Case Report

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Periorbital Oedema as a Crucial Diagnostic Clue for Systemic Lupus Erythematosus in a Young Woman: A Case Report

Internal Medicine Section

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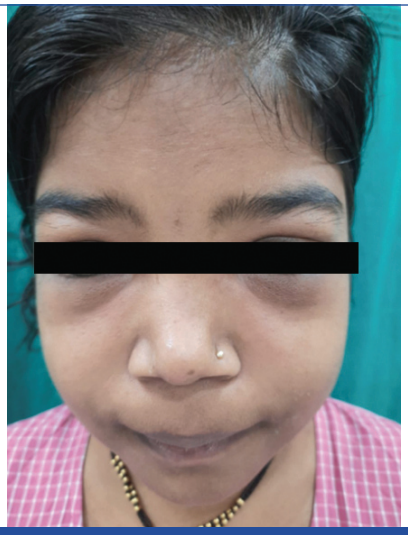
ABSTRACT

Systemic Lupus Erythematosus (SLE) is a polygenic autoimmune disorder characterised by immune-mediated damage to various organs and tissues due to the formation of tissue-binding autoantibodies and immune complexes. This multifaceted disease results from complex interactions between genetic, environmental, and immunological factors, leading to diffuse inflammation and tissue injury. Among the hallmark features of SLE, serositis, a condition involving inflammation of serous membranes such as the pleura, pericardium, or peritoneum, is a key diagnostic criterion. Serositis indicates active inflammation and plays an important role with other diagnostic criteria in guiding the diagnosis and treatment of SLE. Serositis can be challenging to recognise despite its clinical importance, especially when overshadowed by other unusual manifestations. Our patient, a 19-year-old female, presented with persistent periorbital swelling, fatigue, breathlessness and progressive chest pain for the last two months. While, the periorbital oedema was an uncommon presentation of SLE, the identification of serositis was key in establishing the diagnosis. After comprehensive evaluation excluding other systemic causes of periorbital oedema and serositis, a diagnosis of SLE was made. This case showcases the cruciality of recognising serositis as a central feature of SLE, particularly in cases with unusual symptomatology. Prompt recognition and early diagnosis, along with timely intervention, can improve outcomes for patients with this complex autoimmune disease. Clinicians must remain vigilant for SLE in patients presenting with uncommon symptoms like periorbital oedema along with serositis.

Keywords: Autoimmune disease, Immune complex, Serositis, Thoracocentesis

CASE REPORT

A 19-year-old female who was in good health previously, presented with periorbital swelling since 2-3 months, insidious onset, gradually progressing over time, and was accompanied by eye watering. Over the past 15 days, she also experienced joint pain involving the shoulders, elbows, wrists, knees, ankles and small joints, along with breathlessness on exertion and generalised weakness. The patient and her relatives denied any history of malar or discoid rash, oral ulcers, seizures, or cognitive or behavioural disturbances. Her medical history was negative for diabetes, hypertension, thyroid disorders, tuberculosis, or bronchial asthma, and there was no significant surgical or drug history. The periorbital oedema is illustrated in [Table/Fig-1]. Patient permission was taken to display her images.



[Table/Fig-1]: Periorbital oedema in a 19-year-old female.

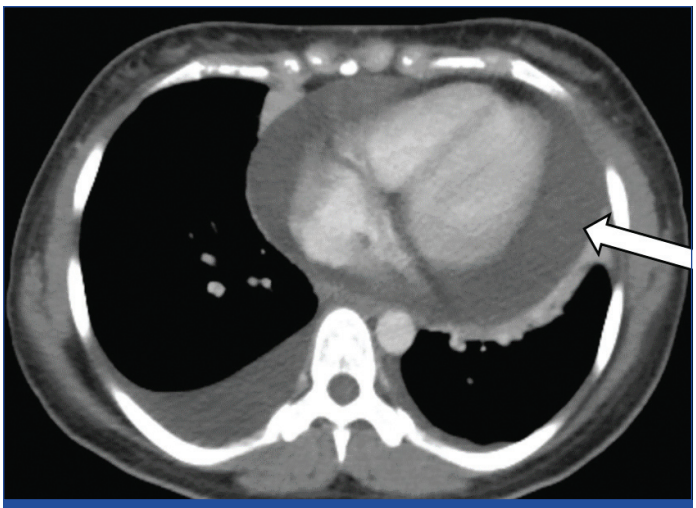
The patient was conscious and oriented to time, place, and person. Her vital signs included a pulse rate of 96 beats per minute and a blood pressure of 110/60 mmHg in both arms. Oxygen saturation was 93% on room air and respiratory rate was 22/min. On clinical examination, there was dullness to percussion and diminished breath sounds in the bilateral infrascapular regions. Routine laboratory investigations were conducted, as outlined in [Table/Fig-2].

