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Case Report

Systemic lupus erythematosus presenting as toxic epidermal necrolysis: a case report

Jaskirat Kaur Sandhu[1], Seema Rai[1], Kirat Kaur Sandhu[2]*

[1]Department of Pediatrics, Guru Gobind Singh Medical College and Hospital, Faridkot, Punjab, India
[2]DD Eye Institute and Lasik Laser Center, Kota, Rajasthan, India

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***Correspondence:**
Dr. Kirat Kaur Sandhu,
E-mail: jaski1989@gmail.com

ABSTRACT

Systemic lupus erythematosus is an autoimmune inflammatory disease with complex etiology. Stevens-Johnson syndrome (SJS)/toxic epidermal necrolysis (TEN) represent a spectrum of skin lesions characterized by rashes, exfoliation, and sloughing usually following drug intake. Occasionally, TEN-like cutaneous manifestations have also been described with systemic lupus erythematosus. Recognition of lupus in a child presenting with TEN-like skin changes is clinically challenging and requires a high degree of suspicion. We present a case of a 9-year-old female with SJS/TEN like lesions following drug intake and on evaluation was found to have systemic lupus erythematosus.

Keywords: Epidermis, Lupus erythematosus, Cutaneous, Blister, Autoimmune

INTRODUCTION

Systemic lupus erythematosus is a prototypic autoimmune disease characterized by the production of antibodies to components of cell nucleus.[1] The exact etiology of SLE remains elusive. An extremely complicated and multifactorial interaction among various genetic and environmental factors is probably involved. The primary pathological findings are those of inflammation, vasculitis, immune complex deposition and vasculopathy.[2] SLE is heterogenous in presentation, with a broad spectrum of clinical manifestations ranging from mild self-resolving symptoms to severe life-threatening organ involvement.

The improved classification criteria used by European league against rheumatism (EULAR) and American College of Rheumatology (ACR) serve as the most precise and advanced criteria to date for the diagnosis of SLE.[3] Toxic epidemal necrolysis is a potentially life-threatening acute muco-cutaneous syndrome, which usually occurs as a reaction to certain drugs. It is characterized by keratinocyte necrosis with separation of epidermis from underlying dermis.[4] While SJS/TEN is rare, cases of SJS/TEN combined with SLE are even less common. The TEN-like presentation of SLE is believed to occur in patients with subacute or acute cutaneous lupus erythematosus that typically develops features of TEN with unusual subacute progression and apparent absence of high-risk drug ingestion. Differentiating between classic drug-induced TEN and TEN-like cutaneous lupus is difficult but important. Here we present a case of a 9-year-old female who initially presented to us with severe anemia and congestive cardiac failure. She was etiologically diagnosed to have autoimmune hemolysis. Subsequently, she came with widespread bullous lesions all over the body and face, along with mucosal involvement without any history of drug intake. She was found to have underlying systemic lupus erythematosus on workup.

CASE REPORT

A 9-year-old female child came to the emergency with complaint of multiple fluid filled lesions all over the body since last 3 days. The child was not well for the past 1

month when she was having fever on and off as per the parents. It was not documented but was found to be low grade. The patient took various medications from the local practitioners for the complaint of fever. She was previously admitted 20 days prior to the current admission with severe anemia and features of congestive cardiac failure. The diagnostic workup for anemia revealed evidence of hemolysis (DCT 3+) along with mild depression of other cell lines. Bone marrow examination was planned but couldn't be done because of non-consenting parents. Blood transfusion was given uneventfully and she was given oral steroids (prednisolone @2 mg/kg/day) for 5 days, following which there was improvement in anemia. 10 days prior to the current admission, patient developed raised red lesions first on the face and then progressed to the trunk, arms, hands and legs. She also developed red raw areas on the lips and in oral cavity which led to difficulty in opening the mouth and swallowing of food. The lesions progressed to develop fluid filled blisters all over the body over the last 3 days prior to the current admission.

