

*Case Report*

# Systemic lupus erythematosus bullosa: A case reported in the Internal Medicine Department of National Teaching Hospital, Cotonou

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**Introduction:** Systemic Lupus Erythematosus (SLE) is an autoimmune disease characterized by a severe damage of skin, joint visceral and hematology systems. Its diagnosis is based on the criteria of the American College of Rheumatology (ACR). The bullous form of lupus is rare; it is less than 5% of lupus cases. We hereby report a particular clinical case of bullous lupus. **Observations:** The patient was a 21-year old woman with sickle cell symptoms. She was admitted for etiological research on a long fever. There were reflection upon several diagnoses including SLE. After six months follow up, she developed diffuse vesicular bullous lesions prevailing at the perineum, abdomen and upper limbs, also affecting the buccal mucosa. Bullous lupus diagnosis was conducted based on Camisa and Sharma criteria. The choice of treatment is corticosteroid therapy and Dapsone. The patient developed steroid-resistant during her monitoring. Therefore, a single 100 mg daily dose of Dapsone was given. The progression revealed the incidence of hemolysis, complicated by severe anemia requiring transfusions. The alternative was Colchicine with slow but good response. **Conclusion:** Bullous Lupus is a rare form of SLE. Its treatment was note easy in our case. Colchicine has been the alternative, with quite slow reaction.

**Keywords:** Systemic Lupus Erythematosus, bullous form of Lupus, Internal Medicine, CNHU-HKM, Cotonou, Bénin.

## INTRODUCTION

Systemic Lupus Erythematosus (SLE) is an autoimmune disease characterized by a severe damage of skin, joint visceral (kidney, nervous and serous) and hematology systems (Meyer, 2005). Ranked among rare orphan diseases from the late 1980, systemic Lupus has been attracting more and more attention from clinicians (Lamoril et al., 2007; Ayme et al., 2007). It presents misleading clinical polymorphism. The diagnosis of SLE is based on a list of 11 clinical and biological criteria for classification, developed in 1982 by (Tan et al., 1982),

and updated in 1997 (Hochberg, 1997; Fujimoto, 2005) by the American Association of Rheumatology (AAR) and the American College of Rheumatology [6,7]. A minimum of 4 criteria are required to maintain the diagnosis with 96% sensitivity and specificity. The grouping of the main clinical symptoms help distinguish mild forms namely skin, joints and serous (pleura-pericarditis), and serious forms namely visceral, renal, neurological, hematologic (thrombocytopenia, hemolytic anemia) and thrombotic (Meyer, 2005). The bullous form of Lupus is rare and rep-

resents less than 5% (Sebaratnam et al., 2011; Hadj and Mernissi, 2013). We hereby report a particular clinical case of bullous Lupus.

## CASE PRESENTATION

The patient was a 21-year old woman with sickle cell symptoms. She was admitted in the Internal Medicine Department for etiological research on a long fever. There were reflection about several diagnoses particularly SLE, based on ACR criteria. This diagnosis was established in accordance with clinical arguments (discoid lesions on the face: **Picture 1**, poly-arthritis, long fever, pleurisy) and biological opinion (microcytic anemia, inflammatory syndrome with accelerated sedimentation rate at 90mm the first hour). SLE diagnosis was confirmed positive by the immunological test (antinuclear antibodies at 1/2560 with speckled fluorescence, and positive anti DNA native antibodies). Researching anti-zone antibodies of the basement membrane and inter-keratinocyte anti-substance as well as histopathology have not been possible due to our technical platform. The synthetic anti-malarial drugs, known as first line therapy were contraindicated in the case of this patient because of the presence of retinal vasculature. She was then put under corticosteroid therapy. The progression initially revealed very frequent relapses and steroid-dependence which motivated the use of methotrexate. After six months follow-up, she developed diffuse vesicular bullous lesions of different age and sizes prevailing at the perineum, abdomen and anus: **Picture 2**; at upper limbs, also affecting the buccal mucosa **Picture3**; the upper right eyelid is besieged by blepharitis **Picture 4**.

Laboratory tests reveal NFS normochromic normocytic anemia with hemoglobin at 8.7g/dl, white blood cells at 4.8g/l with lymphopenia at 0.744g/l and normal platelets at 228g/l. Proteinuria was negative.

Bullous Lupus diagnosis was established on the basis of Camisa and Sharma criteria. A total of five criteria were defined by Camisa and Sharma. In our case, the diagnosis of bullous Lupus is focused on the presence of two criteria (the diagnosis of SLE based on ACR and a vesicular bullous outbreak at both the exposed and unexposed areas). Treatment with Dapsone (DISULONE®) is then implemented.

The progression revealed significant regression of bullous lesions. The incidence of intravascular hemolysis with complicated severe anemia lead to stopping Dapsone. The patient was transfused and showed better improvement in clinical status. Colchicine was introduced later and showed slow but good response.

