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Eosinophilic Fasciitis Unmasking a Lung Cancer

Emilie Vandamme, MD, Philippe Hainaut, MD, PhD

Department of Internal Medicine and Infectious Diseases, Cliniques Universitaires Saint Luc, Catholic University of Louvain, Brussels, Belgium.

PRESENTATION

A 60-year-old man without any relevant medical history was admitted for limb edema and progressive skin induration. Bilateral peripheral edema developed 6 months earlier. It had progressed gradually to cardboard-like textural changes of the skin on both lower limbs and later, on the forearms. The patient denied any systemic complaints. Noteworthy, there was no Raynaud's phenomenon, sclerodactyly, arthralgia, myalgia, muscle weakness, nor breathlessness.

On physical examination, the skin was diffusely thickened and indurated on both legs and forearms and lateral chest wall, with a brownish appearance. Peau d'orange appearance and groove sign were noticed, resulting from the surrounding fascial and subcutaneous sclerosis (Figure 1). The extension of upper limbs was impaired. The face, hands, and feet were spared. The general examination was normal.

ASSESSMENT

Laboratory analysis carried out 6 months prior to admission disclosed peripheral blood eosinophilia up to 1210/μL and a mildly increased C-reactive protein at 23.3 mg/L. On admission, peripheral eosinophilia had normalized at 100 elements/μL. Extractable nuclear antigen, antinuclear antibodies, and antineutrophil cytoplasmic autoantibodies were negative.

A thick skin biopsy down to the muscular fascia was sampled on the left forearm. Histologic examination disclosed an inflammatory infiltrate involving lymphohistiocytic plasma cells and eosinophils in the dermis, hypodermis, and muscular fascia. There was no vasculitis, nor involvement of skeletal striated muscle (Figure 2).

To assess the extension of fascial inflammation in a sensitive and noninvasive way, we ordered a positron emission tomography-computed tomography (PET-CT) scan. Additionally, by disclosing visceral involvement, it enabled the highlighting of an underlying neoplastic or inflammatory disorder like systemic sclerosis, polymyositis, or other connective tissue disorder. Indeed, the PET-CT scan led to the incidental finding of a 2.5-cm-sized right apical lung nodular lesion (Figure 3). A percutaneous transthoracic biopsy identified a localized lung adenocarcinoma, staged T2aN0M0.

DIAGNOSIS

The clinical morphology combined with the earlier observation of peripheral eosinophilia led to suspicion of eosinophilic fasciitis; the diagnosis was fully confirmed by pathological findings. It was likely linked to a lung adenocarcinoma.

MANAGEMENT

The patient underwent a curative right superior lobectomy for the lung adenocarcinoma. Glucocorticoid treatment was preferably omitted prior to and during the first weeks after thoracic surgery. Two months after surgery, due to slow and far-from-complete improvement of skin manifestations (Figure 4), oral methylprednisolone (0.5 mg/kg) and low-dose methotrexate (10 mg weekly) were administered.

DISCUSSION

Eosinophilic fasciitis is characterized by symmetrical cutaneous thickening and induration, predominantly on the limbs and trunk; hands, feet, and face are typically spared. Skin involvement usually starts with edema; swelling is progressively replaced by skin induration and sclerosis, leading to peau d'orange appearance. On palpation, skin looks indurated, with loss of elasticity and inability to pinch it. Erythema, hives, bubbles, hyper- or hypopigmentation,

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Requests for reprints should be addressed to Philippe Hainaut, MD, PhD, Department of Internal Medicine and Infectious Diseases, Cliniques Universitaires Saint Luc, Catholic University of Louvain, 10 Avenue Hippocrate, 1200 Brussels, Belgium.

E-mail address: philippe.hainaut@uclouvain.be

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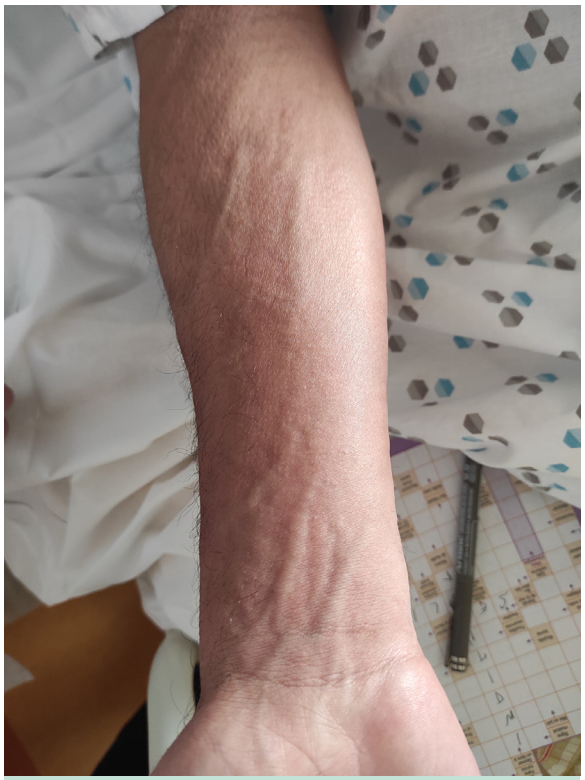