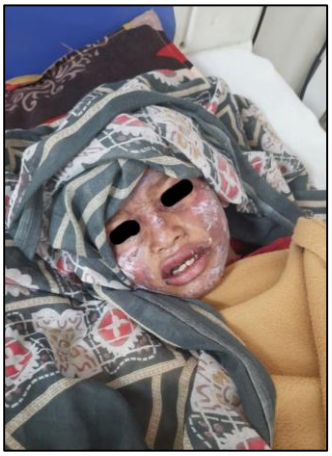

Figure 1: Patient with characteristic lesions over the face, predominantly on the cheeks and bridge of the nose, with swelling and crusting of the lips, angular cheilitis and gum bleeds.

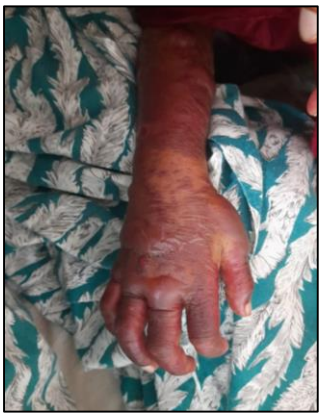

Figure 2: Patient with fluid filled blisters on the hands.

Table 1: Clinical domians.

Clinical domains	Points
Constitutional domain	
Fever	2
Cutaneous domain	
Non scarring alopecia	2
Oral ulcers	2
Subacute cutaneous or discoid lupus	4
Acute cutaneous lupus	6
Arthritis domain	
Synovitis or tenderness in atleast 2 joints	6
Neurologic domain	
Delirium	2
Psychosis	3
Seizures	5
Serositis domain	
Pleural or pericardial effusion	5
Acute pericarditis	6
Hematologic domain	
Leucopenia	3
Thrombocytopenia	4
Autoimmune hemolytic anemia	4
Renal domain	
Proteinuria >0.5 gm/day	4
Class 2 or 5 lupus nephritis	8
Class 3 or 4 lupus nephritis	10

Table 2: Immunologic domains.

Immunologic domains	Points
Antiphospholipid antibody domain Anticardiolipin IgG >40 GPL Or anti-ß2GP1 IgG >40 units Or lupus anticoagulant	2
Complement proteins domain	
Low C3 or low C4	3
Low C3 and low C4	4
Highly specific antibodies domain	6
Anti-dsDNA antibody or	6
Anti-Sm antibody	

On examination of the patient during current admission, her body temperature was 37.8 degree celsius, pulse rate 120/min, blood pressure 106/70 mm Hg and SpO2 98% on room air. She was pale but there was no icterus, clubbing, cyanosis or lymphadenoapthy. The primary lesions were macula-papular, purpuric along with fluid filled bullae which had involved the face, trunk, arms, legs and feet, amounting to 60% of the body surface area. There was ulceration of oral mucosa along with bleeding from the gums and presence of hard palate ulcers. Secondarily, the lesions showed erosion and crusting over some parts of the body. Pseudo Nikolsky's sign was found to be positive. Skin biopsy on Tzanck smear examination revealed mainly inflammatory infiltrates comprising of lymphocytes, neutrophils, few cystic macrophages and rare acantholytic cells. The patient was

diagnosed as toxic epidermal necrolysis and was started on supportive management. Routine investigations were done which showed pancytopenia (Hb 7.6 g/dl, TLC 1700 and platelets 60000). In view of the presence of fever, hard palate ulcers and pancytopenia along with the past history suggestive of autoimmune hemolysis, the workup for systemic lupus erythematosus was planned. There was no joint involvement or any neurological manifestations. Bedside 2D echocardiography didn't reveal any pleural or pericardial effusion. 24 hours urine protein was found to be 0.5 grams which was borderline high.

Table 3: Iinformation regarding the paediatric cases.

