"Eosinophilic fasciitis: typical abnormalities, variants and differential diagnosis of fasciae abnormalities using MR imaging."

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Abstract
Eosinophilic fasciitis is a rare condition. It is generally limited to the distal parts of the arms and legs. MRI is the ideal imaging modality for diagnosing and monitoring this condition. MRI findings typically evidence only fascial involvement but on a less regular basis signal abnormalities may be observed in neighboring muscle tissue and hypodermic fat. Differential diagnosis of eosinophilic fasciitis by MRI requires the exclusion of several other superficial and deep soft tissue disorders.

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Eosinophilic fasciitis is a rare condition that was first described by Shulman in 1974 [1]. Magnetic resonance imaging (MRI) is the ideal imaging modality both for diagnosing and monitoring this condition. MRI findings typically evidence only fascial involvement but on a less regular basis signal abnormalities may be observed in neighboring muscle tissue and hypodermic fat. Such abnormalities further complicate the differential diagnosis of eosinophilic fasciitis over other candidate superficial and deep soft tissue conditions such...
as scleroderma, necrotizing fasciitis or myositis. Following an overview of fasciae anatomy, we will describe the clinical and biological specifics of eosinophilic fasciitis before detailing its typical MRI features, variants and differential diagnosis.

**Fasciae anatomy and physiology**

In the limbs, fasciae consist of a continuous sheet or band of fibrous tissue that entirely covers a group of muscles to form a muscle compartment [2]. Superficial fasciae are underlying to the dermis. Fat may accumulate in this region and form a hypodermic layer of adipose tissue of varying thickness that contains nerves and vessels. Deep fascia, a more compact layer than superficial fascia formed by a dense array of collagen fibers, often cannot be distinguished from the muscle aponeurosis. Intermuscular septa extend from the deep fascia and separate various muscle groups into compartments. Although commonly used, the terms “superficial fascia” and “deep fascia” are considered as incorrect by the FICAT (Federative International Committee on Anatomical Terminology) due to the lack of international consensus on the histological terms used to refer to the different layers of connective tissue [3]. In addition, these terms do not always refer to the same structure when used by an anatomical pathologist, a surgeon or a radiologist.

To maintain consistency and avoid any confusion, it is recommended to use the international terminology that distinguishes cutaneous (superficial) fascia for the hypodermic vascular connective tissue, deep peripheral fascia for the fascia surrounding whole muscle groups and deep intermuscular fascia for intermuscular septa and aponeuroses [2—4].

**Eosinophilic fasciitis (Shulman’s syndrome)**

Eosinophilic fasciitis, also known as Shulman’s syndrome, is characterized by sclerotic skin lesions associated with an increased sedimentation rate, hypergammaglobulinemia and eosinophilia [1,5]. Since the first description, no international consensus has been reached regarding official diagnostic criteria for this condition [6].

Eosinophilic fasciitis is a rare disease, the exact incidence of which is still unknown. Since Shulman’s first description, over 300 cases have been reported in the literature [6]. The average age of onset is approximately 40–50 years [7,8]. Depending on the studies, gender prevalence differences tend to vary, suggesting that the disorder is not sex-related [7—9]. Strenuous physical effort or trauma preceding the onset of symptoms is often among the main causal factors reported [7,8,10]. Some cases have been reported to occur after taking medication (statins, phenytoin, ramipril, subcutaneous heparin) or bacterial infection (borreliosis, mycoplasma) [6]. In one case the condition was found to be associated with lupus [11].

At least 10% of patients with eosinophilic fasciitis show some kind of blood disorder: thrombocytopenia, myelomonocytic leukemia, chronic lymphocytic leukemia and other myeloproliferative disorders [5]. However, it is still not clear whether these blood disorders cause the fasciitis (paraneoplastic syndrome) or if, on the contrary, fasciitis triggers the blood disorder.

The pathophysiology of eosinophilic fasciitis is still unknown. Some authors have suggested that eosinophilia and tissue lesions could be caused by circulating T-cell clones and increased interleukin-5 production [12]. This hypothesis is supported by the fact that the contents of the vacuoles of polymorphonuclear leukocytes and related neurotoxins are involved in fascia fibrosis [6]. Other authors have suggested that mast cells and cytokines cause eosinophilia which is observed in eosinophilic fasciitis patients [13].

