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Etanercept-Induced Juvenile Disabling Pansclerotic Morphea: A Case Report and Literature Review

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ABSTRACT

Morphea as a side effect of tumor necrosis factor-α (TNF-α) inhibitors is a rare phenomenon. Disabling pansclerotic morphea (DPM) is an exceptionally rare and severe subtype characterized by extensive full-thickness skin involvement with potential extension to deeper tissues. We report the case of a 9-year-old boy with polyarticular juvenile idiopathic arthritis (JIA) who developed rapidly progressive pansclerotic morphea eight months after initiation of etanercept therapy. The sclerosis began at the injection site and spread to involve the four limbs, trunk, neck, and face within six months, sparing only the fingertips and toes. Histopathological examination confirmed pansclerotic morphea. Etanercept was discontinued, and treatment with methotrexate and corticosteroids was initiated. At two-year follow-up, the sclerosis has significantly decreased, although hand contracture deformities persist. To our knowledge, this is the first documented case of juvenile pansclerotic morphea induced by etanercept, and only the second case of pansclerotic morphea induced by any TNF-α inhibitor.

KEYWORDS :

Etanercept; TNF-α inhibitors; pansclerotic morphea; localized scleroderma; juvenile idiopathic arthritis; adverse drug reaction; pediatric

MAIN ARTICLE

INTRODUCTION

Morphea is a rare chronic inflammatory connective tissue disorder characterized by inflammation and fibrosis of the skin and underlying soft tissues.[1] Disabling pansclerotic morphea (DPM) is its most severe variant, with extensive sclerosis extending to subcutaneous tissue, muscles, tendons, and bone, typically manifesting before age 14 with a 3:1 female predominance.[2][3] Cutaneous adverse events occur in approximately one in four patients receiving anti-TNF agents.[4] While psoriasiform reactions are the most common, morphea has rarely been described, with only nine cases reported in a 2021 systematic review, including a single case of pansclerotic morphea induced by adalimumab.[5] Only two prior cases of etanercept-induced morphea exist, both plaque-type in adults.[6] We present the first case of juvenile pansclerotic morphea induced by etanercept.

CASE PRESENTATION

A 9-year-old boy with polyarticular JIA presented with rapidly progressive skin tightening and stiffness. Etanercept (25 mg/week subcutaneously) had been initiated eight months prior. The nurse administering injections noted that skin stiffness initially appeared at injection sites before spreading. Within six months, confluent hypopigmented and hyperpigmented sclerotic plaques involved the four limbs, trunk, neck, and face, sparing only the fingertips and toes (Figure 1). Clawlike contracture deformities of the hands developed bilaterally (Figure2). Nailfold capillaroscopy was normal. There was no history of trauma, radiation, or known morphea triggers, and no family history of autoimmune connective tissue diseases.

Skin biopsy revealed marked dermal sclerosis with thickened, homogenized collagen bundles, extension of fibrosis into the panniculus, and sparse perivascular lymphocytic infiltrate, consistent with pansclerotic morphea. Laboratory investigations showed elevated ESR (45 mm/h) and CRP (28 mg/L). Immunological workup was negative (ANA, anti-Scl70, anti-centromere, anti-RNA polymerase III antibodies, and rheumatoid factor).

Given the temporal relationship, injection-site onset, and absence of alternative etiologies, etanercept-induced pansclerotic morphea was diagnosed. Etanercept was discontinued, and methotrexate (15 mg/m²/week) with systemic corticosteroids (prednisone 1 mg/kg/day, tapered over three months) and intensive physiotherapy were initiated. At two-year follow-up, sclerosis has significantly decreased with improved joint mobility, though hand contractures persist.

DISCUSSION

This case is unique in several respects: it is the first pediatric case of etanercept-induced morphea, the first pansclerotic subtype induced by etanercept, and the latency period (8 months) is shorter than the 18–36 months reported in adult cases, possibly reflecting a more aggressive disease course in children.[6]

The pathophysiology of TNF-α inhibitor-induced morphea likely involves disruption of the TNF-α/TGF-β1 balance. TNF-α normally antagonizes the profibrotic effects of TGF-β1; its inhibition may remove this regulatory brake, promoting fibroblast activation and collagen deposition. Additionally, suppression of Th1 responses by anti-TNF agents may shift the cytokine balance toward Th2 dominance, favoring fibrosis.[1][5] The initial appearance of lesions at injection sites suggests a possible role for local tissue factors.