Parameters (units)	Laboratory values	Normal values
Haemoglobin (g/dL)	11.3	13.2-16.6
Total leukocyte count (cells/cu.mm)	8700	4000-10000
Platelet count (cells×10^6/µL)	1.27	4.35-5.65
Serum urea (mg/dL)	33	17-49
Serum creatinine (mg/dL)	0.86	0.6-1.35
Total serum bilirubin (mg/dL)	0.5	0.22-1.20
Direct bilirubin (mg/dL)	0.23	<0.5
AST (IU/L)	36	8-48
ALT (IU/L)	26	7-55
ALP (IU/L)	56	40-129
HbA1c (%)	5.2%	<5.7%
Total protein (g/dL)	7.1	6.4-8.3
Serum albumin (g/dL)	3.6	3.5-5.2
Albumin: globulin ratio	1.3	1.1-2.5
Sodium/Potassium (mmol/L)	140/3.50	135-145/3.5-5.10
ESR (mm/hr)	04	<20
CRP (mg/dL)	3.22	<0.3
HIV antibody	Negative	
Hepatitis B antibody	Negative	
Anti-hepatitis C antibody	Negative	

24-hour urine protein	16.5	<149 mg/24 hr
Serum lactate dehyrogenase (U/L)	270	81-234
Urinary casts	Detected	-

[Table/Fig-2]: Routine laboratory investigations.
ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein; HIV: Human immunodeficiency virus

An ultrasound of the abdomen and pelvis was performed, which revealed normal liver and kidney morphology, with no evidence of free fluid in the peritoneal cavity. The 2D-ECHO was suggestive of large pericardial effusion (posterior > anterior) with 60% ejection fraction. Computed Tomography (CT) thorax was done suggestive of moderate bilateral pleural effusion and large pericardial effusion [Table/Fig-3].



[Table/Fig-3]: CECT showing pericardial effusion.

Thoracocentesis was performed, and the pleural fluid was sent for routine microscopy and Cartridge-Based Nucleic Acid Amplification Test (CBNAAT) studies. The pleural fluid was exudative and results are summarised in [Table/Fig-4].

Pleural fluid routine microscopy parameters (units)	Laboratory values	Normal values
Appearance	Slightly yellowish	Clear to yellow
Cob web	Absent	Absent
Glucose (mg/dL)	99	>60
Proteins (gm%)	4.60	Upto 3
Albumin (g/dL)	2.5	
Red blood cells	Absent	Absent
White blood cells (cu. mm)	900	0-150
Neutrophils	15%	-
Lymphocytes	75%	-
LDH (U/L)	173	
ADA (U/L)	66	0-5
Pleural fluid CBNAAT	Negative	Negative

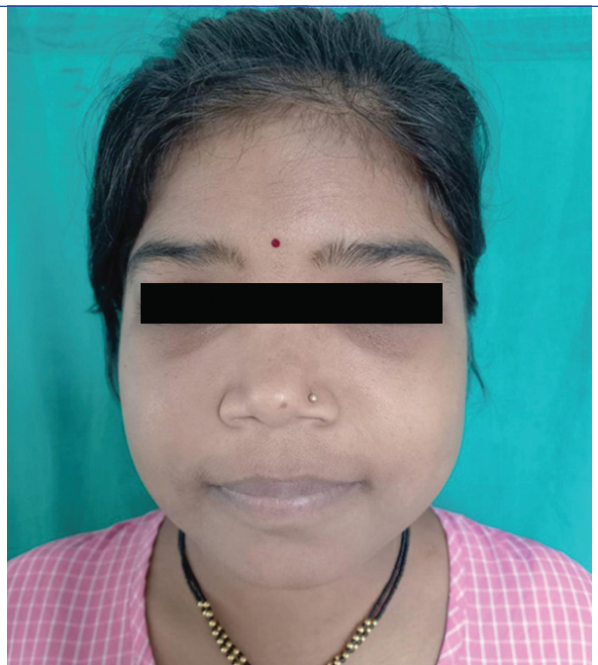
[Table/Fig-4]: Pleural fluid routine microscopy and CBNAAT studies.
LDH: Lactate dehyrogenase; ADA: Adenosine deaminase; CBNAAT: Cartridge-based nucleic acid amplification test

Periorbital oedema can be seen in various conditions, making a thorough differential diagnosis essential. Kidney diseases like nephrotic syndrome, which cause fluid retention and swelling, were ruled out due to the absence of severe proteinuria and hypoalbuminaemia. Infections such as cellulitis or orbital infections were unlikely, as there were no signs of redness, warmth, or pain. An allergic reaction was also considered but excluded due to the absence of itching or other allergic symptoms. Hypothyroidism, another potential cause, was ruled out based on normal thyroid function tests. Given the presence of systemic symptoms, autoimmune diseases were strongly suspected. Imaging studies provided further evidence, as pericardial and pleural effusions are known manifestations of SLE. With a high suspicion of connective tissue disease, an extensive panel of immunologic tests was performed to confirm the diagnosis which was outlined in [Table/Fig-5].