## DISCUSSION

Bullous Lupus is a rare manifestation of SLE. It concerns less than 5% of SLE patients (Hadj et al., 2013). The diagnosis is based on the criteria of Camisa and Sharma (1983). The diagnosis was established on 2 criteria out of a total of 5. Hundreds of cases are reported in the

literature (Lever, 1964). Young adults, generally in their thirties are the most concerned. However, few cases have been reported about female children of ten years Vijayalakshmi and Jayavardhana (2007). Our patient was 21 years old, which is far away from the thirties, and if bullous lupus has been reported about children of ten years, we can say that our patient was an intermediate age, meaning between ten and thirty. Clinical symptoms are vesicular bullous lesions, appearing on healthy skins, both on exposed and unexposed areas and disappearing without any scarring (Abreu Velez et al., 2013). In this particular case, the lesions were more localized on unexposed areas: the abdomen, buttocks, perineum, inner thigh, and the labial mucosa (inside of the lower lip). The upper right eyelid is besieged by blepharitis. These lesions generally occur on healthy skin. Hadj and Mernissien (2013) described a clinical case of Bullous Lupus in a man of 31 years. In this observation, the lesions occurred on a background of urticarial plaque on the torso and limbs. These lesions are grafted by vesicles grouped by location in the form of rosette. The vesicles were also grouped on the abdomen of our patient. He had no impaired renal function and proteinuria was negative. Nephropathy discovered by Iman Haj and Mernissi (2013) in their clinical case was related to SLE because renal biopsy was in favor of stage III Lupus Nephropathy.

Histopathologically, they are sub-epidermal bubbles with infiltrates of neutrophils and eosinophils polynucleus, and often epidermal leukocytoclastic vasculitis. Direct immune-fluorescence is generally positive with deposits of IgG or IgM and IgA at the dermo-epidermal junction Camisa and Grimwood (1986). Cleavage of the bubble is superficial and dermal in electronic microscopy. But considering our technical facilities, histopathology test could not be conducted. The diagnosis was based on clinical suspicion, meaning two Camisa and Sharma criteria (presence of SLE, and bullous lesions) out of 5. But the diagnosis of SLE was confirmed by immunological tests (antinuclear antibodies positive at 1/2560 with speckled fluorescence, and positive anti DNA native antibodies).

The main differential diagnoses are Acquired Epidermolysis Bullosa (AEB) where we find type VII anti collagen antibodies, other autoimmune bullous dermatosis, and bullous skin reactions. They are immunologically related diseases, but have different clinical presentations (Camisa and Grimwood, 1986; Harris-Stith et al., 2003). The AEB seemed less likely due to the absence of preferential impairment of trauma areas and changes without dystrophic scar. Rowell's syndrome is also discussed before the positive antinuclear antibodies speckled fluorescence, frostbite and positive anti-SSA but the skin lesions are not erythema multiform. In the absence of associated visceral impairment, knowing that no topical treatment can control the disease, bullous Lupus treatment is based on corticosteroids. Nevertheless, the therapeutic response to steroids is low, while



**Figure 1.** Discoid lupus of the face: combining: skin erythema, atrophy, and squame.



**Figure 2.** Bullous lesions of the anus.



**Figure 3.** Bullous lesions of buccal mucosa.



**Figure 4.** Blepharitis of the Upper right eyelid.

it is excellent when treatment is made by Dapsone (Abreu Velez et al., 2013)

Dapsone was discovered in 1908 and belongs to the sulfones category. It has been the standard leprosy treatment from the 1940. Its indications were later extended to other infections and in inflammatory dermatoses. Its indications are based on its antibiotic effects: leprosy, pneumocystis and calcineurin inhibitors: autoimmune bullous dermatosis, neutrophil dermatoses (Farhi et al., 2005).

Since our patient developed steroid-resistance, the only alternative was 100 mg/day Dapsone. Its bioavailability and long half-life allows a daily intake (Farhi et al., 2005). In Benin, Dapsone is prescribed in the treatment of leprosy. It is difficult to access when it is indicated in the

treatment of autoimmune pathologies. In our context, its use requires eliminating all causes of red blood cells weakness such as G6PD deficiency and sickle cell disease (Lorcy et al., 2011). Our patient had no G6PD deficiency, but she carries sickle cell symptoms. This is not in contraindication to Dapsone. The progression revealed significant regression of skin lesions and the incidence of intravascular hemolysis followed by anemia which led to stopping Dapsone and correcting anemia with blood transfusion. In fact, Dapsone is metabolized by two enzymatic pathways: N-acetylation and N-hydroxylation. Its N-hydroxylated metabolites are responsible for its dose-related side effects such as hemolysis and methemoglobinemia (Farhi et al., 2005). This may explain the hemolysis observed with our patient.

In case of contraindication or occurrence of side effects associated with Dapsone, the alternative is Colchicine or Sulfasalazine. The patient received Colchicine with a positive but slow response.

Bullous Lupus usually evolves chronically. Severe forms are treated with Cyclosporin and Rituximab. In the forms with visceral impairment, systemic corticosteroids are effective as observed by (Sarrot-Reynauld et al., 1997). (Hadj et al., 2013) in his case-study implemented as treatment: corticosteroid, hydroxichloroquine, and Endoxan bolus with good clinical outcome. Our patient is already steroid-dependent and increase of doses proved no effect on bullous lesions. Colchicine has been efficient albeit slow.

## CONCLUSION

Bullous lupus is a rare form of SLE. Particular attention is needed on the part of the clinician in monitoring SLE patients. Its treatment was not easy in our case with steroid-resistance developed by the patient and his response to Dapsone by hemolysis, hence its termination Colchicine has been the alternative in our case, though the therapeutic response was quite slow

## CONFLICTS OF INTERESTS

Authors Report no Conflict of Interest, and the permission of the patients has been  
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