IBUPROFEN LYELL'S SYNDROME IN AN EIGHT-YEAR-OLD CHILD

SYNDROME DE LYELL À L'IBUPROFÈNE CHEZ UN ENFANT DE 8 ANS

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SUMMARY. Lyell's syndrome or toxic epidermal necrolysis (TEN) is a rare but serious drug-like toxiderma. Treated as a recent extensive burn in intensive care, its management must be urgent, and adapted in order to improve the vital prognosis of patients and reduce their mortality. We report a severe case of Lyell's syndrome occurring 24 hours after oral administration of an anti-inflammatory drug (ibuprofen) as a self-medication in an eight-year-old child.

Keywords: Lyell's syndrome, ibuprofen, self-medication, child

RÉSUMÉ. *Le syndrome de Lyell (nécrolyse épidermique toxique - NET) est une toxidermie médicamenteuse rare mais grave. Son prise en charge, urgente, doit être réalisée en CTB car elle s'approche de celle d'un brûlé. Nous rapportons le cas d'une NET survenue 24h après la prise orale, en automédication, d'ibuprophène.*

Mots-clés : *Lyell, ibuprophène, automédication, enfant*

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Manuscript: submitted 08/10/2021, accepted 16/10/2021

Introduction

Ibuprofen is a nonsteroidal anti-inflammatory drug. It is prescribed for its anti-inflammatory, antiplatelet properties, analgesic for mild and moderate pain, and especially antipyretic in children. It is over-the-counter (without a prescription) in our pharmacies. It is one of the most consumed drugs for self-medication in France, according to the French Observatory of Analgesic Drugs (FOAD), in 2016,[1] and in the United States in 2002.[2,3] Despite its apparent safety, it can induce side effects ranging from the mildest to the most severe, such as toxic epidermal necrolysis (TEN), known as Lyell's syndrome.[4,5] TEN is considered as a drug "allergy" characterized by the brutal destruction of the superficial layer of the skin (epidermis) and mucous membranes (epithelium).

The name Lyell's syndrome is used for the most extensive forms (more than 30% body surface), and Stevens-Johnson syndrome (SJS) for limited forms of epidermal necrolysis that may remain so or progress to Lyell's syndrome.[6,7] In Europe, the joint incidence of TEN and SJS is 2 cases per million inhabitants per year.[8,9] Lyell's syndrome is a severe toxiderma. This is a rare but serious medical emergency.[10] It results from an immuno-allergic mechanism, essentially of drug origin clearly demonstrated in 70% of cases and with potentially a molecule to charge in 20% of cases. TEN without any drugs to accuse is described as "idiopathic". The high-risk drugs of TEN[11,12,13] are: sulfonamides, allopurinol, anticonvulsants, penicillin and nonsteroidal anti-inflammatory drugs of the oxicam family.

Lyell's syndrome evokes in children two very distinct pathologies: epidermal toxin necrolysis (TEN), which is the major form of bubble erythema of drug origin, and "staphylococcal scalded skin syndrome" (SSSS). Its management, usually symptomatic and heavy, is essential in emergency. However, the prognosis remains serious, with 20 to 25% mortality and nearly 50% sequelae, especially ocular, in survivors.[14]

We report the case of an eight-year-old child who developed Lyell's syndrome with ibuprofen during a self-medication.

Observation

An eight-year-old child was admitted to our multi-purpose intensive care unit at the Bouaké University Hospital (BUH) with an extensive rash that occurred about 24 hours after taking ibuprofen administered by her parents in self-medication to treat fever. The clinical examination carried out at the child's admission included: the examination of the history of frequent self-medication carried out by her parents to treat fever and pain; and an absence of asthmatic and atypical terrain. The physical examination found a good general condition, a fever at 38.8°C, a tachycardia at 128 beats/minute and a superficial polypnea at 30 cycles/minute.

Wet laundry skin detachment was observed on discreetly erythematous skin (*Figs. 1 - 4*). Skin detachment occupied more than 65% of the body surface according to Lund and Browder's table (*Figs. 1 - 4*). There was a sign of Nikolsky. It was associated with bilateral eye lesions with symblepharon type and eyelid ulcer and oral lesions with

Fig. 1 - Skin lesions

Fig. 2 - Skin, eye and mouth lesions

Fig. 3 - Topical smeared skin lesions of an unspecified nature

stomatitis type. Pain was rated at 7/10 on the visual analogue scale.

