Case Report on Multiple Connective Tissue Disorder with Features of Overlap Syndrome of Scleroderma with Morphea

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Abstract

Morphea is a rare and unusual skin disorder where an excess of collagen leads to hardening and thickening of the skin. It is more common in Caucasians, but little data exists on Indian patients. Here a 17- year - old boy came to the hospital with symptoms including fever, joint pain, and skin discoloration, initially raising suspicion of a connective tissue disease. After further tests, he was diagnosed with localized Morphea that also showed features of systemic sclerosis, marking it as an overlap syndrome with signs similar to scleroderma. The symptoms included Raynaud's phenomenon, tight skin on the face and arms, and patchy skin pigmentation. This case underlines the complexity of diagnosing and treating overlap syndromes, as they can present with a mix of autoimmune features. Early diagnosis and personalized treatment are key to managing these conditions effectively. This report adds to our understanding of systemic sclerosis with overlapping autoimmune features.

Keywords: *Raynaud's phenomenon, Localised Scleroderma, Multiple Connective Tissue Disorder*

INTRODUCTION

Morphea is an idiopathic inflammatory disorder characterized by intemperate collagen deposition leading to inspissations of the dermis and subcutaneous tissue. It is an uncommon disease relatively with an estimated incidence of 0.4 to 2.7 per 1,00,000 persons and is more often seen in Caucasians. There is a shortage of studies on clinical-epidemiological features of morphea from India, so the study was undertaken to obtain more data. [1] Localized Scleroderma or morphea, is a rare fibrosing skin illness characterized by thickening the skin down to subcutaneous fat due to excessive collagen formation. It may also impact the muscle and bone, in rare occasions it may even impair the Central Nervous System. It is marked by thicker skin bands or inflammatory patches on the limbs, trunk, and head and neck. Raynaud's syndrome involves internal organs alterations in the capillary nail fold and lack of sclerodactyly that distinguish morphea from Scleroderma. [2] The Pathophysiology of Morphea and Systemic Sclerosis is similar, involving auto-reactive T-cells, Th2- associated cytokines such as interleukins 4, and transforming excess growth factor beta (TGF - b). It promotes the formation of extracellular matrix and collagen by fibroblasts. Current therapeutic approaches for Systemic Sclerosis morphea, skin sclerosis, and interstitial lung disease center on identifying and blocking established pathogenic mechanisms. [3] There is difficulty in monitoring the severity and activity of morphea. Modified Rodnan scores validate that systemic sclerosis has limited utility in tracking morphea progression. The localized scleroderma cutaneous assessment tool is currently being evaluated both the disease activity and skin damage. Methotrexate, Mycophenolate mofetil, D – penicillamine, and cyclosporine are considered to prevent complications with the underlying disease for children with progressive cutaneous lesions affecting the face or joints. [2] Because overlap syndromes (OSs) are infrequently reported, a retrospective analysis was conducted to evaluate their frequency and correlations in a Brazilian cohort of 31 patients with dermatomyositis or polymyositis associated with systemic lupus erythematosus (SLE), systemic sclerosis (SSc), or Rheumatoid Arthritis (RA). Myositis-specific autoantibodies (MSAs) and myositis-associated autoantibodies (MAAs), along with autoantibodies related to SLE, SSc, and Rheumatoid Arthritis, were examined in this single-center study, providing insights into the immunological complexity of OSs in these patients. [4]

CASE PRESENTATION:

A 17-year-old male patient was admitted with intermittent fever, joint pain, and skin lesions, initially suspected of having Multiple Connective Tissue Disorder (MCTD). The patient had been treated previously at another hospital with T. Zenapred 8mg OD, T. Pantoprazole 40mg, T. Hydroxychloroquine 200mg OD, and Tenovate cream for 3 days, followed by a regimen of T. Pabatab and T. Revenads for 7 days without improvement. Upon admission, the patient was prescribed T. Cefixime 200mg BD, T. BCT 1tab BD, and T. Paracetamol 500mg BD. Family and menstrual history were normal. On the 4th day of admission, with a positive Anti-nuclear antibody profile, the patient was referred to a dermatologist. The dermatological examination revealed brownish to blackish discoloration of the upper forearm and face, persistent for one and a half months. The patient reported dry mouth, fatigue, body aches after waking up, discoloration of fingers in response to cold (which returned to normal on rewarming within 10 minutes), regurgitation of food for one month, generalized dry skin,

difficulty swallowing, vomiting after consuming excess food, and a history of Raynaud's phenomenon. Cutaneous examination revealed tight skin over the face, salt-and-pepper pigmentation on the forehead and post-auricular region, tight neck skin, no pinched beak-like nose, difficulty in opening the mouth, and tongue protrusion. The patient had taut skin over both forearms and hands, hair loss on the skin, and Raynaud's phenomenon elicited on a cold-water test lasting for 10 minutes. The patient showed signs of an overlap syndrome with features of scleroderma, diagnosed as localized Morphea diffuse systemic sclerosis, a mixed overlap syndrome with features of scleroderma. Further examination revealed bilateral symmetrical hyper-pigmented scaly plaques, 5 x 10 cm in size, with fissures over the anterolateral aspects of the proximal forearm. A hyper-pigmented patch, 2 x 3 cm, was present over the jawline and lower neck, with xerosis over the bilateral lower limbs and salt-and-pepper pigmentation on the frontal region.

