

CASE REPORT

SYSTEMIC LUPUS ERYTHEMATOSUS COMPLICATED WITH CAST
LEMAN DISEASE: A CASE REPORT

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Castleman disease is a rare nonclonal heterogeneous group of diseases involving lymphoid tissue. It often simulates other inflammatory conditions and malignancies. Systemic lupus erythematosus, being a multisystem inflammatory disorder, shares many features with Castleman disease. Here, we report a similar case of a middle age female who was initially diagnosed as SLE with lupus nephritis, for which she was put on prednisolone and mycophenolate mofetil. After commencing treatment, her symptoms resolved and she remained in remission for two years. Then, she stopped taking MMF and did not continue follow up. However, she developed a relapse 6 months later. She was given IV solumedrol pulse therapy and was discharged on prednisolone and MMF. Later on, her condition was complicated with Castleman disease. For diagnostic and therapeutic purpose, she underwent lymph node resection and to our surprise, her condition improved.

Keywords: Castleman disease; Nonclonal heterogeneous group; Lymphoid tissue

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INTRODUCTION

Castleman disease (CD), first defined by Dr. Benjamin Castleman in 1950s, is a rare lympho-proliferative disorder that may present with systemic symptoms.¹ Its spectrum extends from autoimmune conditions including rheumatoid arthritis, SLE and juvenile idiopathic arthritis to malignancies including sarcoma, lymphoma and POEMS (Polyneuropathy, Organomegaly, Endocrinopathy, Monoclonal gammopathy and Skin changes) syndrome.²

Systemic lupus erythematosus (SLE) is a chronic, complex, autoimmune disease involving multiple systems, characterized by a wide range of clinical manifestations. There are two mainly used criteria for the diagnosis of SLE; ACR and SLICC criteria. Both of these criteria have clinical and immunological components; both are required for diagnosis.³ In SLE patients, there are multiple autoantibodies which could be found in the serum. One of the components of immunological criteria for the diagnosis of SLE is the presence of antinuclear antibody (ANA), but ANA testing can sometimes be sensitive as low as 70%, especially in the start of disease.⁴

Both, SLE and Castleman disease are multisystem disorders. SLE has been recognized as a possible risk factor for the development of lymphoma, a condition manifested by lymphadenopathy, resembling Castleman disease.⁵ Hence, for individuals diagnosed with SLE and exhibiting lymphadenopathy, it is essential to undergo a comprehensive evaluation to rule out the possibility of any other associated disease like Castleman disease. Although, both

Castleman disease and SLE can have lymphadenopathy, these diseases have distinct aetiologies and are treated in different ways. These two distinct medical entities, each possessing its own unique challenges, converge to create a diagnostic and therapeutic conundrum.

CASE PRESENTATION

A 40-year-old female presented to Nephrology OPD of Bahawal Victoria Hospital, Bahawalpur in November 2019 with complaints of fever (intermittent, low grade, associated with arthralgias and oral ulcers, and relieved by antipyretics) and generalized body swellings (started from feet then became generalized) for 2 months. She was known hypertensive for the last 3 years and was not taking any regular medication for hypertension. She also had a history of Raynaud's phenomenon and photosensitivity for the past 2 years. On general physical examination, she had pallor, periorbital puffiness and bilateral pedal oedema. Her vitals were; BP 140/90 mmHg, Pulse 86 bpm, Temperature 99 F and Respiratory rate 18/min. On chest auscultation, she had bilateral decreased breath sounds on lung bases. Her abdomen was soft, distended and non-tender. Rest of the examination was unremarkable.

Regarding laboratory investigations, her CBC revealed; Hb 9 g/dl, TLC 10,500 per ul, platelets 150,000 per ul. RFTs were within normal range. Urinalysis showed; 2+ protein and 1–2 WBCs. Serum albumin was 2.4 g/dl and serum cholesterol was 246 mg/dl. 24-hour urinary protein was 2.5 g. ANA was 1:160 (normal value <1:80) and Anti ds DNA was 12

U/ml (normal value <6 U/ml). She had low complement levels and her ESR was 52 mm per hour. Her viral markers were negative for Hepatitis B, Hepatitis C and HIV. Ultrasound abdomen revealed bilateral normal sized kidneys and moderate abdominal ascites. She was managed conservatively and ultrasound guided renal biopsy was performed which showed lupus nephritis class IV+V (active/chronic). She was diagnosed as a case of SLE with lupus nephritis and treated with mycophenolate mofetil 1000 mg BD and tapered dose of oral prednisolone.

