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Eosinophilic fasciitis in a young male auto mechanic exposed to organic solvents

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SUMMARY

We report a case of eosinophilic fasciitis in a teenage auto mechanic who was most likely affected by occupational exposure to organic solvents, including the aromatic hydrocarbons benzene, trimethylbenzene, naphthalene, toluene, and xylene. The patient presented with an 8-month history of painful induration of his extremities and an abnormal gait. A deep excisional biopsy of the fascia was obtained, demonstrating subcutaneous fibrosis with perivascular and interstitial inflammation, with lymphocytes and plasma cells spilling into the sclerosed fascia, and focal fibrinoid necrosis. Treatment was begun with intravenous pulse doses of methylprednisolone, prednisone (20 mg daily), and subcutaneous methotrexate (25 mg weekly), and the patient's painful induration had resolved and gait had normalized at the 6-month follow-up. Our case suggests that exposure to organic solvents could be implicated in the pathogenesis of eosinophilic fasciitis and highlights the importance of a thorough occupational history to prevent repeat exposures to potentially causative agents.

Key words: *Aromatic hydrocarbons, eosinophilic fasciitis, occupational exposure, solvents, systemic sclerosis.*

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INTRODUCTION

Eosinophilic fasciitis (EF) is an autoimmune disease characterized by painful induration of the extremities and thickening of the subcutaneous fascia with inflammation. Initial symptoms include skin edema that may progress to a *peau d'orange*, dimpled, "pseudo-cellulite" appearance. EF is often accompanied by myalgias and reduced range of motion that, in severe or untreated cases, may lead to the development of joint contractures (1). Peak incidence is typically between ages 40 and 50, and EF may rarely occur during childhood (2). While onset is typically associated with strenuous exercise or trauma (in approximately 33-46% of cases), the exact etiology is uncertain (3). However, chemical compounds have been identified as potential triggers (2). We report a case of EF in a teenage auto mechanic, likely influenced by occupational exposure to organic solvents.

CASE REPORT

A 19-year-old Caucasian male with a noncontributory past medical history presented with 8 months of pain and stiffness in his hands, forearms, and legs. He did not have Raynaud's phenomenon. Past treatments with ibuprofen, intramuscular orphenadrine, cyclobenzaprine, intramuscular dexamethasone, intraarticular wrist corticosteroid injections, and intravenous ketorolac resulted in minimal improvement. He denied a family history of autoimmune disease or malignancy. Social history was significant for full-time employment as a brake specialist in an auto mechanic shop. The patient provided material safety data sheets outlining ingredients for 19 products to which he was routinely exposed at work. Most products contained organic solvents, including the aromatic hydrocarbons benzene, trimethylbenzene, naphthalene, toluene, and xylene.

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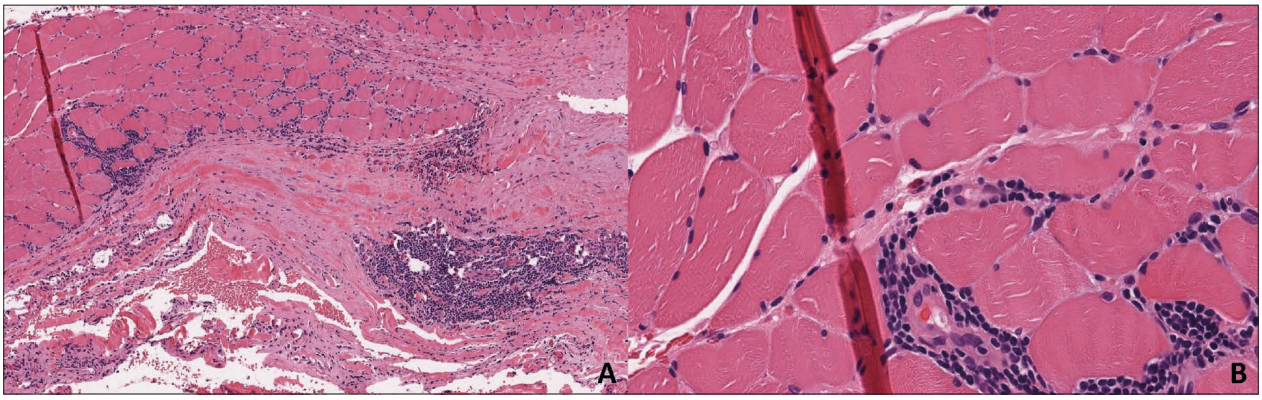

