CASE STUDY

A rare presentation of systemic lupus erythematosus associated with thymoma-induced multiorgan autoimmunity

Jyotsna Oak[1]*, Ojas Unavane[2], Aditya Subramanian[2], Bijal Kulkarni[3], Rajesh Mistry[4]

[1]Department of Rheumatology, Kokilaben Dhirubhai Ambani Hospital, Andheri, Mumbai, India
[2]Department of Medicine, Kokilaben Dhirubhai Ambani Hospital, Mumbai, India
[3]Department of Laboratory Medicine,Kokilaben Dhirubhai Ambani Hospital, Mumbai, India
[4]Department of Surgical Oncology, Kokilaben Dhirubhai Ambani Hospital, Mumbai, India

Abstract

Systemic lupus erythematosus (SLE) is a multisystem autoimmune disease that primarily affects women in their reproductive age. Its typical manifestations include cutaneous symptoms such as alopecia, malar rash, and generalized rash, as well as oral ulcers. The study focuses on a challenging diagnostic case involving an atypical presentation of SLE associated with thymoma-related multiorgan autoimmunity.

Keywords: Thymoma, Systemic Lupus Erythematosus, Paraneoplastic

Introduction

While thymomas are relatively rare, accounting for only 0.2% to 1.5% of all cancers, they do constitute a notable subset of mediastinal tumors.[1] Thymomas are more commonly associated with paraneoplastic autoimmune syndromes than thymic carcinomas.[2] There are certain reports on the rare presentation of pure red cell aplasia, myasthenia gravis, and systemic lupus erythematosus (SLE), in association with thymomas, even after thymectomy.

Case report

A 32-year-old female, working as an accountant and with no known underlying health conditions, presented with a series of chief complaints. She noted a non-resolving hypopigmented lesion on her forearm, accompanied by nocturnal itching, which first appeared approximately three months ago. There were no signs of skin erosions, pus discharge, or inflammation initially. However, over time, similar lesions emerged on her abdomen, back, and chest, eventually transforming into hyperpigmented and indurated patches (Fig. 1). Additionally, multiple lesions were discovered in her oral cavity, specifically on the hard palate, inner lips, and buccal mucosa. The patient also reported significant hair loss over the vertex, resulting in associated balding (Ludwig grade 2). Hair loss was noted to occur constantly during combing, but there were no signs of erythema, scarring, or scaling.

Furthermore, she had been enduring a persistent dry cough for the past three months, which had progressively worsened with no diurnal variation. She complained of pain in both her knees and shoulders, accompanied by swelling. The patient's appetite was poor, and she had lost 8 kg of weight over the last three months, although her bowel habits remained normal. She denied any history of alcohol consumption or smoking, and there was no significant family history of autoimmune diseases. She also reported no history of consuming drugs from outside.

The patient was noted to be undernourished and thin-built, with a BMI of 15. She exhibited pallor but showed no signs of icterus, cyanosis, clubbing, lymphadenopathy, or edema. However, she remained conscious, coherent, and cooperative, displaying orientation in time and place. On examination, she showed arthritis of shoulder and knee joints. Although, breath sounds were bilaterally equal, coarse crepitations were present. The rest of the systemic examination revealed no abnormalities.

Routine laboratory investigations showed: Hb 12.1 g/dl, WBC 8.02 x 10^3/µL, and platelets: 334 x 10^3/µL. Liver and

Fig. 1: Non-scarring alopecia and hyperpigmented patch over the left forearm depicting Wickham's striae

