

# Solitary Morphea Profunda Following Trauma Sustained in an Automobile Accident

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## Practice Points

- Localized trauma to the skin may be an inciting event to trigger morphea.
- Morphea is a clinical diagnosis but should be confirmed through biopsy to differentiate it from other similar entities.

*Solitary morphea profunda (SMP) is a variant of localized scleroderma (LS). We report the case of a 50-year-old white woman with a history of trauma sustained in an automobile accident who presented with SMP on the right upper arm. We also provide a review of the classification, epidemiology, etiology, diagnostic studies, pathogenesis, physical findings, histopathology, treatment, and prognosis of SMP, along with other important details pertaining to the disease. We also provide a brief overview of LS and morphea profunda (MP).*

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## Case Report

A 50-year-old white woman presented to our clinic for evaluation of what she described as a “very hard red line” on the right upper arm. The lesion had developed suddenly overnight. Several months

prior to presentation the patient sustained trauma to the same area in a car accident and she thought the lesion might be related to the resulting nerve damage. Initially she presented to her primary care physician who used ultrasonography of the area to rule out muscle or bone involvement. The patient presented to our dermatology clinic 2 months later with an 18×4-cm, brownish, rectangular, sclerotic, bound-down, hypertrophic plaque that started on the right mid forearm and extended to the right shoulder (Figure 1). Her medical history was notable for high blood pressure, which was controlled with valsartan.

A review of systems was unremarkable. Physical examination revealed a well-developed, well-nourished woman. Examination of the right arm revealed no motion restriction (muscle strength, 5/5) and no pain; however, she described a burning sensation at the site of the lesion. She reported no allergies. A 4-mm punch biopsy was performed and laboratory tests were ordered including an antinuclear antibody (ANA) test with reflex, double-stranded DNA test, DNA antitopoisomerase antibodies test, and Lyme titers (IgM and IgG). Initially, the patient was treated with calcipotriene 0.005%–betamethasone dipropionate 0.064% ointment twice daily; she also was treated empirically for Lyme disease with doxycycline 50 mg twice daily. All laboratory tests were within reference range, and a punch biopsy revealed

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**Figure 1.** An 18×4-cm, brownish, rectangular, sclerotic, bound-down, hypertrophic plaque that started on the right mid forearm and extended to the right shoulder.

markedly thickened fibrous septa within the subcutaneous fat. At the edge of the septa there were nodular aggregates of lymphocytes. Due to clinical presentation, laboratory data, and histopathology, solitary morphea profunda (SMP) was diagnosed.