On the 4th day of admission, the patient complained of abdominal pain and nausea and was treated with T. Domperidone BD, T. Omeprazole 20mg BD, T. Paracetamol 500mg BD, T. Albendazole 400mg OD, T. Zinc OD, T. Calcium OD, cefotaxime IV 500mg BD, and liquid paraffin for local application. The patient's triglyceride level was found to be 548mg/dL, indicating dyslipidemia. On the 6th day, the patient experienced, vomiting and nausea. By the 8th day, the patient's triglyceride level decreased to 340mg/dL, and T. Fenofibrate 120mg HS and T. Nifedipine 10mg OD were added to the treatment regimen. Screening tests revealed a normal chest X-ray, bile reflux gastritis on OGD scopy, and normocytic normochromic anemia with a hemoglobin level of 10.8g/dL, MCV of 80.4fL, MCH of 26.7pg, and MCHC of 33.2g/dL. A 3mm biopsy was taken from the right forearm wound for histopathological examination. On the 10th day of hospitalization, the patient showed symptomatic improvement and was discharged with prescriptions for Liquid Paraffin 30ml, T. BCT, T. Paracetamol 500mg, T. Zinc, T. Calcium, C. Omeprazole, and T. Domeperidone.

DISCUSSION

Comparing to the case, the major criteria of systemic sclerosis, particularly the symmetrical thickening of the skin proximal to the metacarpophalangeal joint, are fulfilled. The patient exhibited Raynaud's phenomenon, which is one of the most common and earliest manifestations of systemic sclerosis, seen in 95% of cases, as noted by Lester et al. [5] This aligns with the patient's presentation, reinforcing the diagnosis of overlap features in this case. Sommer A et al reported the coexistence of "en coup de sabre" or linear scleroderma with Parry–Romberg syndrome in 42% of cases. [6] This reflects the overlapping nature of autoimmune disorders, also present in this case. Tollefson et al also observed a similar overlap in 36.6% of patients, adding to the complexity of the disease seen in this patient. [7] The co-occurrence of these conditions highlights the diagnostic challenges in managing such cases. The differential diagnosis for scleroderma, based on vascular and skin changes, includes primary Raynaud's phenomenon, chemical exposures, amyloidosis, metabolic disorders, and overlap syndromes. [8] In this case, differentiating between these potential diagnoses was critical, as the patient presented with various features that could be attributed to multiple conditions. Visceral involvement further complicates the differential, with sarcoidosis and autoimmune connective tissue diseases being considerations. Research has indicated that the major autoantigens in localized scleroderma are histones, with anti-

topoisomerase II α antibody being frequently detected [9]. In this case, these immunological markers could provide additional insights into the disease, although systemic sclerosis is typically associated with anti-topoisomerase I antibodies. The involvement of B-cells in systemic sclerosis and the potential therapeutic role of RTX (rituximab) have been noting. [10] While RTX is not mentioned as part of this patient's treatment, this case underscores the need for innovative therapies in managing complex scleroderma presentations. Bony resorption, though an uncommon complication, can occur in longstanding scleroderma, particularly affecting the mandible and other facial bones.[11] Although this case did not feature bony involvement, it remains a consideration in the long-term management of patients with extensive cutaneous sclerosis. Sclerodermic or lupus erythematosus panniculitis (SLEP), which shares clinical and histopathological features with localized scleroderma, is rare but has been reported in some cases. [12] While this specific overlap is not present in this case, it reflects the spectrum of autoimmune conditions that can co-occur in patients with systemic sclerosis. Overlap syndromes, as noted in the literature, often occur with connective tissue diseases, sometimes within the same tissue site. [13]This case illustrates the challenge of managing such syndromes, as the patient presented with mixed features of systemic sclerosis and other autoimmune conditions, similar to discoid lupus erythematosus and localized scleroderma. The concept of "sclerosing diseases of the skin" encompasses conditions with fibrotic changes, which manifest in different clinical subtypes based on cutaneous and extracutaneous involvement. [14] This case presents the difficulty in distinguishing between these subtypes, with overlapping systemic sclerosis and localized skin manifestations. Familial autoimmune trends were more common in generalized and mixed subtypes, with neurological manifestations seen in the linear subtype. [15] Although familial history was not important in this case, the overlap of autoimmune diseases in this patient suggests a possible genetic predisposition. [16]

This case mirrors findings in the literature regarding Raynaud's phenomenon, overlap syndromes, and the challenges of differential diagnosis. The rare presentation of overlapping autoimmune features in systemic sclerosis further emphasizes the importance of a multidisciplinary approach to care in such complex cases.

CONCLUSION

This case illustrates the complexity of localized Morphea diffuse systemic sclerosis with overlapping features of scleroderma. The presence of hallmark symptoms such as Raynaud's phenomenon, skin tightening, and systemic involvement emphasizes the need for a comprehensive and multidisciplinary approach. Early diagnosis and tailored therapeutic strategies are essential in managing connective tissue disorders with overlapping autoimmune features, highlighting the importance of personalized care in improving outcomes. This case contributes to a deeper understanding of systemic sclerosis and its clinical variations.

CONFLICT OF INTEREST: The authors declare no conflict of interest.

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