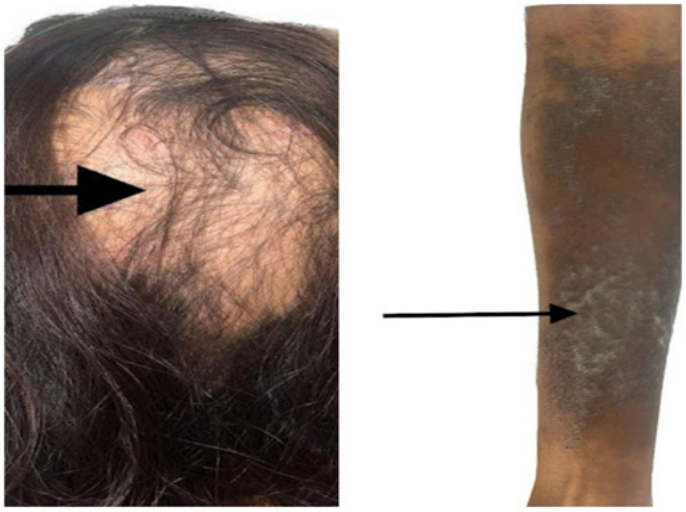
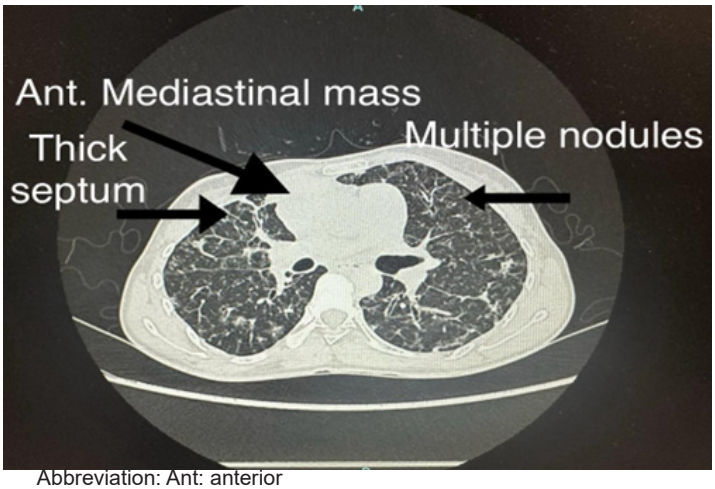


Fig. 2a: HRCT of the chest revealing extensive septal thickening with nodules



Abbreviation: Ant: anterior

kidney function tests were normal. Urine routine showed proteinuria with a protein-to-creatinine ratio (PCR) of 7. Tests for hepatitis C (Anti HCV), hepatitis B surface antigen (HBsAg), and HIV were negative. Antinuclear antibodies (ANA) by immunofluorescence were positive at a 1:640 titer with a homogenous pattern. Ds-DNA was positive with a value of 32 IU/ml.

A high-resolution CT (HRCT) imaging revealed extensive septal thickening in both lungs, with many of the thickened septae showing nodularity, indicative of a non-specific interstitial pneumonia (NSIP) pattern. The scan also indicated the presence of a moderately enhancing right paramediastinal soft tissue (nodal mass), measuring approximately 5.2 x 4.0 x 2.8 cm. Additionally, multiple small nodules were visible along both oblique fissures (Fig. 2a). Pulmonary function tests revealed compromised lung function, with reduced diffusing capacity for carbon monoxide (38%).

Considering the presence of alopecia, skin rash, oral ulcers, bilateral pleural effusion with interstitial lung disease (ILD), albuminuria, and a positive ANA test, a diagnosis of SLE was concluded. A positron emission tomography-computed tomography (PET-CT) scan was performed to investigate the para-mediastinal soft tissue mass. The scan revealed a standardized uptake value maximum (SUV max) of 2.9 in the anterior mediastinal mass, indicating low metabolic activity. Following this, a biopsy was conducted, which confirmed the presence of thymoma (Fig.2b and 2c).

Biopsy of the tumor revealed small, round lymphoid cells intimately mixed with small epithelial cells when observed at 40x magnification. Immunohistochemical staining revealed cytokeratin-positive epithelial cells, CD3-positive cells, and

Fig. 2b and 2c: PET-CT scan of the whole body revealing uptake in the anterior mediastinum