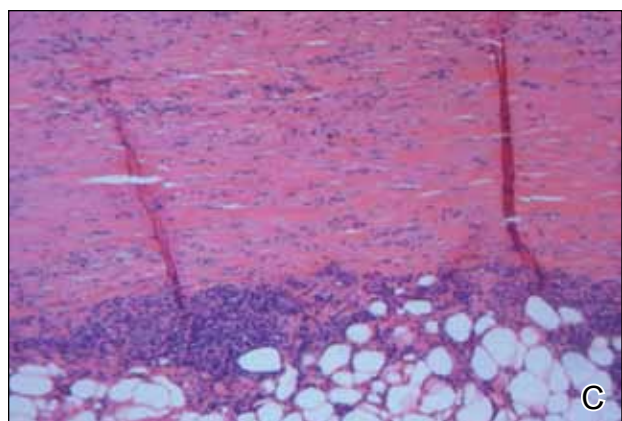
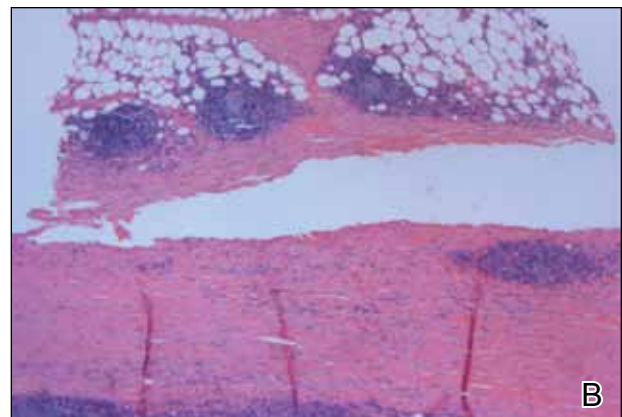
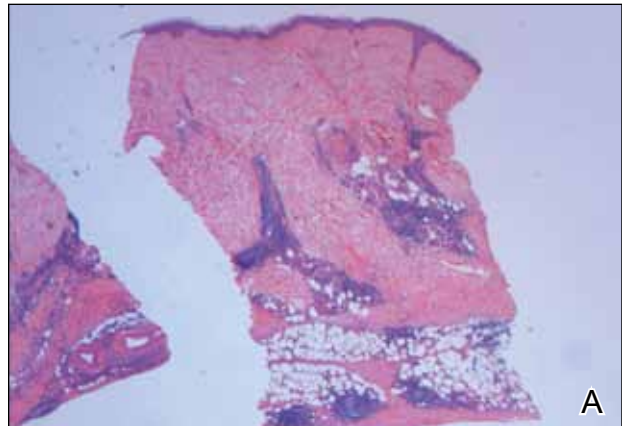
Following histopathologic examination (Figure 2), the patient was instructed to continue treatment with calcipotriene–betamethasone dipropionate as well as doxycycline. A trial of prednisone and/or hydroxychloroquine also was considered pending her response to the initial treatment. At approximately 1-month follow-up, remarkable improvement of the lesion was noted.

### Comment

There is limited literature available about the diagnosis and treatment of SMP. Our case prompted us to further examine the data to emphasize the necessity of greater research surrounding SMP.

*Classification of SMP*—Morphea is a localized form of scleroderma, an inflammatory disease that primarily affects the dermis but can extend down to the bone and also can limit motion. There are several types of morphea that are classified according to the extent, depth, and distribution of the lesions, including plaque, generalized, bullous, linear (including morphea en coup de sabre), guttate, nodular, and deep morphea.<sup>1,2</sup> Other subtypes have been described including subcutaneous morphea, eosinophilic fasciitis (EF), pansclerotic morphea, and morphea profunda.<sup>3</sup> Linear and deep morphea are characterized by involvement of the deep dermis, subcutaneous tissue, fascia, and/or superficial muscle.<sup>2,4</sup>

In 1981, Su and Person<sup>5</sup> first described morphea profunda (MP). In their study, 22 of 23 patients presented with generalized MP. One patient developed a single lesion,<sup>5</sup> which



**Figure 2.** Markedly thickened fibrous septa within the subcutaneous fat with nodular aggregates of lymphocytes (A–C)(all H&E; original magnifications ×2.5, ×5, and ×10, respectively).

ultimately was classified as SMP by Whittaker et al<sup>6</sup> in 1989.

*Epidemiology*—Morphea profunda occurs more frequently in females than in males, with sclerosis manifesting over a period of several months.<sup>7</sup> In 2004, Azad et al<sup>4</sup> suggested that only 9 cases of SMP had been reported in the literature. Although there

is insignificant data to determine the epidemiology of SMP, the authors concluded that it most commonly affects middle-aged individuals with equal sex distribution.<sup>4</sup> The single plaque in patients with SMP most commonly presents on the shoulder, back, or neck or in the paraspinous area.