Figure 1 - Fascial biopsy of the left upper extremity. There is diffuse fascial sclerosis with areas of focal fibrinoid necrosis. Perivascular and interstitial inflammatory infiltrate consist of lymphocytes and plasma cells. The infiltrate spills into the fascia fibrous tissue. Eosinophils were not identified. A) Hematoxylin and eosin stain (H&E), magnification 100×; B) H&E, magnification 200×.

A dermatological exam revealed woody induration with an overlying *peau d'orange* texture of the skin and subcutaneous tissue of his bilateral extremities. Groove sign, referring to a linear depression in the skin parallel to the course of the superficial veins (4), was present bilaterally. There were no additional notable cutaneous, mucosal, or nail findings. A musculoskeletal exam revealed taut distal forearm musculature, including bilaterally limited wrist range of motion and an inability to clench his fists. Additionally, the patient demonstrated upper extremity carriage and decreased lower extremity range of motion, resulting in an abnormal gait.

Laboratory examinations were significant for absolute eosinophil count of 1.09×109/L (reference range 0-0.2×109/L). Complete blood count and erythrocyte sedimentation rate were normal. Rheumatoid factor, antinuclear antibody, and anti-cyclic citrullinated peptide antibodies were negative. Upper extremity magnetic resonance imaging (MRI) revealed bilateral diffuse fascial thickening and edema. A deep excisional biopsy including the left forearm fascia was obtained, demonstrating subcutaneous fibrosis with perivascular and interstitial inflammation, lymphocytes and plasma cells spilling into the sclerosed fascia, and focal fibrinoid necrosis (Figure 1). Eosinophils were not identified.

These clinical, radiological, and histological findings were consistent with EF (2). Jinnin et al. established new diagnostic criteria for EF in 2018, with the major criterion being symmetrical plate-like sclerotic lesions present on the four limbs and two minor criteria being:

1) fascial biopsy demonstrating fibrosis of subcutaneous connective tissue with infiltration of eosinophils and monocytes and
2) fascial thickening seen on imaging such as MRI (Figure 2) (5). As the current case fulfilled both major and minor criteria, the EF diagnosis was confirmed. Additionally, given that our patient demonstrated joint contracture and limited

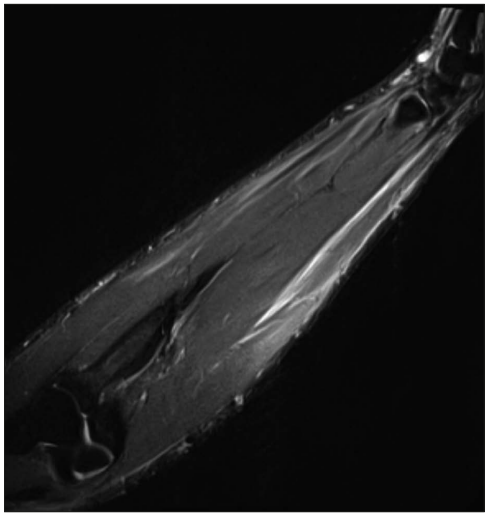

Figure 2 - Magnetic resonance imaging of the left upper extremity showing fascial thickening.

movement of both the upper and lower limbs, his disease was classified as severe (5).

Treatment began with intravenous pulse doses of methylprednisolone, prednisone (20 mg daily), and subcutaneous methotrexate (25 mg weekly). He was encouraged to avoid repeated organic solvent exposure. At the 4-week follow-up, he reported avoidance of organic solvent exposure, decreased pain, and increased extremity range of motion. At the 6-month follow-up, remaining on the abovementioned treatment regimen, his pain and induration had resolved, and his gait had normalized. Upon weaning his steroids below 10 mg daily, he showed clinical evidence of disease activity. He was lost to further follow-up in our tertiary care rheumatology practice due to transportation-related barriers to healthcare and other complicating socioeconomic factors.

