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Case Report

A Case of Amoxycillin-Induced Pediatric Lyell Syndrome in a Provincial Hospital in the Democratic Republic of the Congo

Mireille Ngale[1, 2, 3, *, †], Thierry Mpengani[4, 5, *, †], Percy Velela[3], Jean-Jacques Mbebo[5], Tarcisse Kilara[2], Silva Kasereka[6], Gauthier Mesia[2], Nsengi Ntamabyaliro[2, 3], Samuel Mampunza[2], Gaston Tona[2, 3]

[1]Kimpese Health Research Centre, Evangelical Medical Institute, Kimpese, DR Congo

[2]Clinical Pharmacology and Pharmacovigilance Unit, University of Kinshasa, Kinshasa, DR Congo

[3]National Centre of Pharmacovigilance, Ministry of Health, Kinshasa, DR Congo

[4]Department of Specialties, Otolaryngology Service, University of Kinshasa, Kinshasa, DR Congo

[5]Medical Evangelic Institute, The Church of Christ in the Congo, Kimpese, DR Congo

[6]Dermatology Department of the Uele University Clinics, University of Uele, Isiro, DR Congo

Email address:

ngalemireille@gmail.com (Mireille Ngale), thierrympengani@gmail.com (Thierry Mpengani), percyvk@gmail.com (Percy Velela), tarcissekilara7@gmail.com (Tarcisse Kilara), dermatokasereka@gmail.com (Silva Kasereka), Mesia.kahunu@unikin.ac.cd (Gauthier Mesia), ntamansengi@gmail.com (Nsengi Ntamabyaliro), mampunza552@gmail.com (Samuel Mampunza), tonalutete@gmail.com (Gaston Tona)

[*]Corresponding author

† Mireille Ngale and Thierry Mpengani are co-first authors.

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Abstract: Lyell syndrome is a rare and potentially fatal condition. It represents a serious cutaneous adverse drug reaction, often caused by drugs. Lyell syndrome and Steven-Johnson syndrome have an identical clinical expression and differ from each other only in the body surface area involved. They are characterized by the sudden destruction and detachment of the epidermis and mucous membranes**.** This is a drug allergy for which the mechanisms of onset are complex and involve many poorly understood pathophysiological factors. A 3-year-old girl presented with vulvar pruritus and a rash two days after self-medication with antibiotics and paracetamol to combat a fever. Phlyctenes and bullae then developed all over the body. The chronology of the occurrence of the signs, the spread of the lesions led to the diagnosis of Lyell syndrome. Lyell's syndrome is a rare condition and despite its low incidence, it is increasingly reported on the African continent. Although high, its mortality depends on several factors including the age of the patient, gender, and extent of lesions. Multidisciplinary collaboration and follow-up of the sequelae are crucial for the survival of the patient. Lyell syndrome is potentially fatal, but treatable with concerted management even in rural areas. The community and health workers should be warned of the potential danger of self-medication and irrational use of drugs.

Keywords: Lyell Syndrome, Children, Drug-Induced Toxic Epidermal Necrolysis, Pharmacovigilance, DR Congo

1. Introduction

Lyell's syndrome or toxic epidermal necrolysis (TEN) is a rare and potentially fatal disease. Toxic epidermal necrolysis is a severe mucocutaneous necrolysis with epidermal detachment. Along with Steven-Johnson syndrome (SJS), they represent serious cutaneous adverse reactions resulting from delayed hypersensitivity reactions. The main aetiologies mentioned are drugs, including antibiotics and non-steroidal anti-inflammatory drugs (NSAIDs) [1-3].

However, the mechanism of onset is still poorly understood [1, 2]. Several genetic, immunological and viral factors are thought to be involved in the pathophysiology of Lyell syndrome but remain insufficiently elucidated. Its incidence in the general population is about one to 2 cases per million inhabitants per year [1-5]. Epidemiological and prospective studies are lacking because of this low incidence. In the USA, incidence rates in adults range from 3.96 to 5.3/1000,000 for SJS and 0.4 to 1.45/1000,000. And in children, a US study reported a higher incidence in the pediatric population: 6.3/100,000 for SJS; 0.7/100,000 for SJS/NET overlap syndrome and 0.5/100,000 for TEN. A high mortality rate is observed in children aged 0-5 years. NET and SJS/NET overlap syndrome are associated with a higher mortality rate and longer duration of hospitalization with higher hospitalization costs than SJS.