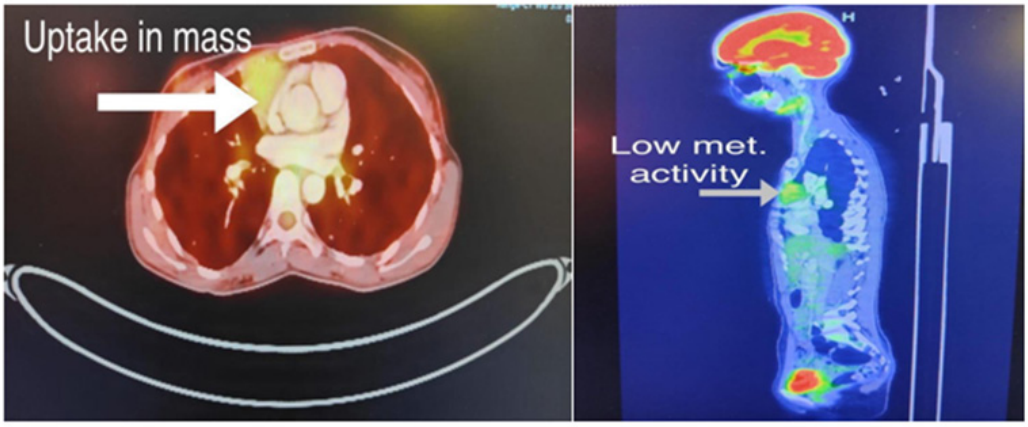


Fig.3: Immunohistochemical staining of the mediastinal mass showing cytokeratin-positive epithelial cells, CD3-positive cells, and TdT-positive thymic 'T' lymphocytes

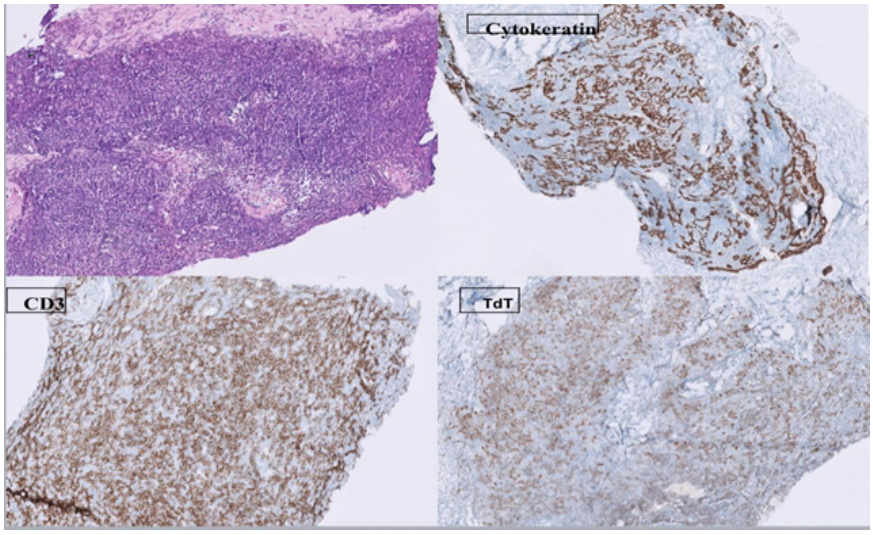
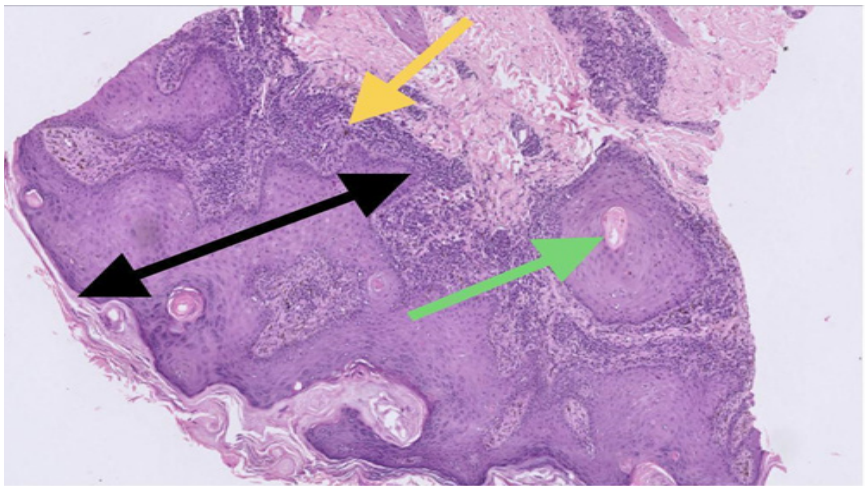
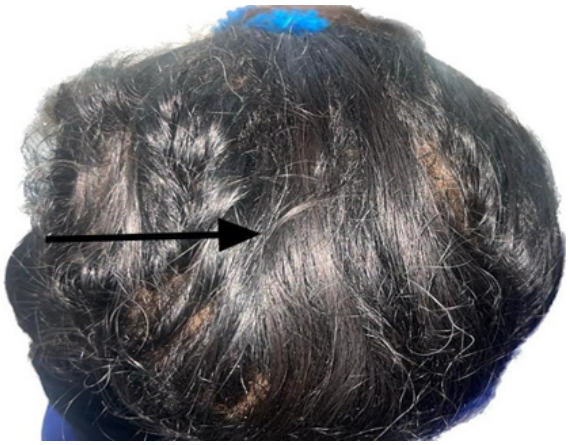