On follow up after 3 months, her body swellings resolved significantly. Her dipstick urinalysis showed no proteinuria and spot urinary PCR was 0.49. However, MMF was continued for the maintenance of remission. She remained in remission and asymptomatic, so she stopped taking MMF after 2 years (in 2021). She did not continue follow up with us during that period.

In March 2022, she was admitted in another hospital with complaints of fever, dry cough, facial puffiness, frothy urine, hair loss and joint pains. She was given solumedrol pulse therapy and discharged on MMF and prednisolone which she took for 6 months but her fever was not relieved. She again presented to us in October 2022 with complaints of fever (high grade, intermittent in nature and associated with enlarged cervical lymph nodes, fatigue and weight loss). She had visited multiple doctors in past couple of months for fever and was treated with antibiotics and antipyretics with no significant response. Her physical examination revealed few enlarged cervical lymph nodes (right anterior cervical group more prominent) and temperature of 102 °F. Her abdomen was soft and non-tender with mild hepatosplenomegaly. Rest of the systemic examination was unremarkable.

Routine blood tests revealed a TLC of 18000 per ul and raised ESR and CRP. Microbial cultures (blood, urine, nasopharyngeal and throat swabs) were negative and complement level was normal. USG abdomen showed moderate hepatomegaly with fatty liver, moderate splenomegaly and mild ascites. USG neck confirmed bilateral cervical lymphadenopathy. She was commenced on antibiotics empirically but fever and inflammatory markers persisted. After much consideration, excision biopsy of cervical lymph nodes was performed. After removal of her cervical lymph nodes, her fever settled. Later on, her lymph node biopsy report came which showed Castleman disease.

Thus, a diagnosis of unicentric Castleman disease overlapping with SLE was made and MMF and prednisolone were continued. On her next visit, her condition had significantly improved and she had

gained some weight. We are regularly following the patient and she is doing well thus far.

DISCUSSION

Castleman disease (CD) has mainly two types; unicentric in which there is localized enlargement of lymph nodes and has minimal symptoms and multicentric in which there is involvement of both lymph nodes and lymphoid organs and has variable symptoms.⁶ Unicentric CD has an excellent prognosis, whereas multicentric CD being a systemic disease, commonly manifests as anaemia, diffuse lymphadenopathy, splenomegaly and systemic inflammatory symptoms.⁷ Regarding pathogenesis, unicentric CD is thought to have a clonal neoplastic etiology and most likely, the origin is stromal, more specifically the follicular dendritic cell.⁸ Whereas, viruses like Human Herpesvirus 8 are likely the etiological factors in multicentric CD, while some patients have idiopathic multicentric CD.⁹

There can be an association between unicentric CD and SLE but the frequency of co-occurrence of CD and SLE is probably under-reported as lymphadenopathy is a common feature in the patients of SLE and these lymph nodes are usually not examined systematically.¹⁰ Multisystem involvement is seen not only in SLE but also in other conditions such as general infections, systemic vasculitis and lymphoproliferative conditions like CD. Therefore, CD can mimic SLE in various ways.¹¹

Our case report discusses the complex presentation of a middle-aged female who was initially diagnosed with systemic lupus erythematosus (SLE) and lupus nephritis. Despite achieving remission with mycophenolate mofetil and prednisolone for lupus nephritis, she relapsed with fever and lymphadenopathy. This later presentation mimicked SLE by its constitutional symptoms but the differentiating feature was persistence of fever despite high dose solumedrol therapy initially. A subsequent excision biopsy revealed Castleman disease, and continued immunosuppressive therapy led to symptom resolution.

Although, a multidisciplinary approach can be used for the diagnosis of SLE and Castleman disease, which involves a careful evaluation by the rheumatologist and haematologist, our patient did not get assessed by a rheumatologist or oncologist. Rather, the diagnosis of SLE was made on the basis of fulfilment of clinical and immunological components of SLICC and ACR criteria. Similarly, Castleman disease was identified on lymph node biopsy. She did not undergo further investigations for the staging of Castleman disease. HHV-8, being related to the Castleman disease, needs to be excluded in these

patients. Unfortunately, HHV-8 serology was not performed in our case.

This case highlights the importance of considering Castleman disease in SLE patients with recurrent fever and lymphadenopathy, even when initial lupus treatment appears effective. The diagnostic challenge posed by overlapping clinical features highlights the critical role of histopathological evaluation in guiding appropriate management strategies.

CONCLUSION

Although lymphadenopathy is a common feature shared by both Castleman illness and SLE, these diseases differ in their etiologies and are treated differently. As lymph node biopsy is rarely performed for the diagnosis of SLE, it makes it very difficult to differentiate between these two conditions. There is a need to understand how to distinguish between these conditions so that risks of treatment intensification could be avoided.

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