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Lyell Syndrome Associated With Lamotrigine

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Summary

Lyell's syndrome or toxic epidermal necrolysis (TEN) is one of the rare major complications of Lamotrigine treatment. Its management has not yet been codified. It requires urgent, extensive intervention adapted to each patient to reduce mortality. We describe a case of Lyell syndrome that occurred eight days after initiation of treatment with Lamotrigine as part of a therapeutic protocol for bipolar disorder in a 36-year-old female inpatient. It is vital to report the importance of raising awareness and providing personalized information to patients and prescribing physicians on the risks associated with the use of antiepileptic drugs in psychiatric disorders.

Keywords:*Lamotrigine, Lyell syndrome, antiepileptic, bipolar disorder.*

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I. Introduction:

Toxic epidermal necrolysis (TEN) or Lyell syndrome is a life-threatening hypersensitivity reaction of the skin. It is a rare form oftoxidermia, with a global incidence of 0.4 to 1.2 million people per year. In Lyell syndrome, more than 30% of the skin surface is affected. It is most often associated with the use of medications [1]. Among psychotropic drugs, antidepressants and antipsychotics are less often responsible for toxidermia than mood stabilizerslike antiepileptics (carbamazepine, oxcarbazepine, lamotrigine), whose extrinsic imputability is well known [2]. Lamotrigine is a new-generation antiepileptic used both in epilepsy and in bipolar I disorder to prevent depressive episodes [3]. We report a case of severe toxic epidermal necrolysis (TEN) after taking lamotrigine, delivered as part of a switchtherapeutic protocol in a patient with bipolar disorder.

Clinical case:

A 36-year-oldfemale inpatient with no medical history was admitted to the burns department of the Mohamed V military training hospital in Rabat for the management of Lyell's syndrome [Fig 1]. On admission, the patient was confused, hemodynamically and respiratory stable, and febrile at 39°. Macular and maculopapular lesions covering 80% of the skin surface with positive Nikolsky's sign and lesions of the labial and genital mucosa were present. The course of action included conditioning the patient with cardiorespiratory monitoring, placement of a central venous line, and a biological and radiological work-up with a protocol for local care and balneotherapy. After interviewing her family, a psychiatric opinion was sought. The patient has been treated in a provincial hospital for bipolar disorder during 1 year by antipsychotics: Quetiapineand Olanzapine. Aftera weight gain of 10 kgs, the previous psychiatrist decided to stop the antipsychotics treatment and to put the patient on Lamotrigine 25 mg. 8 days later, the patient developed a rapidly worsening maculopapular rash with severe skin detachment, requiring hospitalization in an intensive care unit on the burn ward. Treatment was stopped immediately. The patient died six days later following severe infectious complications.

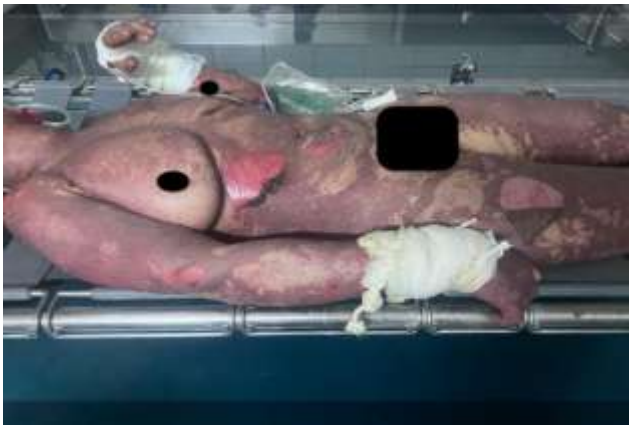

Figure 1: 36-year-old patient suffering from Lyell's syndrome after taking Lamotrigine, 80% of skin surface affected.

II. Discussion:

Toxidermia is a frequent adverse effect of psychiatric drugs, with varying incidence between 2% and 5% depending on the study [4]. Lamotrigine (LTG) is indicated for the maintenance treatment of bipolar disorder. Typical doses for long-term treatment for patients with bipolar disorder range from 50 to 200 mg/day, although higher doses (up to 500 mg/day) are sometimes used. In pregnant women, maintaining treatment is necessary to reduce the risk of recurrence.The rate of congenital malformations, including orofacial cleft malformations, in infants exposed in utero to LTG is similar to general population. Nevertheless, serious life-threatening manifestations were present when plasmatic concentrations exceeded 25 mg/L in adults therefore the recommended doses for adults and children aged ≥ 13 years are 25 mg/d at S1 and S2, then 50 mg/d at S3 and S4, followed by increments of 50 to 100 mg every 1 to 2 weeks.

The risk of skin reactions is well known, estimated at around 10%. Management must be multidisciplinary and take place in a specialized environment. When the toxidermia is a maculopapular exanthema without any signs of severity, extrinsic imputability can be suspected when multiple medications are used so as not to stop all medications whether this decision threatens the treatment of the diseases. On the other hand, in the case of severe toxidermia, all suspect drugs must be stopped, regardless of their notoriety [5]. Late cessation of the medication with long half-lives is responsible for higher mortality. At the same time, the molecule(s) that could extend the half-life of the molecule responsible must also be stopped[6]. The risk of developing Lyell syndrome with Lamotrigine is rare and relatively predictable during the first few weeks of use. It must be remembered that "education in the use of antiepileptic drugs" is an integral part of psychiatric therapy. Those who prescribe antiepileptic drugs for bipolar disorders, particularly Lamotrigine, must warn new patients about the real risk of serious side effects. This risk is particularly high during the first two months following initiation of treatment with Lamotrigine. Immediate cessation of a recently prescribed molecule and urgent medical check-ups are highly important at the onset appearance of any skin or mucous membrane lesion not otherwise explained. Clinicians prescribing this drug must be aware of this high risk.

III. Conclusion:

In psychiatry, the administration of antiepileptic drugs, particularly Lamotrigine, must follow strictguidelines. Prompt recognition of a skin or mucous membrane lesion not otherwise explained in the days or weeks following initiation of treatment must be followed by immediate cessation of suspected medication and urgent medical check-ups to reduce iatrogenic morbidity and mortality.

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