

# Management of Secondary Lyell Syndrome Due to Anti-Covid Vaccine in a Case, at the Renaissance University Teaching Hospital, Ndjamen (CHAD)

Traoré Sory<sup>1</sup>, Adamou Abassi Mana<sup>1</sup>, Abdelsalam Hissein Hassan<sup>1</sup>, Kader Ndjaye<sup>2</sup>, Nouradine Abakar<sup>1</sup>, Abdesalam Mahamt Bahar<sup>2</sup>, Mahamat Ali Bolti<sup>3</sup>, Ngamai Kotyadé<sup>4</sup>, Mwabanyol Loohe Regis<sup>5</sup>, Michel Slama<sup>6</sup>, Hamit Mahamat Alio<sup>7,8\*</sup>

<sup>1</sup>Anesthesia-Resuscitation Department of the Renaissance University Teaching Hospital, N'Djamena, Chad

<sup>2</sup>Emergency Department of the N'Djamena Renaissance University Teaching Hospital, N'Djamena, Chad

<sup>3</sup>Internal Medicine Department, N'Djamena Renaissance University Teaching Hospital, N'Djamena, Chad

<sup>4</sup>Surgery Department of N'Djamena Renaissance University Teaching Hospital, N'Djamena, Chad

<sup>5</sup>Ophthalmology Department of the N'Djamena Renaissance University Teaching Hospital, N'Djamena, Chad

<sup>6</sup>Head of Resuscitation Department CHU Amiens-Picardie, Amiens, France

<sup>7</sup>Laboratory Department of the Renaissance University Teaching Hospital of N'Djamena, N'Djamena, Chad

<sup>8</sup>Faculty of Human Health Sciences of the University of N'Djamena, N'Djamena, Chad

Email: \*hamitalio@yahoo.fr, \*hamitalio@gmail.com

**How to cite this paper:** Sory, T., Mana, A.A., Hassan, A.H., Ndjaye, K., Abakar, N., Bahar, A.M., Bolti, M.A., Kotyadé, N., Regis, M.L., Slama, M. and Alio, H.M. (2022) Management of Secondary Lyell Syndrome Due to Anti-Covid Vaccine in a Case, at the Renaissance University Teaching Hospital, Ndjamen (CHAD). *Journal of Biosciences and Medicines*, 10, 47-54. <https://doi.org/10.4236/jbm.2022.1010004>

**Received:** July 25, 2022

**Accepted:** October 9, 2022

**Published:** October 12, 2022

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## Abstract

**Introduction:** Lyell's syndrome (SL), called Toxic Epidermal Necrolysis is one of the most serious forms of medication accidents. It is an acute, rare pathology, its incidence is estimated at 1 to 2 cases out of one million inhabitants per year and its evolution can be fatal. **Materials and Methods:** We report the observation of a 60-year-old patient, with no significant pathological history, admitted to our intensive care unit at the Renaissance University Teaching Hospital in N'Djamena for the treatment of Toxic Epidermal Necrolysis. In whom the onset of symptoms dates back to few hours after vaccination against COVID-19 with Ag Johnson and Johnson. **Results:** An ophthalmology opinion was requested and the patient was put on Fucithalamic. In our case, in addition to the advanced age of the patient (60 years old), her SCORTEN was  $\geq 5$ . **Conclusion:** The late management as well as the absence of a specific department for severe burns, which condition the presence of a technical plate was fatal to her despite multidisciplinary care: Resuscitators, Traumatology-Orthopedist and ophthalmologist.

## Keywords

Lyell Syndrome, Renaissance University Teaching Hospital, N'Djamena,

## 1. Introduction

Lyell's syndrome (SL), called Toxic Epidermal Necrolysis (TEN) is one of the most serious forms of medication accidents. It is an acute but rare pathology, its incidence is estimated at 1 to 2 cases per million inhabitants per year and its evolution can be fatal [1]. In France, about 120 cases were recorded each year. LS was first described in 1956 by a Scottish dermatologist Alan Lyell in four patients [2]. The disease is manifested by a more or less feverish rash with areas of bullous detachment reaching by definition more than 30% of the body surface. This appearance is that of an extensive deep second-degree burn [3]. TEN and Stevens Johnson Syndrome (SJS) are the same condition but differ in severity. Cutaneous involvement of 10% is the threshold beyond which an increase in mortality is observed. Thus, we attribute to SJS (reputed to be less severe) a skin lesion less than or equal to 10% [3] [4]. Histologically, TEN is characterized by keratinocyte necrosis and alteration of the dermoepidermal junction [5]. According to Siah *et al.* [5], several genetic, immunological and viral factors are supposed to be involved in the pathophysiology of LS, but remain poorly elucidated. Multivisceral involvement (ocular, respiratory, renal, haematological, etc.) complicates the clinical picture [5] [6] [7]. In addition, the management of systemic involvement in the TEN is multidisciplinary in the intensive care units for severe burns (or in the intensive care unit in our case). According to several studies [1] [6] [7] [8] [9], early multidisciplinary management reduces the mortality rate and is currently below 20%. For [5], this remarkable progress is at the cost of good care in intensive care and restrictive nursing.

