Annals of Arthritis and Clinical Rheumatology

Case Report
Published: 05 Jul, 2021

Overlap Syndrome: Dermatomyositis and Systemic Lupus Erythematosus with Cerebral Lupus and Autoimmune Hepatitis: A Case Report

Sulaiman W[1,2], Subramaniam R[1], Sarkan MM[2] and Samhari AA[3]*

[1]Universiti Kuala Lumpur Royal College of Medicine, Malaysia

[2]Perak Community Specialist Hospital, Malaysia

[3]Bone and Joint Specialist, Pusat Bandar Seberang Jaya, 13600, Seberang Perai, Malaysia

[4]Department of Dermatology, Raja Permaisuri Bainun Hospital, Ipoh, Malaysia

Abstract

Dermatomyositis (DM), a rare autoimmune disorder, is a subtype of Idiopathic Inflammatory Myositis (IIM) characterized by classical cutaneous lesions with increased muscle enzyme creatinine kinase. DM has been reported to overlap with other rheumatic diseases, mainly with systemic sclerosis. Data of coexistence of DM and Systemic Lupus Erythematosus (SLE) was however limited. Herein, we described a young girl with overlap severe DM and SLE with mixed cutaneous lesions complicated by lupus cerebritis and hepatitis. The patient fulfilled the American College Rheumatology (ACR) Classification Criteria for SLE 2012 and Systemic Lupus International Collaboration Clinics (SLICC) 2012, and Bohan and Peter criteria for DM. Patient was given the combination treatment of corticosteroid and immunosuppressant and responded well. Our case reported highlighted the rare and complicated overlap autoimmune disorders of DM and SLE, which is yet to be reported in our region. Our case report may help aid early recognition of the overlapping of DM and SLE may provide useful information for a future encounter.

Keywords: Dermatomyositis; Systemic Lupus Erythematosus; Overlap syndrome; Lupus cerebritis; Hepatitis

OPEN ACCESS

Correspondence:
Wahinuddin Sulaiman, Universiti Kuala Lumpur Royal College of Medicine Perak, No. 3, Jalan Greentown, 30450 Ipoh, Malaysia, Tel: 60129289790; E-mail: wahinuddin@unikl.edu.my

Received Date: *03 Jun 2021*
Accepted Date: *30 Jun 2021*
Published Date: *05 Jul 2021*

Citation:
Sulaiman W, Subramaniam R, Sarkan MM, Samhari AA. Overlap Syndrome: Dermatomyositis and Systemic Lupus Erythematosus with Cerebral Lupus and Autoimmune Hepatitis: A Case Report. Ann Arthritis Clin Rheumatol. 2021; 4(1): 1023.

Introduction

Juvenile Dermatomyositis (JDM), subtype of inflammatory myopathies, is a rare autoimmune disorder characterized by cutaneous lesions in most cases, muscle weakness with raised Creatinine Kinase (CK) [1]. JDM as in Dermatomyositis (DM) is a heterogeneous disorder with various clinical phenotypes and clinical outcomes. DM can appear alone or associated with other autoimmune diseases. Literatures reported to commonest association with systemic sclerosis compared to Systemic Lupus Erythematosus (SLE), Rheumatoid Arthritis (RA), and Sjogrën syndrome in patients with DM [2]. Very little information is available in patients diagnosed with co-existence of DM and SLE, as myositis relatively uncommon compared to myalgia [3]. Each disease entity must fulfill the classification criteria, i.e. Bohan and Peter criteria for DM and ACR/SLICC for SLE before being labeled as overlap syndrome [4-7]. Identification of autoantibodies in both JDM and SLE to delineate the phenotypic refinement. We reported a young girl presented with classical DM and overlapping with SLE which was complicated by hepatitis and cerebritis.