DISCUSSION AND CONCLUSIONS

In this case, we present an individual who developed EF with severe clinical findings at a young age following chronic occupational exposure to several organic solvents. The most common potential triggers of EF, including strenuous exercise, trauma, infection (*e.g.*, *Borrelia*, *Mycoplasma*), and certain medications (*e.g.*, statins, phenytoin, ramipril), were not identified (2). Our case suggests that exposure to organic solvents could be implicated in EF pathogenesis and highlights the importance of a thorough occupational history taking to prevent repeat exposures to potentially causative agents.

Organic solvents are carbon-based compounds that dissolve other substances. They are commonly found in dry cleaning agents, paint thinners, and motor vehicle maintenance products. Exposure to organic solvents has been identified as a risk factor for the development of several autoimmune diseases, including systemic sclerosis, primary systemic vasculitis, and multiple sclerosis (6). In particular, several of our patient's organic solvent exposures - benzene (6), trimethylbenzene (7), naphthalene (7), toluene (6), and xylene (6, 7) - have been associated with systemic sclerosis, another connective tissue disease that presents with diffuse cutaneous fibrosis. While EF is rarely linked to chemical exposures, it has been reported to occur following exposure to the organic solvent trichloroethylene (8). Chronic organic solvent exposure could explain the severe clinical findings and young age at presentation.

EF pathogenesis following exposure to organic solvents may be in keeping with theories linking these compounds to the development of systemic sclerosis. Namely, the deposition of chemicals in the skin results in the modification of self-proteins, the development of immunogenic proteins, and the activation of an inflammatory response leading to tissue injury and fibrosis (6). Experimental models have demonstrated that the organic solvents trichloroethylene, benzene, and toluene can affect protein modification, reactive oxygen species generation, nitric oxide production, cellular necrosis, and release of cytokines (9). Additionally, occupational exposure to benzene has been associated with an elevated eosinophil count that grows with increasing years of exposure (10). Further studies are warranted to elucidate the role organic solvents may play in the pathogenesis of EF.

A deep excisional biopsy of the fascia is the gold standard for diagnosing EF, typically demonstrating thickening of the deep fascia with an inflammatory infiltrate composed of lymphocytes, monocytes, plasma cells, and/or macrophages, with or without eosinophils (2). The diagnosis is further supported when a patient fulfills the proposed major diagnostic criteria of EF, which include i) swelling, induration, and thickening of the skin and subcutaneous tissue and ii) fascial thickening with the accumulation of lymphocytes and macrophages, with or without eosinophilic infiltration (2). The primary exclusion criterion for diagnosing EF is a diagnosis of systemic sclerosis. Clinically, EF may be distinguished from systemic sclerosis by the absence of Raynaud's phenomenon, sclerodactyly, and nail-fold capillary changes. Additionally, fascial thickening is rarely observed in patients with systemic sclerosis (2).

The first-line treatment for EF is systemic corticosteroids or pulsed intravenous methylprednisolone. Second-line treatment is immunomodulatory drugs (hydroxychloroquine, colchicine), immunosuppressive drugs (methotrexate, tumor necrosis factor-α inhibitors, rituximab), or ultraviolet A1 phototherapy (11). Delayed EF diagnosis >6 months and lack of pulsed intravenous methylprednisolone therapy are associated with treatment failure or remission with disability (11). We demonstrated in our case report that prompt diagnosis, initiation of appropriate treatment, and avoidance of suspected triggers (including organic solvents) are of utmost importance in initiating clinical disease inactivity. However, further care and management may require other second-line immune-modulating medications and a reassessment with a radiologic survey to assure disease remission.

Contributions
AMT, CBB, conceived and designed the study; AMT, DXZ, drafted the manuscript; GCR, ASZ, WFB, contributed to patient work-up and follow-up. All authors contributed substantially to the revision of the manuscript.

Conflict of interest
The authors declare no potential conflict of interest.

Patient consent for publication
The patient provided written informed consent.

Availability of data and materials
Data and materials are available from the corresponding author upon request.

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