Case	Reference	Demo-graphics	ANA titre	Implicated drug	Treatment given	Outcome
1.	Samini SS	9 year/F	>1:640	Azithromycin	Steroids, immunosuppressors, plasma exchange	Improved
2.	Lee HY	12 year/F	1:800	Not known	Steroids, plasma exchange	Improved
3.	Marija S	14 year/F	1:640	Ampicillin, amikacin, metronidazole	Steroids, immunosuppressors	Died
4.	Yu J	15 year/F	Positive	Hydroxychloro-quine	Steroids, immunosuppressors, plasma exchange	Improved
5.	Yu J	11 year/F	Positive	Hydroxychloro-quine, mycophenolate mofetil, prednisolone	Steroids, immunosuppressors	Improved
6.	Jang	16 year/F	1:640	Not known	Steroids, plasma exchange	Improved

Immunological workup showed high ANA titres done by chemiluminescence immunoassay technique (9.7 test, negative <1.5). Anti dsDNA done by ELISA method was, however, found to be negative (0.87 test, reference cut off 0.90). Complement levels estimated by immunoturbidimetry were found to be low (Complement C3 0.31 gm/l, reference range 0.80-1.7 gm/l and complement C4 0.04 gm/l, reference range 0.12-0.36 gm/l). Thus, as per the new EULAR/ACR criteria for systemic lupus erythematosus, the patient scored 16 points, along with entry criterion of high ANA titres.

She was started on intravenous methylprednisolone @30 mg/kg/day along with intravenous antibiotics for secondary infections. After 5 days of intravenous steroids, patient's cutaneous lesions improved significantly. She was then shifted to oral prednisolone along with hydroxychloroquine. She was subsequently referred to higher centre for renal biopsy to rule out lupus nephritis.

DISCUSSION

This case study illustrates a rare presentation of systemic lupus erythematosus presenting as toxic epidermal necrolysis like picture in paediatric patients. SLE presenting as TEN is a rare manifestation in children. To provide context to this paper's presentation of a recent case of SJS/TEN with SLE, we reviewed relevant case studies, accessed via PubMed database. The keywords for search were Stevens-Johnson syndrome/Toxic epidermal necrolysis AND Systemic lupus erythematosus. The search covers all case studies published from 1985 to 2024. A total of 30 cases were collected, most of which were reported in adults and only 6 were in paediatric age group. Key information regarding the paediatric cases is presented in the Table 3.

As seen in the table, most of the patients had a suspected history of drug exposure before the onset of lesions and their treatment mainly consisted of glucocorticoids, immunosuppressors and plasma exchange. Patient in the current study also had history of drug ingestion (some unknown antipyretics) before the onset of lesions. The differentiation between lupus induced SJS/TEN and classical SJS/TEN is difficult clinically5. Lupus induced SJS/TEN generally has a subacute presentation of weeks without systemic involvement6. Classical TEN has acute evolution within days or sometimes hours, with close drug-related causality.[7] The histo-pathological hallmark is widespread epidermal necrolysis due to death by apoptosis of keratinocytes.[8]

Parperis et al, reviewed records of 30 patients diagnosed with autoimmune rheumatic diseases at an Arizona burn centre from January 2013 to December 2018 and showed that patients with autoimmune rheumatic diseases were more likely to develop SJS/TEN under the influence of a drug.[9] As no guidelines exist for the primary treatment of SJS/TEN, identification and discontinuation of offending medication(s) should be the priority. Attention should be given to adjuvant symptomatic support therapy, pain

management and prevention of secondary infections. Adjuvant therapy includes systemic steroids, immunosuppressants, tumor necrosis factor inhibitors, intravenous immunoglobulin and plasmapheresis. However, a recent meta-analysis suggests glucocorticoids and cyclosporine were the most promising systemic immunomodulating therapies for SJS/TEN.[10]

The patient described in this case report was not a diagnosed case of systemic lupus erythematosus but presented to us with toxic epidermal necrolysis like picture. She was then evaluated for SLE and was found to fulfil the EULAR/ACR diagnostic criteria.[11] She was managed symptomatically and received systemic steroids in pulse doses, after which she showed improvement of cutaneous lesions. Subsequently, she was continued on oral steroids for treatment of SLE.

CONCLUSION

We report a case of a patient who developed toxic epidermal necrolysis following drug exposure and was found to have systemic lupus erythematosus on evaluation. Clinical differentiation between drug induced toxic epidermal necrolysis and acute cutaneous lupus is difficult but important for the proper and timely management of such cases.

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