**Etiology**—Because of the limited amount of literature on MP, a definitive etiology is unknown, but investigators have cited many possible causes. Genetic, autoimmune, hormonal, traumatic,<sup>8</sup> vaccination,<sup>2,8</sup> radiation,<sup>9</sup> viral, neurogenic, and vascular factors all have been implicated,<sup>10</sup> as well as infectious agents such as *Borrelia burgdorferi* in the United States,<sup>11,12</sup> *Borrelia afzelii* in Europe,<sup>2</sup> and *Borrelia garinii* in Japan.<sup>2</sup> Because our patient experienced a traumatic episode several months prior to presentation, it is important to investigate trauma as a likely etiology. Furthermore, traumatic events have been reported in 23% of children with linear morphea.<sup>13</sup>

**Diagnostic Studies**—Morphea profunda is diagnosed clinically and skin biopsy can be used for confirmation. Biopsy requires deep excision down to the muscle, which can aid in determining if the fascia is incorporated. Elevated levels of IgG and IgM have been detected in deep and linear morphea and are known to correlate with disease activity and the development of joint contractures in linear morphea.<sup>2</sup> Serum procollagen type I has been considered by some as a useful indicator of disease severity.<sup>14</sup> Elevated serum levels of antifibrillin-1 antibodies also have been demonstrated in patients with localized scleroderma (LS).<sup>15</sup> Radiography and magnetic resonance imaging can be used for monitoring and analyzing lesion depth. Furthermore, magnetic resonance imaging can be used to differentiate MP from EF.<sup>2</sup>

The presence of ANAs in LS is controversial. According to Nguyen et al,<sup>2</sup> ANAs are present in approximately 46% to 80% of patients with morphea, with a higher prevalence in patients with generalized, linear, and deep subtypes. However, Savoia et al<sup>16</sup> found that patients with morphea typically do not present with ANAs; rather ANAs usually are found in patients with EF.

**Pathogenesis**—After the inflammatory phase in LS, fibrillar collagen types I and III accumulate, causing dermal fibrosis. The extracellular matrix increases due to the activation of connective tissue growth factor, transforming growth factor  $\beta$  (TGF- $\beta$ ), TGF- $\beta$  receptors, IL-4, and several other cytokines.<sup>17</sup> The TGF- $\beta$  receptors combine with the connective tissue growth factor released by fibroblasts to create an autocrine production loop that causes fibroblast and matrix

production.<sup>17</sup> As the inflammation progresses to sclerosis, the CD34 count decreases.<sup>18</sup>

**Physical Findings**—In patients with MP, lesions manifest as thickened taut skin with deep, solitary, and sclerotic indurated plaques. Clinically, plaques are mildly inflamed, hyperpigmented, symmetric, and somewhat ill defined, and the skin feels thickened and bound to the underlying fascia and muscle. Plaques usually are smooth and shiny, but areas of both dermal and subcutaneous atrophy may be present, particularly in chronic lesions.<sup>19</sup> Morphea profunda also can be described as having a cobblestone or pseudocellulite appearance. The groove sign is used to describe a depression along the course of a vein and/or between muscle groups. Both clinical presentations may manifest later in the course of disease.<sup>2</sup>

**Histopathology**—Su and Person<sup>5</sup> described 3 main characteristics of MP that stand out histopathologically. First, there is thickening and hyalinization of collagen bundles in the deep dermis, subcutis, and fascia that are prominent between the junction of the dermis and subcutaneous fat. There also are fewer sebaceous glands and hair follicles. Second, MP presents with an increased inflammatory cell infiltrate composed mainly of lymphocytes located around small blood vessels and the interstitium. In some patients, the lymphocytes consist predominantly of collections of plasma cells. Third, MP contains deposits of mucin in deep portions of the dermis with occasional eosinophils and mast cells. The presence of eosinophils allows EF to be a part of this spectrum and to be included as a differential diagnosis.<sup>5</sup> Eosinophilic fasciitis has a similar presentation to MP because the fibrosis affects the dermis, subcutaneous fat, and underlying structures.<sup>20</sup> Although EF presents with the histopathologic characteristic of fascial fibrosis, a clear distinction between EF and morphea has not been established in the literature. Some authors classify EF as a variant of morphea, whereas others consider it as its own entity. We believe EF is its own entity. Eosinophilic fasciitis can be distinguished from morphea because 60% to 80% of patients with EF have peripheral eosinophilia and 20% to 70% of patients with EF have hypergammaglobulinemia. Additionally, morphea does not present as symmetrically or abruptly as EF.<sup>21</sup>