Fig.4: Biopsy of lichen planus (10x)



Yellow arrow: A thick band of lymphocytes and few plasma cells in the upper dermis,
Black double-headed arrow: Hyperplastic and hyperkeratotic thickened dermis
Green arrow: Keratin pearls in the thickened epidermis

Fig.5: Hair regrowth noted after treatment



TdT-positive thymic 'T' lymphocytes (Fig. 3). Additionally, considering the atypical nature of her skin rash, a skin biopsy was done which led to the diagnosis of lichen planus (Fig. 4).

In light of a Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) score of 26, decreased levels of complement proteins C3 and C4, positive antinuclear antibody (ANA) with a homogeneous pattern, oral ulcers, arthritis, and alopecia, a diagnosis of SLE with high disease activity was established. The patient received a course of intravenous dexamethasone for three days, supplemented with piperacillin-tazobactam. Upon reduction of disease activity, the patient was discharged with an oral regimen consisting of steroids, hydroxychloroquine, and sulfasalazine for ongoing SLE management. Subsequent follow-up demonstrated notable symptom improvement, including hair regrowth (Fig. 5).

Discussion

The thymus plays an integral role in regulating the immune system, primarily by diverting and selecting T lymphocytes, which is necessary for preventing cell-mediated autoimmunity. Thymoma patients with autoimmune diseases such as myasthenia gravis, pure red cell aplasia, and SLE, although relatively uncommon, illustrate the intricate relationship between the thymus and autoimmunity. The efficacy of thymectomy for early-onset myasthenia gravis, with or without thymectomy, has been demonstrated. However, thymectomy and thymomectomy do not affect non-myasthenia gravis autoimmune diseases in 40% of cases. The benefits of thymectomy/thymomectomy are gradual, with remission rates at 20% in the first year, increasing to 50% within 7-10 years.[3] Approximately 15% of thymoma patients exhibit symptoms of myasthenia gravis.[4] Immature T cells formed in thymoma are released from the thymus and may induce autoimmune diseases in patients.[5] Other autoimmune diseases associated with thymoma are complex and often advanced, with episodes of recurrence. SLE patients with thymoma may experience clinical remission of SLE after thymoma resection.[6]

The current patient could not be subjected to thymectomy due to severe restrictive lung disease with low diffusing capacity for carbon monoxide (38%), being undernourished (BMI 15). Plan for surgery would be revisited in the future depending on the response to medical therapy and fitness for surgery. Thymectomy improves the response to treatment for other autoimmune diseases. The efficiency and long-term survival rates of thymectomy in myasthenia gravis are greatest for thymic hyperplasia as compared to thymoma and thymic carcinoma.[7] Extended thymectomy, including the resection of ectopic thymus tissue, has also been proposed.

The current patient initially exhibited multiple skin manifestations, including alopecia and a lichenoid rash. The diagnosis of thymoma was incidental and made during a chest CT scan conducted to investigate interstitial lung disease. Thymoma was later confirmed through histopathology and cytogenetics. The thymus plays a crucial role in T-cell development and the positive and negative selection of T cells. When compromised, it can lead to a spectrum of autoimmune-mediated diseases. In 2007, Wadhera et al. introduced a new term, 'Thymoma Associated Multiorgan Autoimmunity (TAMA),' to describe graft-versus-host-like manifestations in thymoma patients. TAMA is defined as a condition with skin involvement resembling GVHD (graft-versus-host disease) histopathologically, particularly in the context of thymoma.[8] In the current patient, lichen