Case Presentation

A 17-year-old girl, who was previously well, presented with one month of progressive weakness of both lower limbs but was however, able to ambulate with some difficulty. Furthermore, patient has no history of seizures episodes. Her weakness worsened and noted to be inactive and was subsequently hospitalized due to the development of erythematosus rash over the face, palmar and plantar surfaces, fever, and nausea, shortness of breath, non-productive cough, and pain over both thighs. No clinical manifestation of urinary symptoms, abdominal pain, odynophagia, and visual disturbances was observed.

During hospitalization, patient appeared apathy but orientated. Peri-orbital edema with a violaceous maculopapular rash on the malar and supra orbital region with a heliotrope rash was

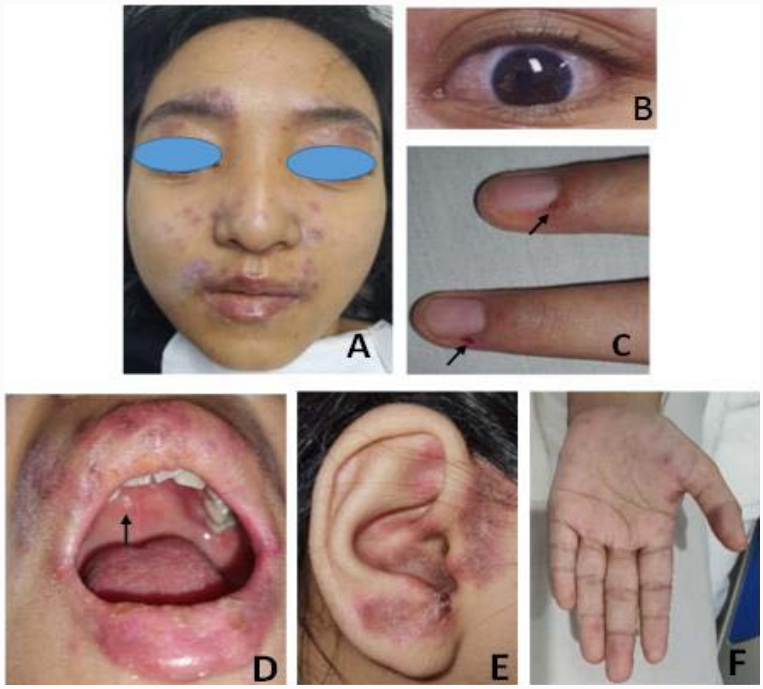

Figure 1: A) Violaceous erythematous rash on the face with a heliotrope rash, B) Episcleritis in eyes, C) Periungual telangiectasia, D) Multiple oral mucosal ulcers with thrush (arrow), E) Discoid rash on both ears, F) Vasculitic rash on the palms.

observed. Vasculitis was noted only on the palms, whilst discoid rash on both ears, but none was observed on the scalp. In addition, the patient also presented bilateral scleritis, oral ulcers with thrush, and periungual edema, and splinter hemorrhage (Figure 1). Coarse crackles were heard in the lower and middle zones of the left lung and lower zone of the right lung. There was no alopecia, Gottron's papules, shawl, or V-signs present. Tenderness was elicited on the quadriceps of the patient with a marked weakness of motor power of grade i.e., three out of five based on the Medical Research Council (MRC) Scale.

Laboratory investigations reveals an elevated serum level of Creatinine Kinase (CK), 14,548 U/L (normal, 44 to 147 U/L), Alanine Transaminase (ALT), 307 U/L (normal, 4 to 34), Aspartate Transaminase (AST), 1,000 U/L (normal, 0 to 26), and ferritin, 5,428 ug/L (normal, 10.0 to 291.0). The inflammatory markers i.e. C-Reactive Protein (CRP) and Erythrocyte Sedimentation Rate (ESR) were 2.7 mg/L and 24 mm/h, respectively. Serum aldolase, however, was not done. Urinalysis data demonstrated the presence of red blood cells 6 u/L, and protein 1.0 g/L, and no myoglobinuria. The Anti-Nuclear Antibody (ANA) was positive with a titer of 1:1280 and homogenous pattern, anti-double-stranded Deoxyribonucleic Acid (ds DNA) antibody-positive with titer >320 U/L. Patient was however negative for Rheumatoid Factor (RF), and Extractable Nuclear Antigen (ENA) (i.e., anti-Sm, anti U1RNP, anti-Jo1, anti Scl70, anti-SSA (Ro), and anti-SSB (La)). The Direct Anti Globulin Test (DAT) was positive (Table 1). The qualitative tests for Myositis-Specific Antibody (MSA) and myositis-associated autoantibody revealed a borderline positive for anti-M2 alpha and anti-M2 beta biomarkers. Tumor markers (i.e., alpha-Feto protein, 26.6 ug/L; CEA, 0.9 ug/L; CA 19-9, 32.1 U/mL; CA125, 13.1 U/mL, and CA15-3, 29.4 U/mL) were normal. Hepatitis B surface antigen (HBsAg), hepatitis C virus antibody, Human Immunodeficiency Virus (HIV), and Coronavirus 2019 (COVID-19) PCR screening were negative.

