

# Case Report

## Phenobarbitone-induced erythema multiforme-macular type in an 8-year-old child - a case report

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**Abstract** Phenobarbitone is an antiepileptic known to cause skin reactions in 1 to 3% of patients. We report a case of erythema multiforme-macular type skin reaction in an 8-year-old female child that occurred immediately following administration of single dose phenobarbitone. The patient presented with confluent erythema with edema on both legs, dorsum of hands and face. The patient was treated symptomatically and given tab. prednisolone. The causal relationship between the drug was 'probable' and the severity 'moderate [level 4(b)] and the preventability to be 'not preventable'.

### **Key words**

Phenobarbitone, erythema multiforme.

### **Introduction**

Phenobarbitone is a commonly used antiepileptic belonging to barbiturate group. The exact mechanism of action of phenobarbitone is not known, but enhancement of inhibitory processes and diminution of excitatory transmission are known to contribute for the antiepileptic activity.<sup>1</sup> The most common adverse effect following administration of phenobarbitone includes sedation, depression, nystagmus, ataxia, paradoxical excitement, restlessness, and confusion. Hypersensitivity reactions

occur in a small proportion of patients. Phenobarbitone is also known to cause skin reactions in 1 to 3% of patients, the common ones being maculopapular, morbilliform, or scarlatiniform rashes.<sup>2</sup> We hereby report a case of phenobarbitone-induced erythema multiforme-macular type skin reaction immediately following the administration.

### **Case report**

An 8-year-old female child, diagnosed to be epileptic 3-4 years ago presented with a history of administration of phenobarbitone for 15 days at the time of diagnosis and discontinued the medicine on assumed recovery.

On May 2, 2006 she visited Dhulikhel

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**Figure 1A**



**Figure 2A**



**Figure 1B**

**Figure 1 (A & B)** Diagram showing erythema multiforme – macular type lesions involving face and hands.



**Figure 2B**

**Figure 2 (A & B)** Disappearance of skin reaction.

Hospital, Dhulikhel, Nepal, with complaints of itching starting from the neck which became generalized, along with swelling of the whole body and development of fever with chills and rigor for 3 days. On interview, it was found that she had epileptic fit 5 days back and received phenobarbitone 30 mg as prescribed by the doctor at a nearby community hospital. The drug reaction occurred within an hour after the first dose. She discontinued the medicine and visited the hospital after 2 days. In between she received Tab. ceterizine 10 mg from dispensary.

On examination, confluent erythema with edema was found on both legs, dorsum of hands and face. However, there was no vesiculation and oral mucosa was not involved. Hematological investigation showed normal renal function and urine analysis. Her total leukocyte count (TLC) was 11,900 and differential leukocyte count (DLC) showed neutrophils 87%, lymphocytes 9% and eosinophils 4%. Patient was admitted in pediatric ward with the diagnosis of phenobarbitone-induced erythema multiforme – macular type. The diagnosis of skin reaction is supported by photograph (**Figure 1A** and **1B**). She was

treated with tab. dexamethasone 2mg four times daily, tab. pheniramine maleate 25 mg three times daily, tab. paracetamol 250 mg three times daily and calamine lotion was applied locally twice daily. After 2 days, swelling and rashes improved by more than 50% (**Figures 2A** and **2B**) and the patient was discharged with the same medications to be continued for total 6 days along with the advice for follow up after 4 days. The causality assessment as per Naranjo algorithm<sup>3</sup> had shown the adverse drug reaction (ADR) to have a probable (Naranjo score 6) association with the drug (phenobarbitone). The severity of ADR was found to be 'moderate [level 4(b)]' as per the modified Hartwig and Siegel Scale.<sup>4</sup> The preventability as per modified Shumock and Thornton scale revealed the ADR to be 'not preventable'.<sup>5</sup>

## **Discussion**

Erythema multiforme (EM) is an acute, self-limiting inflammatory disorder of skin and mucous membrane characterized by distinctive iris or target lesion, usually acraly distributed and often associated with sore throat, mucosal lesions and malaise.<sup>6</sup> Approximately, in 90% of cases EM is minor and usually associated with outbreaks of herpes simplex. However, major type of EM is caused by drugs.<sup>7</sup> The common drugs causing EM include barbiturates, carbamazepine, cimetidine, dapsone, phenytoin, lamotrigine, sulphonamides, NSAIDs, sulphonylureas, isoniazid, rifampicin etc.<sup>8</sup>

Pathophysiology of EM is not completely understood but appears to involve a hypersensitivity reaction that can be

triggered by a variety of stimuli, particularly bacterial, viral, or chemical products. Histopathologic characteristics include a lymphocytic infiltrate at the dermoepidermal junction and around dermal blood vessels, dermal edema, epidermal keratinocyte necrosis, and subepidermal bullae formation.<sup>9</sup> Diagnosis of EM is primarily based on history, clinical appearance and histology. Blood tests are not useful for diagnosis, though skin biopsy may be diagnostic.<sup>7,10</sup> Although our patient's history and clinical feature were very supportive of EM, biopsy could not be performed. Since EM could be a life threatening, an attempt to re-challenge was not done. Treatment of EM is symptomatic and involves treating the underlying causes. However, use of steroid is advocated in severe cases as supported by the dramatic response in our patient i.e. decrease in swelling and disappearance of rashes.<sup>11</sup>

## **Conclusion**

Phenobarbitone is one of the potent antiepileptic drugs used widely in children. Care should be taken while prescribing and patient should be counseled about the possible side effects. Patient should be advised to discontinue the medicine and consult the physician immediately after development of any itch, redness or rash.

## **Acknowledgement**

The authors acknowledge Dr. Smitha Prabhu, Head of the Department, Department of Dermatology and Venerology, and Dr. Mukhyaprana Prabhu, Department of Medicine Manipal Teaching Hospital for reviewing the initial version of

the manuscript and suggesting modifications.

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