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Is there a correlation between Lyell's syndrome and anti-SARS-Cov2 vaccination ? 02 reported cases

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I. Introduction

COVID-19 has affected millions of people around the world since its appearance in December 2019 and has caused a high number of deaths in its severe forms. Although there are no specific therapeutic agents for SARS-Cov2 infection, the anti-COVID-19 vaccine significantly reduces the morbidity and mortality associated with it.

Lyell's syndrome or toxic epidermal necrolysis (TEN) is one of the most serious mucocutaneous drug accidents, its evolution can be fatal. It is rare, however, with an incidence of 0.1% of the general population. **(1)**

The clinical appearance of TEN is an extensive deep second degree burn. It is characterized by a skin detachment and almost a constant mucosal lesions. Fever is present and the general condition is seriously altered, as well as multivisceral damage (ocular, respiratory, renal, haematological, etc.) which complicates the clinical state. **(2)**

TEN and Stevens Johnson Syndrome (SJS) are different degrees of severity of the same condition. 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%. **(2, 3)**

We report a potential complication of the anti-SARS-Cov2 vaccine : 2 cases of Lyell's syndrome appearing after the second dose of the vaccine without exposure to any other drug.

II. Cases Presentation

- **Case N°1 :** 16-year-old patient, presented to the ER for an extensive skin eruption. With no previous medical history, the patient received a second dose of anti-SARS-Cov2 vaccine 13 days previously. Four days before the admission, the patient started to develop an erythematous patch in the upper limbs and trunk, with rapidly progressive extension. Her condition was complicated by the appearance of bullae and vesicles, in addition to generalized edema. **(Fig.1)**

Upon examination, the patient was conscious and stable. Macular and maculo-papular lesions were found on 90% of her body surface area with positive Nikolsky's sign, allergic conjunctivitis with dry eyes; The diagnosis of post-vaccination Lyell Syndrome was then strongly suspected.

Laboratory evaluation showed CRP = 210 mg/l; Procalcitonin > 0.5 µg/l; hypoalbuminemia; D-Dimer: 0.8 mg/l; negative blood culture.

The medical care of the patient involved conditioning and hourly monitoring of the various parameters; Daily skin care and balneotherapy. The ophthalmological follow-up revealed fibrosing conjunctivitis, with burning of both eyelids and a symblepharon which required daily eye care with debridement. The gynecological follow-up had objectified a vulvitis.

Artificial nutrition has led to a gain in skin regeneration. A complete healing of the patient was noted after 27 days.

Figure 1 : Patient N° 1 with Lyell's Syndrome

- **Case N° 2 :** 57-year-old woman admitted for Lyell's syndrome at 85% of her body surface area. Medical previous history : the patient received her second dose of vaccine against SARS-Cov2 twelve days before the onset of TEN symptoms with no notion of drug intake during this period. **(Fig.2)**

Upon examination, the patient was conscious, stable and her temperature was 39°. Macular and maculo-papular lesions are found on 85% of the body surface area with a positive Nikolsky sign and lesions of the labial mucosa. Laboratory evaluation: CRP= 186 mg/l; Procalcitonin > 0.5 µg/l; hypoalbuminemia; Platelets: 69,000/ mm3; D-Dimer : 1.2 mg/l; a positive blood culture for Acinetobacter Baumannii.

The medical care of the patient associated a conditioning and monitoring of biological parameters; Daily skin care and balneotherapy, hydroelectrolytic resuscitation, parenteral then enteral nutrition, prevention of thromboembolic disease was carried out with enoxaparin 0.4 ml/24 h, and intravenous antibiotic therapy was instituted according to the antibiogram combining tazocillin 4g/8h and colimycin 9MUI/d.

Two weeks after her admission, the patient had a septic shock and multi-organ failure with a pulmonary starting point, the angioscan showed pulmonary lesions and ruled out a pulmonary embolism. Her medical condition is now managed in an intensive care unit.

Figure2 : Patient N°2 with TEN

III. Discussion

The physiopathology of Lyell's syndrome or toxic epidermal necrolysis (TEN) is poorly understood, and obeys multiple and varied mechanisms corresponding to unexpected and inexplicable reactions by the pharmacological properties of the product. They are unpredictable, serious, and do not depend on the dosage. **(4.5)**

Medication is the main cause of occurrence of Lyell's syndrome. Among the drugs exposing to a very high risk of TEN : sulfamethoxazole-trimethoprine, aminopenicillins, cephalosporins, quinolones, phenitoin, phenobarbital, carbamazepine, valproic acid, lamotrigine but also NSAIDs, nevirapine and furosemide.