Figure 1 Skin appearance at the diagnosis.

and alopecia can be observed.[1-3] Myalgias and arthralgias have been described, although visceral involvement is typically absent, helping to differentiate eosinophilic fasciitis from systemic sclerosis or localized scleroderma.[1,2]

Peripheral eosinophilia is frequent in early stages, although transient. Acute phase response and hypergammaglobulinemia can be observed. Creatine kinase level is usually normal, even in the setting of myalgias.[2]

Pathologically, inflammation, edema, and thickening and sclerosis of the fascia are the hallmarks of eosinophilic fasciitis. The cellular infiltrate consists of lymphocytes, plasma cells, histiocytes, and eosinophils. The distribution of eosinophils in the fascia can be focal and often correlates with the level of peripheral eosinophilia.[1,2]

An imbalance between the production and degradation of the extracellular matrix has been suggested. A significant increase of tissue inhibitor of metalloproteinase-1 level has been observed in the fascia and serum, leading to a decreased activity of metalloproteinase-13 and, ultimately, to fibrosis by impaired degradation of extracellular matrix proteins.[4,5] An autoimmune origin has been suggested as owing to hypergammaglobulinemia and increased circulating immune complexes. Immune complexes are known to have eosinophilic chemotactic activity, directly or through activation of the complement system.[6] Finally, the ability of eosinophils to stimulate fibroblasts proliferation has recently been demonstrated in vitro.[7]

Although primary cases of eosinophilic fasciitis are more prevalent, secondary forms have been associated with infectious disease (*Borrelia burgdorferi*), medications (statin, ramipril, phenytoin), and autoimmune disorder (eg, Sjögren, Biermer, Basedow, Hashimoto).[1,8] It has also been linked with various hematological (up to 10% of cases in the largest case series from Mayo Clinic[9]) and infrequently, solid[2] malignancies. Indeed, few cases of solid tumors have been so far described: breast cancer,[3] prostate and colic adenocarcinomas,[10] and melanoma.[11] On the average, skin changes precede the diagnosis of cancer by a median of 1 year (range 0 to 3 years).[12]

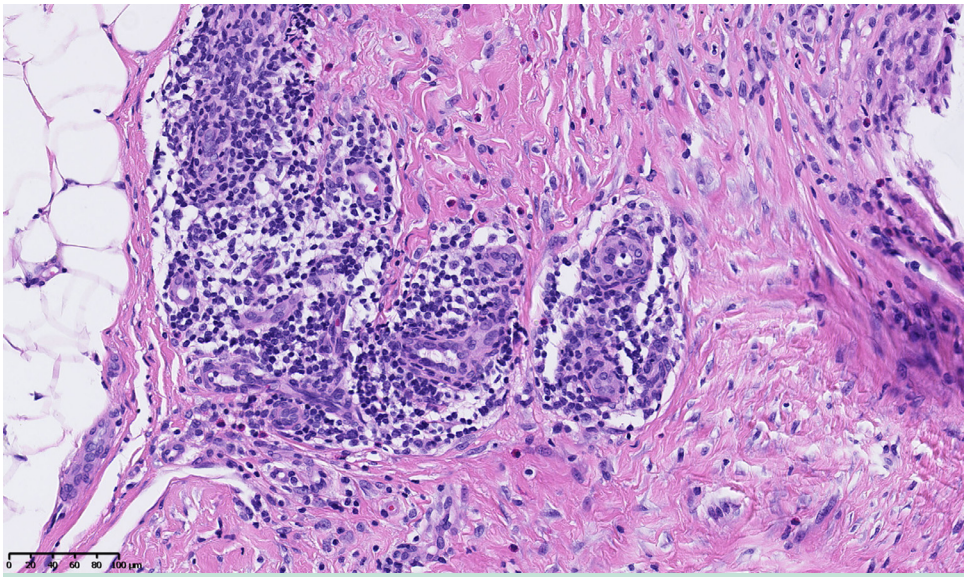

Figure 2 Deep skin biopsy disclosed an inflammatory infiltrate involving lymphohistiocytic plasma cells and eosinophils in the dermis, hypodermis, and muscular fascia.