Clinical manifestations serve as a guide for diagnosis. Up to 90% of patients present with cutaneous manifestations, which include edema, skin induration or so-called orange peel or cobblestone skin with hyperpigmentation [7]. The condition usually comprises two phases: the early phase, characterized by non-specific symptoms such as edema of the limbs that becomes tender and sometimes painful, gradually gives way to the established stage during the course of which edema disappears and is replaced by painless skin induration. Venous furrowing along the veins within the infiltrated area, also called the “groove sign”, is observed in nearly half of the patients and is highly evocative of fasciitis or deep fibrosis [6]. The condition predominately affects the distal parts of the limbs and more rarely the front of the neck and trunk. It is generally symmetric and patients are more likely to have symptoms on the arms (88%) than on the legs (70%) [10,14]. The head is generally not affected, and the hands and feet are rarely involved [15,16]. Typically Raynaud’s phenomenon is not present and normal findings are observed with capillaroscopy [6]. Skin manifestations are often associated with myalgia (67—86% of patients) and joint contractures or inflammatory arthralgia (up to 40% of patients) [10,14].

Eosinophilia is observed in 63 to 93% of patients and, although important in nature, tends to decrease or even disappear as the condition becomes established. Therefore, although highly evocative, eosinophilia is not indispensable for diagnosis [10,14,17]. No relationship has been found between the degree of eosinophilia and the severity of the disease [7,8,17].

An inflammatory syndrome is common with increased C-reactive protein levels (55%), a greater erythrocyte sedimentation rate (up to 63%) and generally polyclonal hypergammaglobulinemia (more than 50% of patients) [6].

Autoimmune screening for ANCA and anti-DNA/ENA antibodies is negative, although anti-nuclear antibodies may be detected in 15—20% of cases [6].

In practice, diagnosis is made based on deep skin biopsy (skin and muscle) of skin abnormalities, which evidences a thickening of the fascia due to lymphocyte and plasma cell infiltration with a varying percentage of eosinophil granulocytes. Eosinophils can actually be absent in fascia biopsies although eosinophilia is observed in blood samples. For this reason, it seems preferable to designate the condition as “fasciitis with eosinophilia” rather than “eosinophilic fasciitis” [18].

In the same way as for diagnostic criteria, there is no general consensus with regard to therapy and assessment of the patients’ response to treatment. In practice, high doses of corticosteroids are given as first-line line treatment (0.5—1 mg per kg and per day). The dose is gradually
Eosinophilic fascitis is a chronic inflammatory condition characterized by swelling and tenderness of the fascia, a layer of connective tissue that surrounds muscles. Although the prognosis is generally favorable, treatment can be challenging, and various diagnostic and therapeutic approaches are employed. This section focuses on the use of MRI in the evaluation and management of eosinophilic fascitis.

**MRI findings in eosinophilic fascitis**

**Typical form**

Although not strictly required for diagnosis, MRI is carried out on a regular basis as part of the initial assessment of eosinophilic fascitis. It is the ideal imaging modality both for diagnosing and monitoring the course of this condition.

In accordance with published data, the minimal acquisition protocol consists in T1-weighted SE images and short tau inversion recovery (STIR) images in the axial plane. Injection of a gadolinium-based contrast agent is not performed systematically. However, when performed, it is followed by a fat-saturated T1-weighted SE sequence in the axial plane. The condition is generally bilateral so both limbs should be studied on a comparative basis.

Prior to the injection of contrast agent, MR images typically show a thickening of deep fasciae (peripheral deep fasciae and more rarely intermuscular fasciae) on T1-weighted sequences that appears with a relatively higher signal intensity than that of muscle tissue on fat-suppressed or fat-saturated T2-weighted sequences. Following injection of a gadolinium-based contrast agent, thickened fasciae appear with markedly enhanced signal intensity (Fig. 1). Abnormalities are typically limited to the fasciae, sparing muscles and hypodermic fat. MRI also helps to identify the most affected regions where biopsies should be collected. MRI is also useful to follow the course of the disease in treated patients. Although the evolution of laboratory abnormalities following treatment was variable, Baumann et al. found that MRI findings were closely correlated with the disease’s clinical evolution with complete disappearance of imaging abnormalities in fully remitted patients and incomplete regression in patients who responded only partially to treatment (Fig. 2). Nevertheless, no strict criteria have been defined to assess the response to treatment using MRI, the response to treatment being simply referred to as partial or complete depending on whether fascia abnormalities persist following treatment.