The diagnosis is based on the appearance of cutaneous bullae and or mucosal erosions preceded by prodromal symptoms which appear on average 48 hours before the specific signs. **(4.6)**

In the state phase, the NET typically looks like a "wet cloth" epidermal detachment. NIKOLSKY's sign is positive on most of the integuments, exposing an oozing dark red dermis **(Fig. 3)**. All of the integuments except the scalp can be affected with 30 to 100% detachment of the epidermis (must be greater than 30%, which differentiates TEN from Stevens-Johnson syndrome (SJS) where the peeled off surface is less than 10%). **(4, 6,7)**

As far as our patients are concerned, the extension of the cutaneous detachments was on a surface of 92% for the first patient and 85% for the second, which pleads in favor of Lyell's syndrome.

Figure 3 : NICOLSKY Sign

The SARS-Cov2 vaccine provides increased immunity against COVID-19 infection. Clinical trials revealed elevated levels of RBD-specific IgG antibodies with a geometric mean concentration of 8 to 46.3 times that of convalescent serum. Mild and transient local reactions and systemic events were observed without adverse effects. However, data analysis did not assess safety and immunological responses 2 weeks after administration of the second dose. **(8)**

Rare cases of Lyell's syndrome have been associated with some vaccines, including the smallpox vaccine ; vaccination against chickenpox and measles, mumps and rubella; and influenza vaccination. **(9, 10,11)**

Analytical studies carried out on the adverse effects of anti-SARS-Cov2 vaccines covering data validated between November 12 and 25, 2021, the results of which were presented and discussed during the ANSM monitoring committee with the French network of CPRVs of December 02, 2021, reported 4 cases of Lyell's syndrome out of 95,153,900 injections. (12)

Articles published in 2021 and 2022 revealed cases of Stevens-Johnson syndrome post-COVID-19 vaccines : 1 case after an injection of a 2nd anti-Covid-19 dose PFIZER in Saudi Arabia, 1 case after a 1st vaccine dose received by a 60-year-old patient in India, 1 case in Morocco induced by the SINOPHARM vaccine. (13, 14, 15)

An article published in 2021 reported the existence of 1 case of Lyell's syndrome post-SARS-Cov2 vaccine PFIZER involving a 49-year-old woman. (16)

Publication's date	Authors	COVID-19 Vaccine	Dose	SJS/TEN	Number of cases
16/08/2021	Bakir M, Almeshal H, Alturki R, et al.	PFIZER	1st	TEN	1
19/07/2021	Mohamed Omar Elboraey, Emad El Said Fahim Essa	PFIZER	2nd	SJS	1
19/08/2021	S Dash, C S Sirka, S Mishra, P Viswan	-	1st	SJS	1
03/12/2021	ANSM	MODERNA PFIZER	- -	TEN TEN	1 3
06/01/2022	L Boualila, B Mrini, A Tagmouti, N El Moubarik, M Benchekroun Belabbes, N Boutimzine, L O Cherkaoui	SINOPHARM	-	SJS	1

Summary table of reported numbers of Stevens-Johnson syndrome and Lyell's syndrome post-COVID-19 vaccines

In our study, we observed that 2 Lyell's syndromes were reported out of 52,000,000 injections of anti-COVID-19 vaccine with no notion of drug intake before the appearance of the symptoms.

The management of patients with TEN must be early and multidisciplinary within a burns intensive care unit, the foundations of which are based on rigorous asepsis, hydroelectrolyte and nutritional intake, prevention of infection and its treatment with appropriate antibiotic therapy, and local nursing and care. The supposed effectiveness of intravenous immunoglobulins is based only on isolated cases and there are no randomized studies yet. **(17)**

Prognosis: With current management, mortality rates are now below 20%. However, TEN remains a very serious disease, with a vital prognosis at stake in the acute phase and frequent disabling sequelae. Mortality is linked firstly to septic shock and secondly to lesional pulmonary edema, and often occurs in an array of multiorgan failure, with ARDS in particular. **(7)**

The SCORTEN score **(Fig.4)** is predictive of prognosis, and is the most widely used: a score less than or equal to 2 indicates a probability of survival of 90%, a score greater than or equal to 4, is associated with a probability survival less than 50%.

Our patients had a SCORTEN score of 3 on the 2nd day of their admission.

Prognostic factors	Points
Age > 40 years	1
Tachycardia > 120 bpm	1
Neoplasia	1
Initial detachment > 10%	1
Serum urea > 10 mmol/L	1
Serum bicarbonate < 20mmol/L	1
Blood glucose > 14 mmol/L	1

SCORTEN	Mortality (%)
0-1	3
2	12
3	35
4	58
≥ 5	90

Figure 4 : SCORTEN score

IV. Conclusions

Lyell's syndrome and Stevens-Johnson syndrome represent an extremely rare but particularly serious disease. Although some studies conducted since the start of the pandemic on the adverse effects of SARS-Cov2 vaccines have reported cases of induced SJS/TEN ; These syndromes are considered to be an extremely rare sequela.