Blood samples showed lymphopenia at 2000 lymphocytes/mm^3, inflammatory syndrome with C-reactive protein increased to 80 mg/l, high sedimentation rate at 26 mm at the first hour and normal procalcitoninemia. Blood glucose was 14.50 mmol/L. There was a renal note with a urea level of 3g/l. The blood ionogram objected to hypernatremia at 165 mmol/l with hyperkalemia at 5.8 mmol/l. The thick drop was positive at 1100 trophozoids/mm^3. The three blood cultures performed were sterile. Skin swabs for staphylococcal deposits were negative. HIV viral serology was negative. Direct immunofluorescence examination could not be performed. The histological study of the skin biopsy performed showed an intra-epidermal skin detachment with keratinocyte necrosis on a healthy dermis. The diagnosis of Lyell's syndrome secondary to ibuprofen was therefore retained. The patient benefited from hydro-electrolytic resuscitation with crystalloids according to the Carvajal formula, antimalarial treatment, skin lesion dressing, oxygen therapy, eye damage treatment and nursing care. The re-administration of ibuprofen has been formally prohibited. Intensive care lasted five days. The evolution has been favorable with persistence of achromic skin scars (*Figs. 5 & 6*). She was transferred to dermatology for further management.

Fig. 4 - Topical smeared skin lesions of an unspecified nature 1: Nikolsky sign

Fig. 5 - Dyschronic scar skin lesions

Fig. 6 - Dyschronic scar skin lesions

Discussion

This serious case of Lyell's syndrome illustrates the danger of self-medication increasingly practiced by the population. Many drugs are involved in the occurrence of Lyell's syndrome. European case control epidemiological studies conducted by the EuroSCAR group have identified the drugs that cause SJS/TEN, which most often are: sulfonamides, allopurinol, carbamazepine, phenobarbital, phenytoin and nonsteroidal anti-inflammatory drugs (NSAIDs).[15] Other drugs such as nevirapine, lamotrigine, sertraline, pantoprazole and tramadol are sometimes implicated.[16] Cases of Stevens-Johnson syndrome and Lyell's syndrome following ibuprofen are known, but very rare.[17,18,19] A few very rare cases of TEN of infectious origin (viral or bacterial) have been described.[20] In our observation, we did not find a bacterial infectious cause after the completion of the brief infectious assessment. Our patient had no allergic risk factors. She was neither asthmatic nor atypical.

Lyell's syndrome is very often fatal. The mortality rate remains high. It is of the order of 20 to 25% in the acute phase despite urgent and adapted treatment, with sequelae in 50% of patients.[21,22] The main risk factors for mortality identified are high age, the size of the body surface peeled off, the continuation of the drug and the long half-life of the drug responsible.[2] This girl had two risk factors for a poor prognosis. The SCORTEN score is a predictive score for the prognosis of TEN (*Table I*). It has seven items, each of which brings 1(one) point to the score. HIV infection and AIDS are not factors with a poor prognosis. A score less than or equal to 3 (three) indicates a favorable

Table I - Severity-of-illness score for toxic epidermal necrolysis (SCORTEN)

Risk Factors*	Score	Score
	0	1
Age	< 40 years	≥ 40 years
Associated cancer	No	Yes
Heart rate (beats/minute)	< 120	≥ 120
Serum urea nitrogen	≤ 28 mg/dL (10 mmol/L)	> 28 mg/dL (10 mmol/L)
Body surface detached or affected	< 10%	≥ 10%
Serum bicarbonate	≥ 20 mEq/L (≥ 20 mmol/L)	< 20 mEq/L (≥ 20 mmol/L)
Blood glucose	≤ 250 mg/dL (≤ 13,88 mmol/L)	> 250 mg/dL (≤ 13,88 mmol/L)

prognosis. From 4 (four), there is a major vital risk.[23] Our patient had an estimated SCORTEN score of 4 (four), with a mortality rate of 58.3%.

Taking into account the anamnesis, the clinical examination, the paraclinical examinations and the ALDEN imputability score, we can affirm that the role of ibuprofen is very likely and even certain.[15,24] Also, this side effect could have been avoided if the parents had avoided self-medication and consulted a pediatrician. The management of Lyell's syndrome is mainly based on hydro-electrolyte rehydration, correction of metabolic disorders and discontinuation of the causative drug. Peeled skin is a huge gateway for germs, and infection prevention is based on the application of very strict aseptic measures. Skin care and dressings should be performed under sedation - analgesia in order to reduce pain due to therapeutic acts. Immunoglobulin (IVIG) therapy has often been discussed in the medical literature, but its effectiveness in the paediatric population is based on only a few isolated cases.[25] The largest study looking at the management of toxic epidermal necrolysis (EuroSCAR) reported no improvement in mortality rate in the 75 patients treated with IVIg (1.5 to 1.9 g/Kg).[26] Results were recently confirmed by a retrospective study of 64 patients treated with IVIg.[27] The use of corticosteroids is also discussed but does not seem to be recommended. They may promote infectious complications and delay the healing of skin lesions.[28]

Conclusion

Lyell's syndrome is a rare and severe toxiderma associated with significant morbidity and mortality. It is usually secondary to taking medication, including ibuprofen. The identification of the drug responsible is an important step, because its definitive eviction avoids any recurrence of toxiderma in an even more severe form. In addition, raising awareness among the population against the dangers of self-medication is necessary.

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