**Variants**

On a less regular basis, abnormalities of both the fasciae and neighboring tissues are observed on MRI. In some cases, the hyperintense signal intensity on T2-weighted images and enhancement have been reported to extend to the muscle fibers and subcutaneous fat adjacent to the affected fasciae (Fig. 3). In a group of eight patients studied...
by Baumann et al., such abnormalities were visible in the muscles adjacent to the fasciae in 3 cases (37.5%) and in subcutaneous tissue in 2 cases (25%) [16]. In the series by Moulton et al., the abnormalities extended to muscle fibers adjacent to the fasciae in the 12 cases assessed during the acute phase (less than 6 months) and in 2 out of 3 cases assessed following implementation of corticosteroid therapy during the subacute phase (between 6 and 12 months after the onset of symptoms) [23]. Nonetheless, such signal abnormalities in muscle or hypodermic tissue remain of lesser importance and fascia abnormalities are still the main MRI finding. In addition, these secondary abnormalities are always limited to neighboring tissues and therefore probably reflect the extension of inflammation to the muscles directly next to the fascia, as can be observed at histological analysis [16,24]. As for the hypodermic signal abnormalities observed in the report by Baumann et al., they could be explained by panniculitis-like sclerotic and fibrous changes [16]. The exact frequency of these atypical presentations of eosinophilic fasciitis has yet to be determined and no relationship has been reported up to date between the severity of the condition and extended MRI abnormalities.

**MRI and differential diagnosis**

The main differential diagnoses for eosinophilic fasciitis using MRI include superficial and deep tissue (dermis, hypodermis, muscle) conditions such as the following.

**Cutaneous scleroderma or morphea**

The MRI findings of cutaneous scleroderma or morphea are generally limited to the skin and subcutaneous fat but can however frequently extend to the deep fasciae and muscles, and rarely to bone marrow and joints (Figs. 4, 5) [25]. During the inflammatory phase of these conditions, lesions consist of a thickening of the dermis and a variable degree of subcutaneous tissue infiltration that appears as a hypointense signal on T1-weighted sequences and a hyperintense signal on T2-weighted STIR sequences or T1-weighted sequences following administration of a gadolinium chelate. Fascia thickening is however limited compared to that observed in the typical form of eosinophilic fasciitis [25]. Calcifications (calcinosi) may be observed in soft tissue, but are not disease-specific [26].

Other connective tissue diseases may show abnormalities of deep soft tissues. For example, systemic lupus erythematosus and Sjögren’s syndrome are sometimes associated with myositis-like abnormal MRI muscle signal intensities [27]. The distribution of such abnormalities can be variable, focal or diffuse [27,28] and may be associated with bone abnormalities [29].

**Stasis edema**

Stasis edema is characterized by an infiltration of hypodermic tissue that appears as a hyperintense signal on T2-weighted images, of generally diffuse and symmetric distribution, that is not enhanced after injection

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**Figure 2.** Typical MRI features of eosinophilic fasciitis in a 52-year-old man before and after treatment. a. Axial STIR-weighted sequence showing bilateral symmetric thickening and high signal intensity in peripheral deep fasciae (arrows) and intermuscular fasciae (arrowheads), mainly in the posterior muscle compartments of the thigh. b. Identical sequence performed 12 months later following long-term corticosteroid therapy showing clear regression of the lesions. The latter are barely visible with only very mild focal high signal intensity in the deep intermuscular fasciae (arrowheads).

**Figure 3.** MRI variant of eosinophilic fasciitis in a 36-year-old man. STIR-weighted axial sequence of the upper (a) and medium (b) thirds of the legs showing asymmetric predominantly left-sided involvement with moderate thickening (high signal intensity) of the deep intermuscular fasciae (arrows) associated with infiltration (high signal intensity on STIR-weighted sequence) of the anterior portion of the left medial gastrocnemius muscle (asterisk) and hypodermic tissue (arrowheads).
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Figure 4. Fasciitis of the right forearm of a 39-year-old woman with systemic sclerosis. Axial STIR and T1SE-weighted sequences. Diffuse fascial thickening (high signal intensity on STIR-weighted sequence) (arrowheads) with adjacent muscle infiltration (arrows).

Figure 5. Myositis of the lower limb in a 54-year-old woman with systemic sclerosis. Axial STIR-weighted sequences clearly reveal edematous infiltrated hypodermic fat next to the gluteus maximus (a: arrows) associated with edema-like signal abnormalities of the muscles of the anterior compartments of the left, and to a lesser extent right, thighs (b: asterisks).