Test description	Observed values
Anti nuclear antibody by immunofluoroscence	Positive 3+ at a titre of >1:10,000
Anti smith autoantibody	Positive
Anti dsDNA	Positive
Nucleosomes	Positive
AMA M2 antibody	Positive
C-ANCA	Negative
P-ANCA	Negative
Anti-Phospholipid antibodies	Negative
Compliment proteins	Negative
Direct and indirect coombs test	Negative
RA factor	Negative
Anti CCP antibody	Negative

[Table/Fig-5]: Results of immunologic tests.
dsDNA: Double standed DNA; AMA: Anti-mitochondrial antibody; C-ANCA: Cytoplasmic-anti-neutrophil cytoplasmic body; P-ANCA: Perinuclear-anti-neutrophil cytoplasmic antibody; RA: Rheumatoid factor; CCP: Cyclic citrullinated peptide

The Systemic Lupus Erythematosus Collaborating Clinical Criteria for Classification of Systemic Lupus Erythematosus (SLICC) score is positive. The score of American College of Rheumatology/European League Against Rheumatism (ALR EULAR) criteria is 18. Thus, based on these criteria, the patient is diagnosed with SLE. In SLE, anaemia, low white blood cell count, low platelets, and elevated lactate dehydrogenase often occur due to the immune system attacking blood cells. Consequently, the patient was initiated on a treatment regimen of methotrexate, supplemented with folic acid, and hydroxychloroquine. The patient completed a 3-month course of treatment, which resulted in significant improvement, culminating in the complete resolution of the periorbital oedema [Table/Fig-6].



[Table/Fig-6]: Resolution of periorbital oedema following treatment.

DISCUSSION

The SLE is a chronic and autoimmune disease that predominantly affects females with a prevalence ratio of 8:1, when compared to males. The disease is influenced by genetic, epigenetic, ecological, and environmental factors. The peak incidence occurs during early reproductive age, but the reason for the marked female predominance remains largely unexplained [1]. Despite advances in