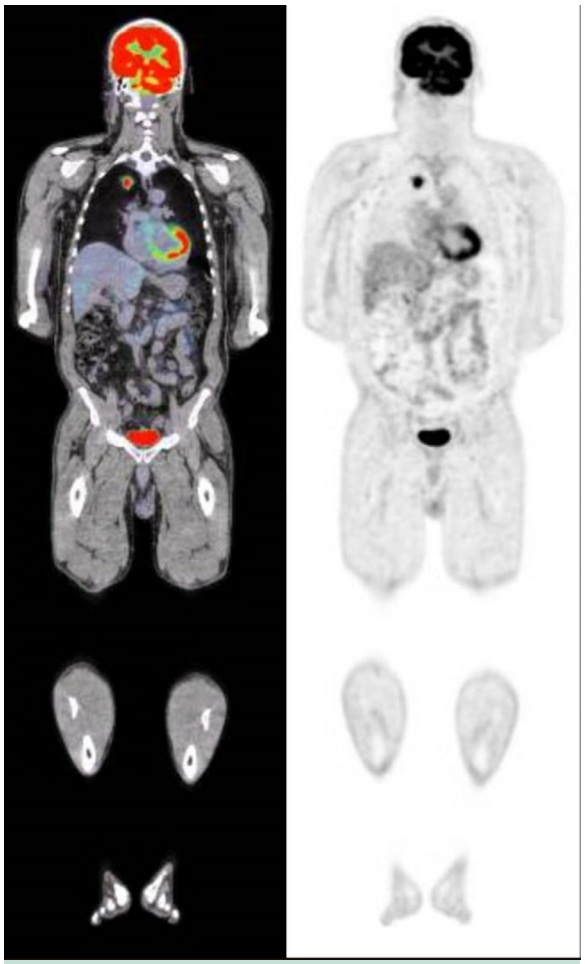

Figure 3 Positron emission tomography–computed tomography disclosed a 2.5-cm-sized right apical lung nodular lesion.

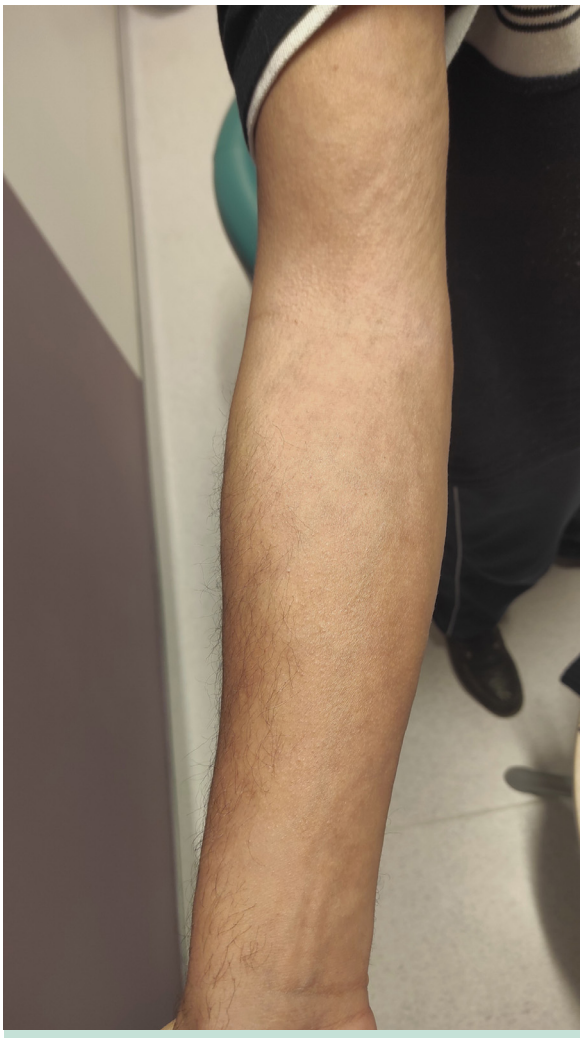

Figure 4 Skin appearance 2 months after surgery.

Corticosteroids remain the cornerstone treatment. After failure of corticosteroids, other immunosuppressive treatment may be tried.[2,12] Treatment of paraneoplastic eosinophilic fasciitis remains challenging because corticosteroids and other immunosuppressive agents commonly fail; this may be a clue for a neoplastic origin. Treatment of the underlying cancer may improve skin manifestations.[12] Immunosuppressive treatment can be attempted prior to final resection of the solid tumor. However, we decided to postpone the corticosteroids after surgery to secure the healing of the bronchial wall after lobectomy.

CONCLUSION

We describe a patient suffering from eosinophilic fasciitis unmasking a pulmonary adenocarcinoma. The association is supported by partial improvement of cutaneous damage after surgical removal of pulmonary tumor. The finding of eosinophilic fasciitis in a middle-aged patient with no comorbidity probably warrants the search for an underlying malignant disease.

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