

## **Eosinophilic Fasciitis Following COVID-19 Vaccination**

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## Abstract

A 60-year-old female developed symptoms of eosinophilic fasciitis 10 days after receiving the second dose of the COVID-19 vaccine, characterized by sclerotic and hyperpigmented lesions, hypereosinophilia, and positive antinuclear antibodies. The diagnosis was confirmed through deep skin biopsy and MRI, and treatment with prednisone and methotrexate showed great improvement. This case highlights the potential for eosinophilic fasciitis to be triggered by the COVID-19 vaccine, although the exact mechanisms and relationship remain unclear.

Keywords: Eosinophilic Fasciitis, COVID-19 Vaccine, Eosinophilic Reaction

Eosinophilic fasciitis or Shulman syndrome, is a rare entity first described by Shulman in 1974. It is characterized by an inflammatory and fibrotic disorder of the fascia, associated with hypereosinophilia, elevated sedimentation rate and hypergammaglobulinemia. The diagnosis is suggested by the clinical presentation, supported by MRI, and confirmed by histology. Its pathophysiology remains unknown 50 years after its initial description. However, several eosinophilic reactions following COVID-19 vaccination, whether cutaneous, pulmonary, or myocardial, have been reported.

A 60-year-old female patient with a history of hypertension under treatment, presented 10 days after receiving her second dose of the AstraZeneca COVID-19 vaccine, an intense pruritus accompanied by hyperpigmented indurated lesions on her coxal and pubic regions, which progressively spread across her body.

Clinical examination revealed extensive, symmetrical lesions that were sclerotic, confluent, and infiltrated, with areas of hyperpigmentation. The lesions spared the face, extremities, breasts, and buttocks. Additionally, there was bilateral indurated edema in both thighs, with no detectable signs of mucosal or visceral involvement (Figure 1).

Biological assessment showed minimal inflammatory syndrome with significant hypereosinophilia at  $2950/\mu$ L and positive antinuclear antibodies at 640.



Figure 1: Sclerotic and Symmetrical Lesions, Hyperpigmented in Some Areas, Associated with Bilateral Edema in the Thighs

Deep skin biopsy demonstrated significant fibrosis extending to the hypodermis with a sclerodermic appearance, associated with a perivascular inflammatory infiltrate rich in lymphocytes and eosinophilic granulocytes. MRI findings were suggestive of thickening with edematous infiltration of the soft tissues and superficial and deep muscular fasciae. The patient was treated with prednisone at a dosage of 1 mg/kg/day in combination with methotrexate at 15 mg/week. A total treatment period of 2 years led to good improvement.

Eosinophilic fasciitis is a rare connective tissue disease with over 300 reported cases in the literature. The average age of onset is between 40 and 50 years, with no gender predisposition [1]. It initially manifests as painful, indurated edema that gives a "orange peel" appearance, typically bilateral and more or less symmetrical, sometimes associated with hyperpigmentation. This evolves towards induration and sclerofibrosis of the muscle fascia and subcutaneous tissue [2]. Hypereosinophilia is the most consistent and characteristic sign, observed in over 80% of cases from the acute phase [3]. Moderate elevation of sedimentation rate and a polyclonal hypergammaglobulinemia involving either IgG or IgM are present in about one-third of cases. Rheumatoid factors and antinuclear antibodies are generally negative [4].

The onset is often abrupt and can be triggered by various factors. In approximately half of the cases, eosinophilic fasciitis occurs after unusual intense physical exertion, trauma, surgery, or medication use (statins, phenytoin, ramipril, subcutaneous heparin) or following a bacterial infection (such as borreliosis or mycoplasma), as well as some reported post-vaccination cases [4].

The pathophysiology of eosinophilic fasciitis remains unclear, although an autoimmune mechanism is presumed. This assumption arises from the frequent presence of hypergammaglobulinemia, the response to corticosteroids and immunosuppressants, the detection of rheumatoid factor, antinuclear antibodies, and immune complexes in certain cases, as well as the deposition of IgG and C3 in the fascia in some patients [5].

Although no direct link between the COVID-19 vaccine and eosinophilic fasciitis has been established, it is hypothesized that vaccination may induce an eosinophilic immune response. In this response, eosinophils infiltrate the fascia, and their degranulation leads to the release and accumulation of cationic eosinophil granules, which are involved in the development of fascial fibrosis [6]. Several publications in the literature report eosinophilic reactions in the skin, lungs, or myocardium triggered by the COVID-19 vaccine [7-8-9-10-11-12-13-14-15-16]. This supports our hypothesis; however, no definitive relationship has

been established to date.

Eosinophilic fasciitis continues to present diagnostic challenges due to its various triggering factors and unclear pathophysiology. In our case, eosinophilic fasciitis is likely triggered by COVID-19 vaccination, but this requires further investigation. The presence of eosinophilic reactions following vaccination, as reported in the literature, supports this hypothesis. However, additional research is needed.

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