Magnetic Resonance Imaging (MRI) of the brain and the thigh muscles reveals the right cerebro-occipital cerebritis (Figure 2) and consistent with vasculitis and myositis changes respectively (Figure 3). The High-Resolution Computed Tomography (HRCT) showed minimal thickening of pleura at the bases of the lung. The abdominal ultrasound was unremarkable. However, muscle biopsy and electromyography were not performed in this patient. Patient was treated with intravenous methylprednisolone 1 gm daily for three days followed by oral prednisolone 60 mg daily (1 mg/kg/day). Subsequently, hydroxy chloroquine 200 mg daily, nystatin oral suspension 100,000 units, mycophenolate mofetil 500 mg twice daily, and cyclosporine 50 mg twice daily (0.8 mg/kg/day) were added. Upon completion of pulse IV methylprednisolone, the CK level decreased to 4281 U/L, and AST decreased to 754 U/L), whilst an increase serum level was observed for ALT (347 U/L). Serum ferritin decreased to 2189.9 ug/L. However, the CRP level remained normal (1.1 mg/L).

Patient was discharged after two weeks hospitalization without proximal myopathy, and discoid rash on both ears resolved gradually. Her scleritis, rashes and pulmonary crackles were completely resolved. Patient was alert and has regained her muscle power to ambulate without assistance. No complication in lung was observed. The serum level of laboratory parameters was as followed: CK was 108 U/L, LDH 356 U/L, serum ferritin 307.2 ug/L, ALT 38 U/L, AST 121 U/L and GGT 727 U/L, ESR 55 mm/h, and CRP 19.5 mg/L. The combination treatment of corticosteroid and immunosuppression was continued, and patient has been remaining in remission without any signs of relapse.

Discussion

We reported a young female patient aged 17 years old with distinctive features of both DM and SLE, who were diagnosed based on the clinically and serologically criteria of the respective Bohan

Table 1: Laboratory results on admission.

Complete blood count		**Serological tests**	
Hemoglobin (g/dL)	12.3 (12–16)	CRP (mg/L)	2.7 (<5.0)
Hematocrit, %	39 (36–46)	ESR (mm/hr)	24 (<38)
White blood cells (x 10^9/L)	9.4 (4.0–11.0)	C3 (mg/dL)	36 (92–180)
N, %	82.3 (40–75)	C4 (mg/dL)	14 (11–40)
L, %	12.3 (20–45)	DAT	Positive
M, %	5.2 (2.0–10.0)	**Immunology**	
Platelet (x 10^9/L)	285 (150–400)	ANA	1:1280 (Homogenous)
Biochemistry		Anti-ds DNA	Positive >320
Total protein (g/L)	60 (64-86)	Anti-SS A antibody	Negative
Albumin (g/L)	24 (38-56)	Anti-SS B antibody	Negative
Globulin (g/L)	36	Anti-Jo1 antibody	Negative
Total bilirubin (umol/ L)	10.5	Anti-Mi-2 alpha	Borderline positive
ALP (U/L)	139 (82–169)	Anti-Mi-2 beta	Borderline positive
AST (U/L)	1000 (0–26)	**Microbiological test**	
ALT (U/L)	307 (4–34)	Blood culture	Negative
GGT (U/L)	402 (5–19)	**Urinalysis**	
LDH	n.d.	Color	Clear
Creatinine kinase (U/L)	14,582 (28-142)	Protein	1.0 g/L
Creatinine (umol/L)	85 (40–100)	Red blood cell	6/hpf
BUN (umol/L)	6.7 (3.2–7.5)	White blood cell	nil
Sodium (mmol/L)	120 (132–141)	Urine for myoglobin	Negative
Aldolase	n.d		
Ferritin (ug/L)	5,428 (10.0– 291.0)		