Lyell syndrome and Stevens-Johnson syndrome are clinically similar. They are the evolution of the same pathology and differ from each other in the proportion of the body surface area affected. A Steven-Johnson syndrome can become a Lyell syndrome [1-4, 6]. Thus, we speak of Stevens-Johnson syndrome if the affected body surface is equal to 10% of the body surface, and of Lyell syndrome if it is greater than 30%. And when this involvement varies between 10 and 30%, it is an overlap SJS/TEN.

The diagnosis is clinical, confirmed by anatomopathological examination (skin biopsy) [5]. This toxidermia, which presents as a deep second-degree burn [1-4], begins with a prodrome of dysphagia, ocular pruritus, fever, and respiratory symptoms. This is followed by inflammation and dryness of the mouth and genitals, and finally by acute and extensive destruction of the skin and mucous membrane epithelium. The diffuse eruption usually begins on the trunk with purpuric macules succeeding vesicles and/or bullae, and evolves into superficial skin detachments with a "wet linen" appearance; associated with Nikolsky's sign, detachment of the apparently healthy epidermis under finger pressure. Mucosal erosions then follow, followed by total necrosis of the epidermis over its entire thickness.

2. Case Presentation

This is a 3-year-old girl with a history of bronchial asthma, with notion of self-medication at home, with amoxycillin, paracetamol, multivitamin, martial treatment. She was transferred from a peripheral medical center to the Kimpese general referral hospital for management of fever, skin rash and vulvar pruritus. The disease history dated back to 5 days prior to the consultation with fever for which her mother administered amoxycillin, paracetamol, multivitamin and martial therapy. After two days, the evolution was highlighted by the occurrence of vulvar pruritus, leading to a consultation at the medical centre where she was treated as severe malaria with quinine infusion and other drugs: Artemether-Lumefantrine combination, Gentamycin, Cefotaxime. The apparition of pruritic rashes justified the transfer to the KIMPESE/EMI hospital for further treatment.

On physical examination, the condition of the girl was altered by physical asthenia, sore face and fever. She presented with facial puffiness, severe eyelid oedema leading to occlusion of the eyes, and labial lesions: wounds on the upper and lower lips reaching the commissures with hypersalivation. There were phlyctenes, some ruptured in places, at the level of the eyes, and all over the body; vulvar ulcerations; extending to the perineal-anal margin; and purplish spots (Figure 1). The body surface area affected by the lesions was estimated to be over 30% (Figure 2).

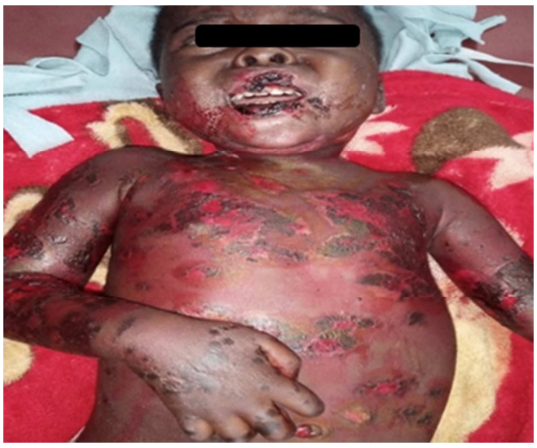

Figure 1. *Necrotic lesions of the buccal mucosa. Cutaneous lesions associating epidermal necrosis, leaving the dermis bare, on the neck, the trunk and upper limbs.*

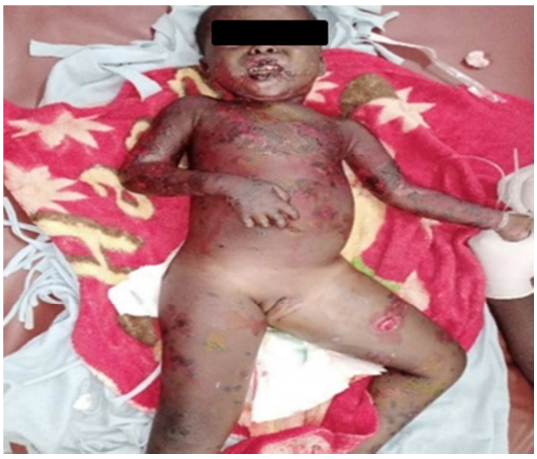

Figure 2. *Cutaneous lesions associating epidermal necrosis at perineal area and lower limbs.*

She was hospitalized in the Paediatric Intensive Care Unit for drug-induced toxidermia: Lyell syndrome complicated by

sepsis and severe malaria. The stomatology and ophthalmology teams concluded respectively to a drug-induced stomatitis and chemical eye burns.

She was given paracetamol infusion, Lincocin, ceftriaxone and Metronidazole. Skin trimming, oral care, eye care and nutritional supplies were provided.