Table 1: Review of previously published similar cases

Author, year	Jorunal	Number of cases	Findings
Mollaeian et al., 2020[5]	*Clinical Rheumatology*	1	Compared to thymic carcinomas, thymomas are more frequently associated with autoimmune disease and paraneoplastic syndromes.
Zhang et al., 2022[6]	*Medicine (Baltimore)*	1	A 27-year-old woman with SLE having associated thymoma. After thymectomy, the patient's blood count and immune function gradually returned to normal.
Gubod et al., 2021[11]	*Cureus*	1	A 45-year-old Chinese man presented with ulcerative oral lichen planus that was associated with a thymoma. Thymectomy was performed and blood investigations revealed pure red cell aplasia.
Noël et al.,2020[12]	*Autoimmunity review*	14	Around 93% of the patients were women, and the median age was 43.5 years at the time of thymoma diagnosis. Among the clinical features of SLE, the most common was joint involvement in 78.6% of the patients, followed by autoimmune cytopenia in 35.7%, and cutaneous manifestations in 28.6%.12
Bernard et al.,2016[13]	*Autoimmunity review*	85	They studied 85 patients with thymoma between 2005 and 2011 and found that 47 of them had autoimmune diseases. Out of these, 2 patients had SLE and 2 had lichen planus. Six patients had at least two autoimmune diseases.13
Genty et al., 2001[14]	*La Revue de Médecine*	2	They studied two cases of thymoma associated with SLE. One case was of a 41-year-old man with SLE with pleurisy. He underwent thymectomy followed by chemotherapy without affecting SLE. Another case was of a woman with SLE and incidental thymoma. SLE remained stable 4 years post thymectomy14
Alarcón-Segovia et al.,1963[15]	*Lancet*	2	A 32-year-old woman with myasthenia gravis developed features of SLE 6 years after thymectomy done for myasthenia gravis. She presented with joint pains, urticaria, high ESR and urine positive for protein. She was treated with steroids and chloroquine.
Boonen A et al.,2000[16]	*Rheumatology (Oxford)*	19	A 76-year-old woman presented with spindle cell type thymoma and SLE. Antinuclear antibodies tested positive. Ten days post-thymectomy, her clinical features of SLE resolved without any medication for SLE.

planus is considered a manifestation of TAMA, and it significantly improved following the initiation of intravenous methylprednisolone. Current treatment options for TAMA include thymectomy, systemic glucocorticoids, intravenous immunoglobulins, cyclosporine, and narrow-band ultraviolet B therapy. Thymectomy can directly influence the outcome of cutaneous autoimmune disorders.[9]

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Thymoma is associated with various cutaneous disorders, including pemphigus vulgaris, lichen planus, vitiligo, alopecia areata, and lupus erythematosus.[10] A rare condition known as paraneoplastic autoimmune multiorgan syndrome (PAMS) is characterized by variable clinical phenotypes in the presence of neoplasms. The manifestations of PAMS depend on the activation of humoral and cellular immune responses. Patients with thymoma may present with a spectrum of antibody-driven skin conditions, including pemphigus-like lesions, lichen planus, and erythema multiforme. A study conducted by Darshini Satishkumar et al compared the clinical features of PAMS across various countries, revealing lichen planus as the most common skin manifestation, along with oral involvement observed in 100% of cases, with thymoma being the second most common neoplasm.[11] A comprehensive review of previously published similar cases is presented in table 1.

Conclusion

Although thymectomy effectively eliminates the source of autoantibodies responsible for autoimmunity, managing SLE associated with thymoma in patients unsuitable for surgery may benefit from glucocorticoids and DMARDs, as indicated by the current study. Further research on PAMS with SLE manifestation is necessary to determine the most effective treatment approach. The incidence rate of thymoma is estimated to be between 0.13 to 0.32 per 100,000 people per year, while that of SLE is between 14 to 60 per 100,000 people per year. Since the simultaneous occurrence of thymoma and SLE is rare based on their individual incidence rates, further research is needed to explore and understand this potential association between thymoma and SLE.

Conflicts of Interest

The authors declare that they have no conflict of interest.

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*Correspondence: Dr. Jyotsna Oak. Department of Rheumatology, Kokilaben Dhirubhai Ambani Hospital, Andheri, Mumbai, India. jyotsnaoak@gmail.com

Citation

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