Abbreviation: N: Neutrophil; L: Lymphocyte; M: Monocyte; ALP: Alkaline Phosphatase; AST: Aspartate Transaminase; ALT: Alanine Transaminase; GGT: Gamma-Glutamyl Transpeptidase; LDH: Lactate Dehydrogenase; BUN: Blood Urea Nitrogen; CRP: C-Reactive Protein; ESR: Erythrocyte Sedimentation Rate; C3: Complement 3; C4: Complement 4; DAT: Direct Antiglobulin Test; ANA: Anti-Nuclear Antibody; dsDNA: double-stranded Deoxyribonucleic Acid Antibody; n.d: not done

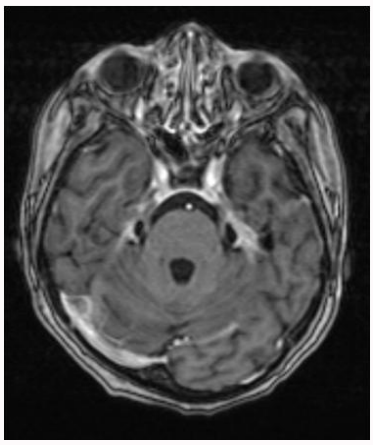

Figure 2: T1 weighted MRI showing hyperintense at the right cerebro-occipital area suggestive of vasculitis.

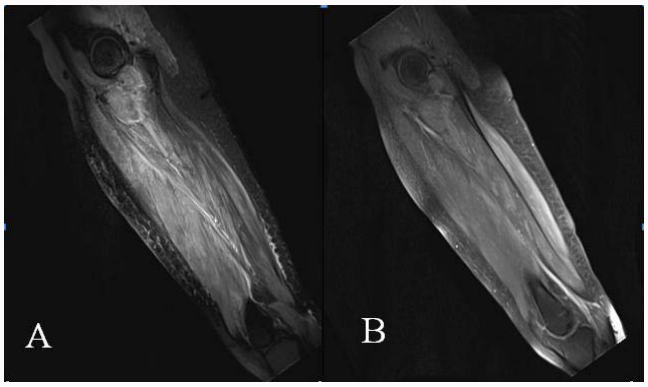

Figure 3: MRI of the right (A) and left (B) femur showing hyper vascularization in the subcutaneous layer bilaterally. Minimal free fluid noted in the posterior soft tissue just above the knee joints, extending to the skin.

and Peter, and ACR/SLICC classification criteria. To the best of our knowledge, there have been no reported literatures of the overlapped DM and SLE developed simultaneously and complicated by lupus cerebritis and hepatitis at the onset of presentation. The co-existence of both entities may be indistinguishable due to shared common features.

The association between DM and autoimmune diseases has been described in the literature and systemic sclerosis was reported to most common. The presence of mixed clinical and laboratory markers with distinctive clinical features defined the overlapped nature of these autoimmune diseases. The incidence of myositis is low (4% to 16%) in patients with SLE, compared to myalgia (50% to 80%) [8,9]. The association between myositis and SLE, however, is rare, although the former may occur before, after, or coexisting with SLE [10-13].