During the six weeks of hospitalization, she has developed two successive iatrogenic abscesses: the first on the jugular vein catheter and the second on the right thigh, and have received a blood transfusion. The wounds have gradually healed (Figure 3). She was discharged with appointments for adaptive physiotherapy for lower limbs and ophthalmologic follow-up. The girl and her parents disappeared without paying the fees.

Figure 3. *Healing mucocutaneous lesions. On day 20 of hospitalization.*

3. Discussion

Lyell's syndrome and Toxic Epidermal Necrolysis (TEN) are Type B or "Bizarre" cutaneous adverse reactions: i.e. not predictable and not dose-dependent on the of the drug. These are delayed, Type IV hypersensitivity reactions. Some require a first administration, known as sensitisation, which often goes unnoticed. Lyell syndrome differs from SJS in the percentage of body surface area affected [1, 5, 6]. It is a rare disease with a worldwide incidence estimated at 1-2 cases per million, too low for epidemiological studies to be carried out. Nevertheless, more and more case reports are emerging from Africa. This shows the increasing interest in serious cutaneous adverse reactions [7–10]. It is reported more in adults than in children [11, 12]. Lyell's syndrome differs from SJS in the percentage of the body surface affected. Mortality varies from country to country10 to 50 % [5, 13], but depends on several factors including age, gender, extent of lesions, and multidisciplinary management with supportive treatment including nutrition and nursing care. Nutritional supply is crucial, as the more area affected, the more loss of water, electrolytes and protein will occur. Although the use of antibiotics is not essential, it ensures the prevention of wound superinfection [1, 14–16].

In this case report, we describe the occurrence and course of Lyell syndrome in a 3-year-old girl in Kimpese, a rural town in the Central Kongo Province, approximately 250 km from Kinshasa, the capital of the DRC. As far as we know, this is the first reported case of Lyell syndrome in children in the DRC. The history of the condition and the clinical presentation are consistent with a diagnosis of drug-induced anaphylaxis. The first symptoms (vulvar then generalized pruritus and rash) appeared after the parents treated a fever with antibiotics and paracetamol. The girl was then taken to a health center where she was given quinine and several antibiotics for three days before being transferred to the Kimpese Evangelical Medical Institute (EMI). Self-medication and irrational use of antibiotics are common in the DRC. Among the many recognized causes, free access to medicines, low population affordability and ignorance of the harm of medicines are highlighted.

The precise diagnosis is anatomopathological [5]. However, in limited-resources areas, a clinical classification of the affected skin is useful. This enables early diagnosis and management. The first symptoms appeared two days after the medication was taken. This is consistent with the literature, which describes an initial average interval of one to seven days after administration of the medication [2]. However, an infectious cause (bacterial or viral) cannot be excluded, especially as the patient had presented with a fever [12]. In this case, ocular, stomatological and genital involvement are consistent with toxic epidermal necrolysis (TEN) [12, 16-18]. Despite many outstanding questions about the mechanism of occurrence, drugs are the most common etiological group involved, especially in adults. While many studies in children have found bacterial or viral infections (adenovirus or enterovirus) to be the cause of skin lesions [19]. Several studies mention antibiotics and non-steroidal anti-inflammatory drugs, but paracetamol is not exempt [20, 21]. Several reports by Mockenhaupt and Broyles have found an association between gender and hypersensitivity reactions [1, 14, 19]. In addition, the girl's history of asthma may suggest an individual susceptibility that could explain this delayed hypersensitivity reaction [13].

The EMI is a health complex that includes the Kimpese general referral hospital, two medical-nursing institutes and a research center. The hospital has several departments and an equipped laboratory. Collaboration between the different teams (paediatric resuscitation, surgery, dermatology, ophthalmology, stomatology and nutrition) allowed a potentially life-threatening clinical condition to be successfully treated. After six weeks of treatment and gradual resolution of the wounds, the parents and the girl left the hospital room, abandoning a bill that seemed too expensive. The socio-economic level of a rural population, living mainly on subsistence farming, does not always allow them to pay for long hospital stays. This increasingly recurrent situation is discouraging the managers of this Protestant and missionary hospital, which has been working for decades for the well-being of the people of the sub-region.

4. Conclusion

Despite its rarity, Lyell syndrome is present in the DRC in the rural areas, both in adults and children. Its evolution depends on early and inclusive care, even in remote localities. Public awareness messages should be addressed to health workers and the community on the rational use of antibiotics and the danger of self-medication. More case reports should be published to establish its epidemiological profile in our country and in Africa.

ORCID

Mireille Ngale: 0000-0001-9395-613X

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Conflicts of Interest

The authors declare no conflicts of interest.

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