**Treatment**—To date, there is conflicting literature regarding the treatment regimen for MP. There is controversy regarding whether MP responds to corticosteroids.<sup>19</sup> Different treatment regimens have been discussed for LS, but there is a lack of reports specifically describing therapies for MP and SMP. Because MP and SMP fall under the umbrella of LS, many investigators have reported using the following

treatment regimens for patients with MP and SMP: bosentan,<sup>22</sup> D-penicillamine,<sup>23</sup> phototherapy,<sup>24-26</sup> retinoids,<sup>26</sup> oral steroids,<sup>27</sup> methotrexate,<sup>27-29</sup> vitamin D<sub>3</sub> (oral calcitriol),<sup>30,31</sup> cyclosporine,<sup>32</sup> mycophenolate mofetil,<sup>33</sup> and extracorporeal photochemotherapy.<sup>34</sup>

Falanga and Medsger<sup>23</sup> reported 64% (7/11) treatment success with D-penicillamine in patients who exhibited severe LS. Psoralen plus UVA,<sup>24</sup> methoxsalen, and UVA1 therapy are widely used in the treatment of LS.<sup>25</sup> Kreuter et al<sup>25</sup> advocated for phototherapy as the first approach in the management of LS after reporting improvement in all participants in their study (N=64), 2 participants with deep morphea while the rest exhibited other forms of morphea. Ozdemir et al<sup>26</sup> proposed that retinoic acid combined with psoralen plus UVA is a good treatment choice for plaque-type LS; however, UVA only has the ability to target the epidermis and dermis, which may not be useful for deep forms of morphea.

Several studies have shown positive results in patients treated with methylprednisolone combined with low-dose methotrexate sodium.<sup>27-29</sup> Kreuter et al<sup>30</sup> and Elst et al<sup>31</sup> proposed that calcitriol is effective in treating LS, whereas Hulshof et al<sup>35</sup> indicated that it is not. It should be noted that none of these studies specifically mentioned MP. Martini et al<sup>33</sup> demonstrated success with mycophenolate mofetil in the treatment of 10 LS patients who were resistant to methotrexate sodium and corticosteroids. Although none of the participants in the study had MP, 2 patients had disabling pansclerotic morphea, 3 had generalized morphea, and 5 had linear scleroderma (morphea en coup de sabre) affecting the limbs (n=2) and face (n=3).<sup>33</sup> Because there is no established therapy or consensus for the treatment of MP, we have found success in starting with corticosteroids and then trying alternative therapies.

**Prognosis**—Morphea has transitioned into systemic scleroderma in a small number of reported cases.<sup>10,16,20,36</sup> Therefore, patient follow-up is imperative to consistently identify systemic evolution. Although visceral complications are rare in the setting of LS, associated clinical findings have been reported, including arthralgia, arthritis, contractures, and carpal tunnel syndrome, as well as pulmonary, esophageal, and cardiac abnormalities.<sup>7,34</sup>

## Conclusion

The morphologic features observed in our patient appear to correspond most closely to the type of lesion described by Su and Person<sup>5</sup> and Whittaker et al.<sup>6</sup> Although our case was clinically difficult to distinguish from linear morphea, the histology suggested SMP over other causes. If our patient's SMP

progressed to the joints, physical therapy would be needed to maintain range of motion and function of the extremities,<sup>2</sup> and mandatory long-term follow-up would be required due to the risk for relapse after discontinuation of therapy. Our case highlights the inherent difficulties in the treatment of MP. Due to limited reports of SMP and MP in the literature as well as the conflicting views regarding effective and appropriate treatment options, additional investigation of these conditions and therapeutic options are necessary to further understand this debilitating condition.

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