Previously, it has been reported cases of DM with characteristic cutaneous phenotype, with normal CK (clinically amyopathic), which is commonly associated with the presence of anti-Melanoma

Differentiation-Association gene 5 (MDA5) antibody, overlapped with SLE which may develop much later [14]. It is notably that cutaneous lupus may be indistinguishable from DM clinically and histologically as in a previous case report of anti-MDA5 antibody associated with rapidly progressive interstitial lung disease [15]. In contrast to this patient whom CK was markedly raised with the presence of anti-Mi 2 alpha and beta antibodies although it was borderline positive qualitatively.

Anti-Mi2 autoantibody is associated with classical DM, and patients are often presence with severe muscle disease and low incidence of other organs involvement [16]. In patients with DM, only 4% to 10% of anti-Mi2 was reported. Nevertheless, the prognosis of DM patient is good as a patient usually responded to the conventional treatment [17]. Anti-U1RNP antibody is commonly found in patients with lupus and/or Mixed Connective Tissue Disease (MCTD), is also typically identified in 4% to 6% of DM [1]. However, this autoantibody was not detected in this patient.

In patients with SLE, the presence of lupus cerebritis is well-known associated systemic manifestations or complications, which has not been described in patients with DM. While co-existence liver involvement or Auto Immune Hepatitis (AIH) in SLE without prior exposure to hepatotoxic agent or viral hepatitis is rarely reported, and usually identified by raised liver enzymes at presentation [18,19]. This patient illustrated similar findings although Immunoglobulin G (IgG) level, histological evidence was not available which is part of the International Autoimmune Hepatitis Group Criteria [20]. Common serological markers i.e. ANA, anti-dsDNA antibodies are present in both SLE and AIH. Hepatic histopathological evidence of AIH remains as an important diagnostic tool to distinguish between both conditions although there are specific biomarkers for AIH available [21]. In contrary, hepatitis in DM has been commonly associated with hepatitis B or C viruses which lead to hepatocellular carcinoma [22]. Thus, close surveillance is important in this patient despite absence of such evidence at presentation.

Lupus cerebritis has been a diagnostic conundrum due to its heterogeneous neurological manifestations from non-specific to severe symptoms which occur in 16% of SLE patients [23,24]. Cerebral vasculitis has not been reported in DM alone but usually in association with lupus. Clinical assessment with ancillary laboratory and radio imaging, although it is not diagnostic, may facilitate the diagnosis as shown by this patient.

We concluded that early recognition of this rare overlap of DM and SLE with the presence of specific autoantibodies is important as it responds well to standard conventional immunosuppressants. Myositis autoantibody test should be considered in patient with SLE. The current availability of qualitative measurement of myositis auto antibody helps in prognosticates the underlying disorder though. Nevertheless, long-term surveillance is required to assess the vulnerability of both conditions towards undesirable complications.