Figure 6. Stasis edema from the ankle of a 79-year-old woman with heart failure. Axial T1 (a) and STIR-weighted (b) sequences of the distal third of the right leg. Diffuse fluid infiltration of dermal (arrowheads) and hypodermal (arrows) tissue is visible (low signal intensity on T1-weighted and high signal intensity on STIR-weighted sequences). No muscle involvement (asterisks) was observed.

Erysipelas

Erysipelas is a common dermo-hypodermitis caused by bacterial infection that is clinically diagnosed. MRI is not indicated for its typical form, but if performed, reveals subcutaneous infiltration of high intensity on T2-weighted images extending to the fasciae, of typically asymmetric and more or less localized distribution, that is enhanced following injection of gadolinium-based contrast agent ("cold edema") [4] (Fig. 6).

Necrotizing fasciitis

Necrotizing fasciitis is a rare but potentially lethal infection. MRI assessment is used to evaluate the depth of the lesions, localize abscesses in soft tissues and guide surgical management. Although in theory easy, it is often more difficult in practice to differentiate between superficial lesions that can be managed medically and deep lesions that require surgical management [4]. Necrotizing fasciitis is characterized by deep intermuscular fasciae involvement, a sensitive but fairly non-specific sign that can be associated...
with abscesses that are generally better visualized following injection of gadolinium-based contrast agent (Fig. 8) [4]. Diffuse muscular edema is often observed [28]. An additional but inconsistent feature is the presence of gas (a hypointense signal whatever the sequence) that is strongly evocative of necrosis.

**Myositis or inflammatory myopathies**

Myositis or inflammatory myopathies are general terms used to qualify several conditions, the main subcategories being dermatomyositis, polymyositis and inclusion body myositis [30]. The MRI findings for these myopathies are hyperintense muscle signal on fat-suppressed T2-weighted sequences with contrast enhancement. Bilateral and symmetric involvement is generally observed in dermatomyositis and polymyositis, less frequently in inclusion body myositis and the condition is generally localized within a muscle in patients with focal myositis [27]. T1-weighted sequences are used to evaluate the chronic manifestation of the disease, i.e. amyotrophy and fatty involution of affected muscle groups. Dermatomyositis is characterized clinically by the presence of skin lesions which were, in the 14 cases described by Yoshida et al., systematically associated with fascia involvement (Fig. 9) [31]. In the population of 25 patients with progressive polymyositis studied by Dion et al., muscle signal abnormalities predominated along the fasciae.
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Disclosure of interest
The authors declare that they have no conflicts of interest concerning this article.

References


Figure 10. Polymyositis in a 33-year-old woman with muscle pain in all four limbs. MRI of the thighs: a. Axial T1-weighted sequence showing discrete symmetric fatty involution of the anterior-medial and posterior compartments (arrowheads). b. Axial T2 STIR-weighted sequence showing symmetric muscle infiltration (high signal intensity) especially in the rectus femoris (arrows) and adductor longus (stars) muscles. Symmetric infiltration (high signal intensity) of the deep peripheral fasciae was also observed (arrowheads).

(usually global involvement) or the posterior compartments of the thigh (Fig. 10) [32].

The signal abnormalities of deep fasciae observed on T2-weighted MR images are therefore not specific and can be observed in various conditions such as from ruptured popliteal cyst or necrotizing fasciitis [33]. It is therefore essential that imaging results be combined with clinical, laboratory and if necessary anatomical pathology data before making diagnosis.

Conclusion

Eosinophilic fasciitis is a rare disease. Diagnosis is guided by its clinical manifestations and then further confirmed by anatomical pathology examination of deep skin biopsies. MRI is the ideal imaging modality both for selecting the best site for biopsy and monitoring the course of the disease following initiation of treatment. MRI findings for the typical form generally evidence only fasciae involvement, but less frequently MRI signal abnormalities may be observed in the muscle and hypodermic tissue adjacent to the fascia. Differential diagnosis of eosinophilic fasciitis by MRI requires the exclusion of other superficial and deep subcutaneous tissue conditions that produce abnormal signal intensities for the fascia. It is therefore crucial that imaging be combined with all other data (clinical, laboratory and anatomical pathology) if eosinophilic fasciitis is suspected.