We report the observation of a 60-year-old patient, with no significant pathological history, admitted on 09/04/2022 to our intensive care unit at the Renaissance University Teaching Hospital in N'Djamena for the treatment of Toxic Epidermal Necrolysis (TEN) following a vaccination against Covid-19 (Figure 1).

## 2. Patient and Observation

The onset of symptoms dates back to the evening of 03/24/2022 after vaccination against COVID-19 with Ag Johnson and Johnson, Lot number 652 which expires in 10/2023, marked by the occurrence of a fever with chills accompanied by generalized pruritus followed by bullous rashes giving progressively extensive toxic epidermal necrolysis to the whole body associated with dysphagia to solids occurring a few hours later, having motivated a consultation in a local Health Center where she would have benefited medical treatment based on Dexamethasone and Chlorpheniramine without success. It was in the face of the worsening of the symptoms that she was referred to the R-UTH for better care. On



**Figure 1.** Patient after the first dressing (picture by Nouradine, dated 09/04/22).

admission, there is an alteration in general condition, preserved consciousness, PA: 132/72 mmHg; HR: 125 bpm; SpO<sub>2</sub>: 97% on room air; eupneic; a diuresis preserved with very dark urine and a fever of 40.5°C. Extensive epidermal necrosis with Burnt Body Surface (SCB) estimated at 100% including 40% to 50% of deep 2nd degree with positive NIKOLSKI's sign. There was also inflammation of the oropharynx and synechia of the eyelids with significant tearing.

### 3. Biology

NFS: Leukocytes: 5100/mm<sup>3</sup>, Hemoglobin: 9.1 g/dL hypochromic microcyte, Platelets: 196,000/mm<sup>3</sup>; GS/HR: A+; an inflammatory syndrome with CRP: 100 mg/L; impaired renal function: Urea: 17.85 mmol/L, Creatinemia: 310.8 μmol/L (GFR: 17.095 ml/min); ionic disorders (Na<sup>+</sup>: 123 mmol/l, K<sup>+</sup>: 2.3 mmol/l, Cl<sup>-</sup>: 82.30 mmol/l) and hypoalbuminemia at 21.2 g/l.

The TEN is retained before the clinical, anamnestic and biological arguments with a SCORTEN ≥ 5.

Mesasure taken:

- Septic isolation;
- Oxygen therapy by bezel;
- Placement of a VVC in the right femoral and filling with Ringer Lactate and Nacl 0.9% according to the Parkland formula;
- Placement of an arterial catheter in the left radial for invasive blood pressure
- Analgesic: paracetamol, tramadol and morphine then Ketamine with PSE;
- Antibiotic therapy: Meropenem and Metronidazol;
- Correction of ionic disorders by supplying sodium and potassium ions;
- Anticoagulant: Enoxaparin;
- Gastric protection: Omeprozole;

- Enteral/SNG and Parenteral Nutrition with Perikabiven;
- Daily dressings in bed.

An ophthalmology opinion was requested and put on Fucithalmic.

A J1: patient stable on hemodynamic and respiratory plan under O<sub>2</sub> 2 l/m, conscience conserved and apyretic.

On D3: Control assessment: Hb deglobulization: 8.4 g/dl, slight improvement in renal function: creat = 243 µmol/l, urea = 15 mmol/l.

On D5: worsening by respiratory distress, hemodynamic instability and hypothermia

CAT: O2/MHC, and amine vasopressor (noradrenaline).

Evolution was marked by septic shock refractory to noradrenaline and the patient died on D6 of hospitalization (04/14/22) at 01:05 in a picture of septic shock with multi-visceral failure.

#### 4. Discussion

TEN occurs at any age, with a slightly elevated incidence in the elderly [4] [7]. As in our case, Bastusji-Garin [10] and Bonnetblanc *et al.* [11] reported an incidence of LS 2.7 times higher in subjects over 60 years old than in a younger population. The elderly present a fragile ground (pathological antecedents), often polymedicated. The originality of our observation lies in the rarity of severe drug eruption due to the anti-COVID-19 vaccine and particularly Lyell's syndrome. Indeed, to our knowledge, this is the first case reported in Chad during the anti-COVID-19 vaccination campaign with the Jhonson and Jhonson vaccine. Cases of Toxidermia linked to vaccines have been reported by certain observations, in particular linked to: Pzifer, Moderna, Sinopharm, as is the case with the following authors: Elboraey *et al.* [12] in Egypt, Mardani *et al.* [13] in Iran and Dash *et al.* [14] in India. As we note, all the different types of COVID-19 vaccines can be responsible for this syndrome.