References

1. Mendez EP, Lipton R, Ramsey-Goldman R, Roettcher P, Bowyer S, Dyer A, et al. US incidence of juvenile dermatomyositis, 1995-1998: results from the National Institute of Arthritis and Musculoskeletal and Skin Diseases Registry. 2003;49(3):300-5.
2. Pearson CM, Bohan A. The spectrum of polymyositis and dermatomyositis. Med Clin North Am. 1977;61(2):439-57.
3. Garton MJ, Isenberg DA. Clinical features of lupus myositis versus idiopathic myositis: A review of 30 cases. Br J Rheumatol. 1997;36(10):1067-74.
4. Bohan A, Peter JB. Polymyositis and dermatomyositis (first of two parts). N Engl J Med. 1975;292(7):344-7.
5. Bohan A, Peter JB. Polymyositis and dermatomyositis (second of two parts). N Engl J Med. 1975;292(8):403-7.
6. Aringer M, Costenbader K, Daikh D, Brinks R, Mosca M, Ramsey-Goldman R, et al. 2019 European League Against Rheumatism/American College of Rheumatology classification criteria for systemic lupus erythematosus. Ann Rheum Dis. 2019;78(9):1151-9.
7. Petri M, Orbai AM, Alarcón GS, Gordon C, Merrill JT, Fortin PR, et al. Derivation and validation of the systemic lupus international collaborating clinics classification criteria for systemic lupus erythematosus. Arthritis Rheum. 2012;64(8):2677-86.
8. Atzeni F, Cazzola M, Benucci M, Di Franco M, Salaffi F, Sarzi-Puttini P. Chronic widespread pain in the spectrum of rheumatological diseases. Best Pract Res Clin Rheumatol. 2011;25(2):165-71.
9. Di Franco M, Guzzo MP, Spinelli FR, Atzeni F, Sarzi-Puttini P, Conti F, et al. Pain and systemic lupus erythematosus. Reumatismo. 2014;66(1):33-8.
10. Maazoun F, Frikha F, Snoussi M, Kaddour N, Masmoudi H, Bahloul Z. Systemic lupus erythematosusmyositis overlap syndrome: Report of 6 cases. Clin Pract. 2011;1(4):e89.
11. Rostić G, Paunić Z, Vojvodić D, Petronijević M, Glisić B, Stefanović D, et al. Systemic lupus erythematosus and dermatomyositis-case report. Srp Arh Celok Lek. 2005;133(Suppl 2):137–40.
12. Isenberg DA, Snaith ML. Muscle disease in SLE: A study of its nature, frequency and course. J Rheumatol. 1981;8:917–24.
13. Dayal NA, Isenberg DA. SLE/myositis overlap: Are the manifestations of SLE different in overlap disease? Lupus. 2002;11(5):293-8.
14. Milam EC, Futran J, Granks Jr AG. Anti-MDA5 antibody dermatomyositis overlap with systemic lupus erythematosus: A case report and review of the literature. Open Rheumatol J. 2016;10:122–8.
15. Huang Y, Mao M. Rapidly progressive interstitial lung disease originating from clinically amyopathic dermatomyositis associated with positive anti-MDA 5 antibody: A case report and literature review. SN Compr Clin Med. 2019;1:915–20.
16. Petri MH, Satoh M, Martin-Marquez BT, Vargas-Ramírez R, Jara LJ, Saavedra MA, et al. Implications in the difference of anti-Mi-2 and -p155/140 autoantibody prevalence in two dermatomyositis cohorts from Mexico City and Guadalajara. Arthritis Res Ther. 2013;15(2): R48.
17. Tansley SL, Simou S, Shaddick G, Betteridge ZE, Almeida B, Gunawardena H, et al. Autoantibodies in juvenile-onset myositis: Their diagnostic value and associated clinical phenotype in a large UK cohort. J Autoimmun. 2017;84:55-64.
18. Runyon BA, LaBrecque DR, Anuras S. The spectrum of liver disease in systemic lupus erythematosus. Report of 33 histologically proved cases and review of the literature. Am J Med. 1980;69(2):187-94.
19. Beisel C, Weiler-Normann C, Teufel A, Lohse AW. Association of autoimmune hepatitis and systemic lupus erythematodes: A case series and review of the literature. World J Gastroenterol. 2014;20(35):12662-7.
20. Alvarez F, Berg PA, Bianchi FB, Bianchi L, Burroughs AK, Cancado EL, et al. International autoimmune hepatitis group report: Review of criteria for diagnosis of autoimmune hepatitis. J Hepatol. 1999;31(5):929-38.
21. Lohse AW, Mieli-Vergani G. Review autoimmune hepatitis. J Hepatol. 2011;55(1):171-82.
22. Han J, Wang S, Kwong TNY, Liu J. Dermatomyositis as an extra hepatic manifestation of hepatitis B virus-related hepatocellular carcinoma: A case report and literature review. Medicine(Baltimore). 2018;97(33):e11586.

23. Kajs-Wyllie M. Lupus cerebritis: A case study. J Neurosci Nurs. 2002;34(4):176-83.

24. Goswami D, Chatterjee S, Ahmad BI, Das S. Two case reports indicating the dilemma in diagnosing lupus cerebritis. J Family Med Prim Care. 2013;2(1):111-14.