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CASE REPORT

# Antiepileptic drugs toxicity: A case of toxic epidermal necrolysis in patient with phenytoin prophylaxis post-cranial radiation for brain metastases

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**KEYWORDS**

Antiepileptic drugs (AED);
Stevens–Johnson syndrome (SJS);
Toxic epidermal necrolysis (TEN);
Cranial radiation

**Abstract** *Background:* Treatment of epilepsy with antiepileptic drugs (AED) is effective and remains the principal mode of management. A group of adverse effects and drug toxicity can develop immediately or later in the course of treatment. AEDs also have the potential of precipitating idiosyncratic adverse effects including serious cutaneous, hematological and hepatic events. Stevens–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are rare but severe cutaneous adverse reactions are related to or caused by a variety of medications including AEDs, they carry a high mortality and morbidity rate, accurate diagnosis and rapid treatment may improve the prognosis.

*Objective:* To characterize the clinical features and methods of differentiating Stevens–Johnson syndrome from toxic epidermal necrolysis using a case study and to identify other factors that may contribute to this critical illness.

*Conclusion:* Clinical knowledge of potential sever adverse reaction of AEDs is essential and may overcome treatment failure with major impact on health-related quality of life in people with epilepsy.



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## 1. Introduction

Antiepileptic drugs (AED) are known for a variety of adverse reactions. Stevens–Johnson syndrome and toxic epidermal necrolysis (SJS, TEN) are among the severe cutaneous drug reactions reported in the literature that can be initiated by different classes of anticonvulsants, especially in the background of other high-risk factors such as advanced age, malignancy or radiation exposure. Prescribing such medications should be done with caution, especially if the underlying medical condition could increase the risk of developing SJS–TEN.

## 2. Case presentation

A 45-year-old female presented to the emergency department with progressive non-pruritic macular rash. The rash started on her face and over 3 days spread in a caudal direction to involve her entire body, sparing her legs below the knee (and affecting more than 80% of total body surface area). The rash was vesicular with large bullae on the face and swollen eyes and lips. It was associated with photophobia, a burning sensation in the eyes and visual impairment, dysphagia, dyspnea, and dysuria. These symptoms preceded for 2 weeks duration with prodromal manifestations of fever, malaise, and sore throat.

The patient had been on phenytoin treatment (100 mg tid) for 1 month prior to developing this rash, as a management of secondary partial seizures. She had been diagnosed with brain metastases secondary to breast cancer 2 months earlier and received cranial radiotherapy. The right breast cancer was diagnosed 18 months prior to brain metastases. At that time management included modified radical mastectomy of the right breast followed by 25 sessions of chemo-radiotherapy and tamoxifen hormonal therapy.

In addition to the phenytoin therapy, the patient was on dexamethasone (4 mg bid) and ranitidine (150 mg tid). On admission, physical examination revealed a toxically ill and distressed patient with a temperature of 38.7 °C, pulse rate of 128 beats per minute, blood pressure of 93/57 mmHg and respiratory rate of 18 breaths per minute. Skin examination showed discrete irregular vesicular rash with multiple large bullae on the face extending to the knees with a positive Nikolsky's sign. On the third day of admission, bullae started to slough leaving areas of exposed skin surface (Figs. 1.1 and 1.2). She had edematous lips with necrotic mucus membranes and oral ulcerations. Eyes were also edematous with mucoid discharge. Chest examination showed that the mastectomized right breast scar was hyperpigmented but clear with no evidence of chest wall recurrence. The other breast was normal. Lungs were clear bilaterally with no localizing signs, heart with regular rhythm and no added sounds or gallop rhythm; abdomen was soft, benign with no tenderness or acute findings. No peripheral edema. The neurological exam was unremarkable.

Initial laboratory tests showed a normal white blood cell count and differential, hemoglobin level and platelet count. Serum liver enzymes were abnormal with slightly elevated alanine aminotransferase (81 IU/L) and aspartate aminotransferase (62 IU/L), alkaline phosphatase (71 IU/L), and gamma glutamyl transpeptidase (624 IU/L). Total bilirubin was

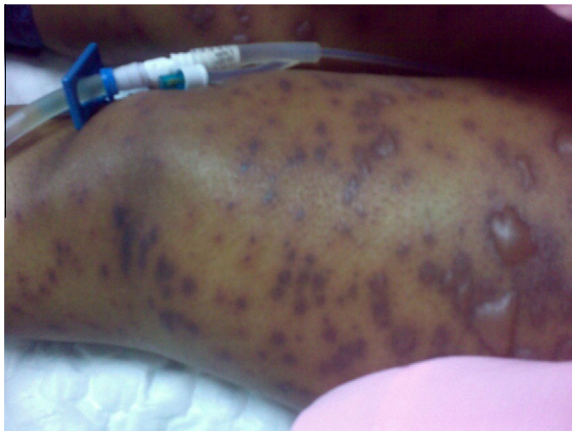

**Figure 1.1** Left lower limb showed irregular vesicular rash with multiple large bullae.

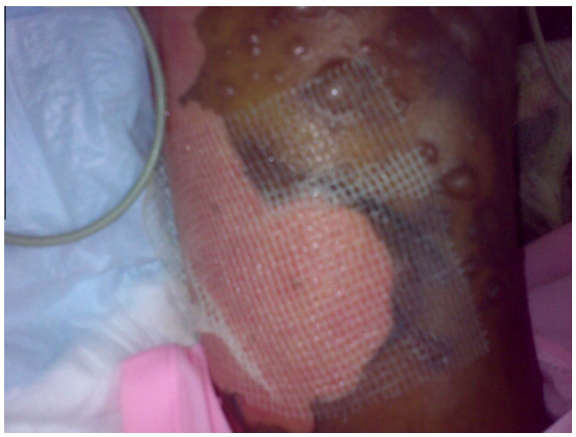

**Figure 1.2** Vesicular rash with bullae started to slough leaving areas of exposed skin surface.

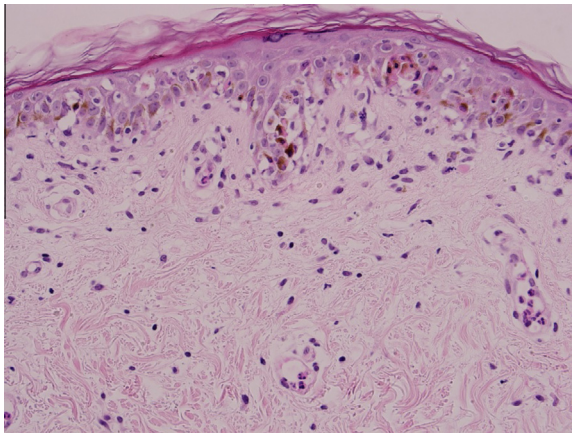

**Figure 2.1** (Microscopic description) Section shows epidermal spongiosis, and basal cell hydropic degeneration. Scattered dyskeratotic cells are seen. Mild lymphocytic infiltration of the dermo-epidermal junction is also identified. The upper dermis shows mild edematous change and mild lymphocytic infiltration. The capillary lumina contain neutrophils. No bullae formation is identified.