Drug combinations are also responsible for LS, but in our case, this possibility was ruled out by the anamnesis. Our patient was not polymedicated.

Several results reported a slight female predominance, with a sex ratio of 0.6 [8] [15] [16] [17] and indeed our case is female. The work, among others, of [5] [6] [18] [19] [20] has shown that patients suffering from HIV, systemic lupus erythematosus or having undergone a bone marrow transplant (immunocompromised) are subjects at risk of SJS or TEN. In the same vein, Mokline *et al.* [21] have shown that in addition to the factors including the comorbidities mentioned above, advanced age, the surface area of the skin detachment, the delay in diagnosis and treatment, the late discontinuation of the drug in question and the proven complications, in particular infectious, are formidable because they are responsible for a high mortality rate. Although our patient was of an advanced age and did not present any of these risk factors, the onset of the symptoms dates back to the evening after a vaccination against COVID-19 (Ag Johnson and Johnson) marked by the occurrence of a fever with chills accompanied generalized pruritus followed by bullous rashes giving progressively extensive toxic

epidermal necrolysis throughout the body associated with dysphagia to solids. However, there was a delay in diagnosis and good care because our patient was consulted in a local health center where she received medical treatment based on Dexamethasone and Chlorpheniramine. The first drug is a nonsteroidal anti-inflammatory drug from the corticosteroid (glucocorticoid) family, and the second is an antihistamine from the pyridine class. Several studies, among others 12, 13 and 14, have shown the role of vaccination, although very rare, in the occurrence of TEN. Although in our case neither Dexamethasone nor Chlorpheniramine are incriminated, in the literature [22] [23] [24] [25] the drugs most frequently imputed are anti-infective sulfonamides, anticonvulsants, nonsteroidal anti-inflammatory drugs and allopurinol. For [24] [25], the occurrence of TEN is independent of the dose received and a minor exposure may be sufficient to cause the disease. In the same order, several studies have instead incriminated anti-infective sulfonamides [23] [24] [25] [26]. On the other hand, for the authors Surbled *et al.*, Melde *et al.*, Mandal *et al.*, Mame *et al.* [27] [28] [29] [30] almost all of the risks are incriminated with particular frequency for penicillins, followed by quinolones, vancomycin, macrolides and antituberculosis drugs. As for most of the studies [31] [32] [33] [34] [35], the diagnosis of our case is based on the clinic, the anamnestic arguments and the data of the biological examinations. There is currently no specific treatment of demonstrated validity [8] [9] [35].

Systemic corticosteroid therapy remains controversial; various immunosuppressive treatments (cyclophosphamide, ciclosporin) have been tried in a few cases [11], without proven proof of their effectiveness. The benefits of high doses of intravenous immunoglobulins have not been confirmed [18]. The prognosis of SL remains reserved, it depends on several pejorative factors including advanced age, the surface of the skin detachment, the delay in diagnosis and management, the late discontinuation of the drug and the complications, in particular infectious, proven and formidable. Because they are responsible for a high mortality rate [35] [36]. The most important sequelae are dyschromic scars such as hyperpigmentation and corneal sequelae (cases that may require a graft, and recur on the graft). Whatever the incriminated drug, the management is multidisciplinary, and requires hospitalization in an intensive care unit. It is mainly based on rehydration, nutrition, local skin care and mucous membranes (oral, ocular and genital), as well as the treatment of secondary infections [34] [35] [36]. The severity and the prognosis (vital or not) are evaluated by the SCORTEN [31] [33] [34] [35] [36]. In our case, in addition to the advanced age of the patient (60 years old), the late management and the absence of a specific service for severe burns, which determines the presence of a technical platform, were fatal to her. Moreover, the SCORTEN of our patient was  $\geq 5$ .

## 5. Conclusion

Lyell's syndrome or toxic epidermal necrolysis is a rare but serious pathology, responsible for significant morbidity and mortality. Early and multidisciplinary

care in an intensive care unit dedicated solely to burns patients improves the prognosis of this condition. Through this observation, we are appealing to the country's health authorities to be more vigilant about the side effects linked to vaccines, and above all an early and adequate management strategy. For doctors, the thoughtless and unfounded drug prescription especially that of antibiotics, could lead to the risk of the occurrence of TEN. To the authorities responsible for Health in Chad, the creation of a center dedicated to severe burns is essential. All these means of prevention will help to further reduce the frequency of this condition and improve the prognosis.

### Acknowledgements

Our gratitude goes to Mr Yerima Mahamat Isma for his invaluable help in translating the study into English.

### Conflicts of Interest

Conflict of interest was not revealed in this study.

### Author's Contribution

All authors contributed to the conduct of this work and to the drafting of the manuscript. All authors have read and approved the final version of the manuscript.

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