluid by measuring the activity of the fluid. These results were confirmed by Stolzenberg [8], who reported the successful use of lymphoscintigraphy for the detection of a lymphocutaneous fistula with attending lymphorrhoea after a left-sided carotid–subclavian bypass operation for subclavian steal syndrome.

In general, lymphoscintigraphy presents the disadvantage of an ionising radiation exposure and poor spatial, as well as temporal, resolution, limiting its value for an accurate delineation of the lymphatic anatomy. As demonstrated in all four patients in this study, MRL is highly

Table 1. Clinical findings in four patients with lymphocutaneous fistulas

	Location of lymphocutaneous fistulas	Cause of lymphocutaneous fistulas	Lymphorrhoea through lymphocutaneous fistulas	Ipsilateral leg	Contralateral leg
Patient 1	Right groin	Diffuse lymphangiomatosis	Alternating chylous and clear liquid	Lymphoedema (Stage 1)	Latent lymphoedema (Stage 0)
Patient 2	Right forefoot	Primary lymphoedema	Clear liquid	Lymphoedema (Stage 2)	No lymphoedema
Patient 3	Right groin	Traumatic (earlier radiation therapy)	Clear liquid	Lymphoedema (Stage 1)	No lymphoedema
Patient 4	Left groin	Diffuse lymphangiomatosis	Clear liquid	Lymphoedema (Stage 2)	Latent lymphoedema (Stage 0)

Table 2. Magnetic resonance lymphangiography findings in four patients with lymphocutaneous fistulas

	Detection of lymphocutaneous fistulas (high signal intensity)	Diffuse lymphangiomatosis (high signal intensity)	Ipsilateral lymphoedema lower extremity (high signal intensity)	Ipsilateral lymphatic collectors lower extremity (high signal intensity)	Contralateral lymphatic collectors lower extremity (high signal intensity)
Patient 1	Right groin (T_1 and T_2 sequence)	T_1 and T_2 sequence	T_2 sequence	Enlarged up to 5 mm (T_1 sequence)	Enlarged up to 4 mm (T_1 sequence)
Patient 2	Right forefoot (T_1 sequence)	N/A	T_2 sequence	Aplasia (T_1 sequence)	Not enlarged (T_1 sequence)
Patient 3	Right groin (T_1 and T_2 sequence)	N/A	T_2 sequence	Not enlarged (T_1 sequence)	Not enlarged (T_1 sequence)
Patient 4	Left groin (T_2 sequence)	T_1 and T_2 sequence	T_2 sequence	Enlarged up to 6 mm (T_1 sequence)	Enlarged up to 5 mm (T_1 sequence)

N/A, not applicable; T_1 sequence (after intracutaneous contrast material injection at the region of the forefoot).

superior to lymphoscintigraphy when taking into account the detailed description, with high resolution of small lymphatic pathologies that are only a few millimetres in size and consecutive affection of the adjacent structures. Furthermore, MRL is able to delineate dermal back-flow areas precisely, indicating a lymphatic outflow

obstruction [11–13]. Additionally, similar to a lymphoscintigraphy study, it is possible to obtain functional information for a MRL study, since the image acquisitions of the T_1 weighted 3D spoiled gradient echo sequence are obtained sequentially 15, 25, 35, 45 and 55 min after intracutaneous contrast material injection [11–13]. As seen

(a)

(b)

(c)

Figure 1. 17-year-old man with lymphocutaneous fistulas in the right inguinal region. (a) Coronal three-dimensional (3D) T_1 weighted gradient echo source image, obtained 25 min after gadoteridol injection, reveals extensive lymphangiomatous changes in the region of the right groin (large arrows) with afferent lymphatic vessels (arrowhead). Note the partially enhanced, inconspicuous inguinal lymph nodes on the left side (small arrow). (b) Axially reconstructed 3D T_1 weighted gradient echo source image, obtained 25 min after gadoteridol injection, demonstrates the lymphocutaneous fistulas in the region of the right groin (small arrows), extending from the adjacent lymphangiomatous changes (large arrows). Note the partially displayed femoral head and right inferior pubic ramus showing a low signal intensity. (c) Axial reconstructed heavily T_2 weighted 3D turbo spin echo source image at the pelvic region depicts multiple lymphangiomatous changes on the right parailiacal side (large arrows) extending from the inguinal region. Furthermore, free perisigmoidal fluid is detected (small arrow).

Figure 2. 48-year-old woman with lymphocutaneous fistulas at the level of the right forefoot. Coronal three-dimensional T_1 weighted gradient echo maximum intensity projection image, obtained 35 min after gadoteridol injection, reveals several lymphatic collectors with a typical beaded appearance at the level of the inconspicuous left lower leg (small arrows). The right lower leg demonstrates an enlarged diameter with lymphoedematous changes (arrowhead). Furthermore, no lymphatic collectors are visualised at the level of the right lower leg with consecutive lymphatic outflow obstruction and a severe network of lymphatic collateral vessels at the level of the forefoot (large arrow).

in the presented patients, in contrast to lymphoscintigraphic examinations, it is possible to exactly evaluate and delineate the distribution of an existing lymphoedema using the 3D-TSE sequence [11–13]. Finally, owing to the minimal invasiveness and lack of radiation, a diagnostic

MRL follow-up can be performed routinely without risk for the patient.