Treatment of pansclerotic morphea remains challenging. Methotrexate combined with systemic corticosteroids is the mainstay for juvenile localized scleroderma. For refractory cases, tocilizumab and abatacept have shown promise.[3] Our patient's significant improvement after etanercept discontinuation and immunosuppressive therapy underscores the importance of early recognition, though persistent hand contractures highlight the consequences of delayed intervention.

CONCLUSIONS

This first case of juvenile pansclerotic morphea induced by etanercept highlights the importance of vigilant cutaneous monitoring in pediatric patients receiving anti-TNF therapy. Clinicians should carefully examine injection sites and promptly investigate any new-onset skin induration. Early recognition and discontinuation of the offending agent are essential to prevent irreversible sequelae.

FIGURES

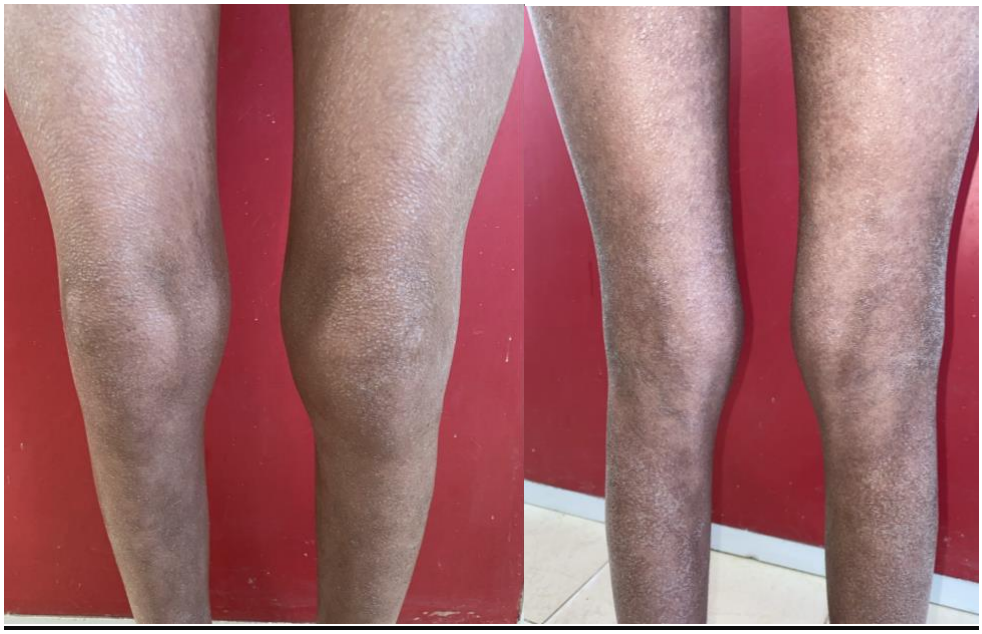

Figure 1: Diffuse sclerosis of the lower limbs with depilation and scattered punctate white macules.

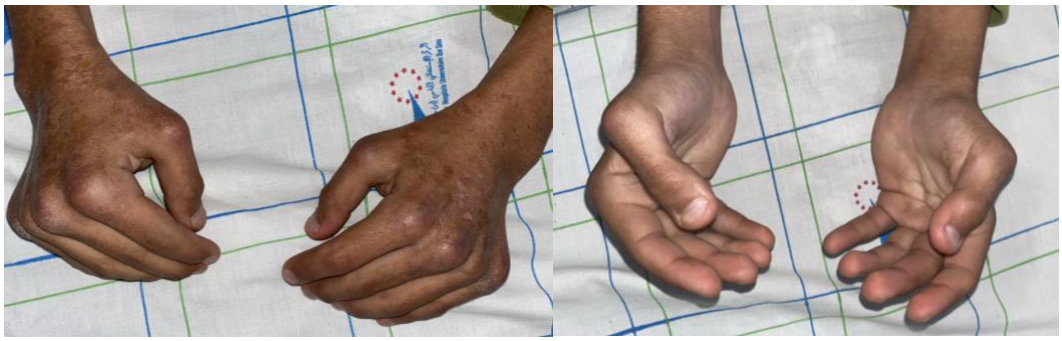

Figure 2: Clawlike contracture deformities of both hands with sclerotic skin changes. Note the sparing of the fingertips.

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The authors declare that they have no conflicts of interest.

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