As soon as the diagnosis is made, we emphasize the absolute importance of early and multidisciplinary management in intensive care units for severe burns.

References

[1]. Couadau E., Carles M., Ichai C. Conférence d'actualisation. Paris: Elsevier; 2001. Troubles cutanés en réanimation. pp. 551–570.
[2]. [Lyell's syndrome and its ophthalmologic manifestations in Cameroon]. Moussala M, Beharcohen F, Dighiero P, Renard G ; J Fr Ophtalmol. 2000 Mar; 23(3):229-37.
[3]. Dikhaye Siham. Syndrome de Lyell et syndrome de Stevens-Johnson: l'expérience du service de dermatologie du centre hospitalier universitaire Ibn-Sina, Rabat, Maroc. Thèse N° 107. 2005.
[4]. FRENCH LE. Toxic epidermal necrolysis and Stevens Johnson syndrome : our current understanding. Allergol Int. 2006 Mar ; 55(1) : 9- 16.
[5]. PAQUET P, PIERARD GE New insights in toxic epidermal necrolysis (Lyell's syndrome): clinical considerations, pathobiology targeted treatments revisited Drug Saf 2010;33: 189-212.
[6]. HARR T, FRENCH LE. Stevens-Johnson syndrome and toxic epidermal necrolysis. Chem Immunol Allergy.2012 ; 97:149-66.Epub 2012 May 3.
[7]. E. RIVERS, B. NGUYEN, S. HAVSTAD, J. RESSLER, A. MUZZIN, B. KNOBLICH, E. PETERSON, M. TOMLANOVICH. Early Goal Directed Therapy in the Treatment of Severe Sepsis and Septic Shock. November 8,2001 ; N Engl J Med 2001 ; 345:1368-1377.
[8]. Mulligan MJ, Lyke KE, Kitchin N. Phase I/II study of COVID-19 RNA vaccine BNT162b1 in adults. Nature. 2020 ; 586:589–593.
[9]. Shetty SR, Chatra L, Shenai P, Rao PK. Stevens-Johnson syndrome : a case report. J Oral Sci. 2010 ; 52:343–346.
[10]. Oluwo AO, Irewole-Ojo FO, Mabogunje CA. Oral manifestations of herbal medicine induced Steven Johnson syndrome in 3 Nigerian paediatric patients : case report. PAMJ-Clin Med. 2020 ; 4:92.

[11]. Harr T, French LE. Toxic epidermal necrolysis and Stevens-Johnson syndrome. Orphanet J Rare Dis. 2010 ; 5:1–11.
[12]. ANSM. Point de situation sur la surveillance des vaccins contre la Covid-19 - Période du 12/11/2021 au 25/11/2021. PUBLIÉ LE 03/12/2021.
[13]. Mohamed Omar Elboraey, Emad El Said Fahim Essa. Stevens-Johnson syndrome post second dose of Pfizer COVID-19 vaccine: a case report ; Oral Surg Oral Med Oral Pathol Oral Radiol. 2021 Oct; 132(4): e139–e142.
[14]. S Dash, C S Sirka, S Mishra, P Viswan. COVID-19 vaccine-induced Stevens-Johnson syndrome ; Clin Exp Dermatol. 2021 Dec;46(8):1615-1617. doi: 10.1111/ced.14784. Epub 2021 Aug 19.
[15]. L Boualila, B Mrini, A Tagmouti, N El Moubarik, M Benchekroun Belabbes, N Boutimzine, L O Cherkaoui. Sinopharm COVID-19 vaccine-induced Stevens-Johnson syndrome ; J Fr Ophtalmol. 2022 Jan 6;S0181-5512(22)00004-3. doi: 10.1016/j.jfo.2021.12.005.
[16]. Bakir M, Almeshal H, Alturki R, et al. (August 16, 2021) Toxic Epidermal Necrolysis Post COVID-19 Vaccination - First Reported Case. Cureus 13(8): e17215.
[17]. doi:10.7759/cureus.17215
[18]. S. Siah, A. Baite, H. Bakkali, M. Atmani, K. Ababou, H. Ihrai. Prise en Charge du Syndrome de Lyell ou Necrolyse Epidermique Toxique ; Ann Burns Fire Disasters. 2009 Sep 30; 22(3): 142–146.

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