Regarding the method of blue dye staining, a study including four patients with lymphocutaneous fistulas following vascular procedures has been presented by Schwartz et al [9]. These patients received a dye-assisted ligation, which showed a clear and precise identification of the transected lymphatic vessels. The authors concluded that the use of isosulfan blue, in conjunction with operative exploration, allows rapid and accurate ligation of the damaged lymphatic vessels with no additional side effects. The results were underlined by the study of Weaver and Yellin [10], who reported the successful use of isosulfan blue in six patients with inguinal lymphatic leaks after arterial revascularisation procedures, and in two further patients after renal transplantation and a thoracoabdominal aneurysm repair. However, in contrast to these two studies, Tyndall et al [1] reported that intra-operative blue dye staining did not help to identify the leak sites in 10 patients, who had undergone a surgical repair of lymphocutaneous fistulas.

Therefore, in order to decide whether an operative approach is rational for the individual patient presenting a lymphocutaneous fistula prior to surgery, we recommend performing an exact overview of the lymphatic pathologies with high resolution. This information can be obtained by means of MRL.

According to Foeldi et al [4], in the first stages of the disease, the lymphatic vessels respond to the lymphatic load in lymphoedema, with a dilatation and a fast lymphatic outflow. Therefore, in two of the presented patients with diffuse lymphangiomatosis, using the T_1 weighted 3D spoiled gradient echo sequence after intracutaneous contrast material application, MRL was able to detect enlarged lymphatic vessels in the contralateral, inconspicuous lower extremity with a diameter of up to 5 mm. Clinically, these extremities demonstrated no signs of lymphoedema. Hence, MRL was able to diagnose a “Stage 0 (latency) lymphoedema”, according to the “Foeldi and Foeldi classification” (Tables 1–3). By using these important diagnostic MRL results, an optimal treatment plan can be established prior to the occurrence of clinical symptoms.

Table 3. Lymphoedema staging according to the Foeldi and Foeldi classification

Stage	Pathological mechanism	Clinical character
0 Latency	Focal fibrosclerotic tissue alterations	None
1 Reversible	High protein oedema; focal fibrosclerotic tissue alterations	Pitting oedema; elevation reduces the swelling; possibly “pain of congestion”
2 Spontaneously irreversible	Extensive fibrosclerosis; proliferation of adipose tissue	Brawny, hard swelling that does not recede with elevation
3 Elephantiasis	Extensive fibrosclerosis; proliferation of adipose tissue	Like Stage 2; invalidism

Table 4. Treatment plan in four patients with lymphocutaneous fistulas

	Surgery	Compressive decongestive therapy	Middle-chain triglyceride diet	Skin hygiene with disinfection	Antibiotics for infection
Patient 1	No	Yes	Yes	Yes	No
Patient 2	Reduction operation of the forefoot	Yes	No	Yes	Yes
Patient 3	Ligation of lymphocutaneous fistula	Yes	No	Yes	No
Patient 4	No	Yes	No	Yes	Yes

In the later stages of lymphoedema, the lymphatic vessels increasingly decompensate with valvular insufficiency, lymph stasis and delayed lymphatic outflow [4]. At this later stage, MRL findings should be identical to a single fluid column with no visibility of a beaded appearance of the lymphatics. Corresponding to the increasing stages of lymphoedema, the lymphatic fluid retention increases, which is visible in the MRL examinations using the 3D-TSE sequence acquisitions [11–13].

In all presented patients, the evaluation of the lymphatic system at the level of the lower and upper leg contrast-enhanced T_1 weighted images were superior to the heavily T_2 weighted images. To demonstrate the complete extent of the lymphangiomatous changes in the region of the pelvis and retroperitoneum, the heavily T_2 weighted images showed better results, since the intracutaneously applied contrast media at the level of the forefoot did not reach all these areas sufficiently. Therefore, our findings have confirmed previous study results, which demonstrated an excellent delineation of lymphatic vessels by heavily T_2 weighted sequences if the lymphatic flow was very slow [14,15]. These premises usually exist in a diffuse reticular network of lymphangiomatous changes.

A variety of treatment options has been described in the medical literature for lymphocutaneous fistulas, including leg elevation, continuous local pressure, negative pressure dressing therapy, radiotherapy and surgical therapy, including microsurgical and debulking procedures [4,16–19]. On the basis of the MRL findings, two patients in the presented series were treated with surgical procedures. In two patients with diffuse lymphangiomatosis, a surgical intervention of the lymphocutaneous fistula was not indicated on account of MRL revealing an infiltration of the lymphangiomatous changes into the adjacent structures and distant organs. The risk of recurrence with even more severe lymphorrhoea was estimated to be too high. As reported in these two patients, in order to minimise the risk of infection in conservatively treated patients, meticulous skin hygiene with constant disinfection was performed on the sites of the lymphocutaneous fistulas and lymphocysts [4]. Furthermore, as seen in the presented patient series, the underlying lymphatic disease should also be treated, *e.g.* primary lymphoedema with CDT [4].

Conclusion

MRL has proved to be a safe and accurate imaging modality for a comprehensive evaluation of the lymphatic system in the examined four patients suffering from lymphocutaneous fistulas. Since the localisation and extension of the lymphocutaneous fistulas with adjacent lymphatic pathologies are important prognostic factors, it is crucial to perform a minimally invasive radiological evaluation with high resolution, to acquire optimal patient therapeutic planning. To estimate the precise value of MRL for this patient group, further studies with a larger patient series are necessary.

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