treatment leading to a 95% 5-year survival rate, individuals with SLE experience higher morbidity and mortality compared to the general population. Additionally, their quality of life tends to be lower than that of both the healthy population and those with other chronic diseases [2]. SLE is a multisystem disorder with diverse manifestations affecting the skin, musculoskeletal system, haematological system, heart, lungs, nervous system, gastrointestinal tract, kidneys, and vascular system [3]. Skin involvement is the second most common feature in SLE, and it may present as photosensitive malar rash, psoriasis, tinea corporis, discoid lupus erythematosus, non scarring alopecia, mucosal ulcers, bullous lesions, pyoderma gangrenosum, or subcutaneous nodules. The immunosuppressed state in SLE increases susceptibility to infections, and in some cases, necrotising fasciitis may mimic or coexist with severe lupus-related skin lesions, requiring early recognition and aggressive treatment [4]. Although cutaneous manifestations are common, periorbital oedema in SLE is rare, and cases of periorbital oedema without other cutaneous features are even more unusual [5]. SLE primarily leads to the activation of both innate and adaptive immune responses, which in turn activate autoreactive B cells through T cells. This activation results in the deposition of immune complexes in various tissues, initiating an autoimmune cascade that may be confined to a single organ or can lead to widespread systemic involvement [6]. The variety of clinical presentations and laboratory parameters of SLE creates a challenge for its accurate diagnosis. For patients presenting with clinical features of SLE, ANA immunofluorescence serves as an effective screening assay, detecting most associated autoantibodies. To confirm the diagnosis of SLE, ANA-positive blood samples should undergo further testing with specific assays. A more accurate detection of SLE can be achieved by combining ANA testing via immunofluorescence with ANA (Ro/La/Sm/RNP) and anti-dsDNA assay [7]. The American College of Rheumatology and the European League Against Rheumatism jointly proposed a new set of criteria, referred to as the EULAR/ACR criteria. This criteria employs ANA positivity as an entry requirement and consists of two domains: clinical and immunological. Each domain includes multiple criteria, with scores ranging from 2 to 10. A patient is diagnosed with SLE if they meet the entry criteria and achieve a total score of 10 or more [8]. The Systemic Lupus International Collaborating Clinics (SLICC) group revised and validated the SLICC classification criteria. In their validation set, the SLICC criteria demonstrated fewer misclassifications compared to the current ACR classification criteria. Moreover, the EULAR/ACR criteria offer improved accuracy in diagnosing SLE [9]. Serositis, defined as inflammation of serous membranes, is a hallmark feature of SLE. It typically manifests as pleuritis, pericarditis, or, less commonly, peritonitis. Pleuritis is characterised by pleuritic chest pain and pleural effusion, while pericarditis may present with chest pain, pericardial friction rub, or pericardial effusion. In our patient, moderate bilateral pleural effusion and large pericardial effusion were evident on imaging studies. These findings align with serositis-related complications in SLE, underscoring the systemic nature of the disease. SLE is the most likely diagnosis due to the presence of periorbital oedema without nephrotic syndrome, which has been documented in SLE flares. The multisystem involvement, including serositis, supports an autoimmune aetiology. Additionally, the absence of other clear causes (e.g., allergy or infection) makes SLE with an atypical cutaneous manifestation the most plausible explanation. Similar to the study by Jarek MJ et al., our patient had periorbital oedema without proteinuria or hypoalbuminaemia, suggesting inflammatory cause rather than a nephrotic one [10]. However, unlike their cases, our patient did not have Mees' lines but did present with serositis, indicating more widespread inflammation. This case supports the idea that periorbital oedema can be a marker of SLE activity, even without kidney involvement. Bilateral eyelid oedema is a cutaneous sign linked to numerous aetiologies, such as infections, tumours, trauma, facial dermatitis, and autoimmune diseases. Several alternative diagnoses could not be completely ruled out in this case. Dermatomyositis can present with periorbital oedema and a heliotrope rash, but it typically involves muscle weakness, which was not a prominent feature here. Angioedema could cause sudden swelling, though it is usually transient and associated with allergies or hereditary C1 esterase deficiency [11]. Angioedema was unlikely due to the absence of allergic triggers, drug exposure, or recurrent episodes. The lack of response to antihistamines further ruled out an allergic cause [12]. Hypothyroidism (myxoedema) may lead to facial and periorbital oedema, but other systemic hypothyroid symptoms were not noted. Renal or hepatic dysfunction, despite the absence of significant proteinuria or hypoalbuminaemia, could still play a subtle role in oedema formation. Idiopathic orbital inflammatory syndrome (orbital pseudotumour) can also cause periorbital swelling, but it typically presents with pain and restricted eye movement. While SLE remains the most likely diagnosis, these conditions could not be entirely excluded.

The association of eyelid oedema with SLE was first reported by Tuffanelli DL and Dubois EL [13]. The aetiopathogenesis of periorbital oedema in SLE remains poorly understood. However, the presence of dermal mucin has been attributed to this oedema [13]. The dermal mucin deposition and mucin accumulation in the skin, seen in lupus, can contribute to swelling and thickening of tissues. While periorbital oedema is an uncommon initial presentation in SLE, its occurrence could indicate underlying inflammation and immune complex deposition, which are hallmark features of the disease [14]. Periorbital oedema in SLE may be due to increased dermal mucin deposition or vasculitis, and it can serve as a subtle but important clue in patients with other nonspecific symptoms. Inflammatory vasculopathy in SLE can increase vascular permeability, causing periorbital oedema. Lupus nephritis-related hypoalbuminaemia may contribute to fluid retention. Direct autoimmune inflammation and corticosteroid use can also lead to localised swelling.

CONCLUSION(S)

Periorbital oedema should raise suspicion for SLE, particularly when associated with other systemic or cutaneous manifestations suggestive of autoimmune activity. Clinicians should consider SLE in the differential diagnosis of periorbital oedema, especially in young females or individuals with a personal or family history of autoimmune disorders. Early recognition and further investigation with immunological tests, including ANA, anti-dsDNA, and Extractable Nuclear Antigen (ENA) panels, are crucial for timely diagnosis and treatment, potentially preventing more severe systemic involvement. Early intervention in SLE is crucial to preventing severe complications. In this case, prompt treatment with methotrexate and hydroxychloroquine led to significant improvement, highlighting the importance of early immunosuppressive therapy in controlling disease activity and preventing long-term damage. Future studies should evaluate periorbital oedema as a potential early marker of SLE flares, its correlation with disease activity, and response to treatment.

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