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Case Report

Phenobarbital induced erythroderma: a case report

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ABSTRACT

Phenobarbital (PHB) (International Non-proprietary Name) or Phenobarbitone (British Approved Name) is a long acting barbiturate and the most widely used anti-seizure medication globally. Fever, skin reactions, limb edema, and drug-induced hypersensitivity have been reported in children because of various drugs, mainly aromatic antiepileptic drugs such as phenytoin, PHB, carbamazepine, and primidone. The skin reactions differ in severity and range from a mild maculopapular erythema to exfoliative dermatitis. A 2-month-old male baby was brought to the dermatology out-patient department with complaints of redness and scaling all over the body (erythroderma) after 2-3 weeks of PHB treatment for convulsions. PHB was stopped, and corticosteroids (topical and systemic) were started. The baby improved over a period of 2 weeks. According to Naranjo's adverse drug reaction probability scale, the causality relation between erythroderma and PHB was found to be a probable one.

Keywords: Antiepileptic drugs, Convulsions, Corticosteroids, Drug-induced hypersensitivity, Erythroderma, Naranjo's adverse drug reaction probability scale, Probable, Phenobarbital, Seizures

INTRODUCTION

Phenobarbital (PHB) or phenobarbitone is a long-acting barbiturate and the most widely used anti-seizure medication globally.[1] The World Health Organization recommends PHB as a first-line medication for partial and generalized tonic-clonic seizures in developing countries.[2] The most important adverse effects of PHB are behavioral and cognitive alterations. PHB has been reported, from the early fifties, to be associated with adverse effects like exfoliative dermatitis, morbilliform or scarlatiniform rash.[3] Here, we present the case of a child under therapy with PHB developing erythroderma.

CASE REPORT

A 2-month-old male baby was brought to the dermatology out-patient department with complaints of redness and scaling all over the body after 3 weeks of treatment with PHB (Figure 1). The baby was admitted 1 month before for obstructed inguinal hernia on the right side. The baby was taken for surgery immediately after intubation. After a successful surgery, the baby developed 4-6 episodes of convulsions and was started on injection phenytoin and injection PHB. After 10 days, injection phenytoin was stopped and injection. PHB was tapered to 8 mg/kg. At the time of discharge, syrup PHB 3 mg/kg was prescribed. The baby developed eruptions and scaling all over the body, scalp and face 1-week after discharge.

Erythroderma or exfoliative dermatitis is a generalized erythema of the skin accompanied by variable degree of scaling affecting more than 90% of the body surface. On examination, extensive non-uniform erythematous scaly patches involving the scalp, face, trunk, arms, legs, palms, and soles were noticed. On clinical examination, there was no lymphadenopathy or hepatosplenomegaly. Family history was negative for similar conditions or skin disorders.

PHB was stopped. Treatment advised was topical corticosteroid, desonide cream to be applied twice daily for

5 days, syrup prednisolone 2 ml/day (2 mg) and cetaphil cleansing lotion to be applied all over body. (Cetaphil ingredients: Water, cetyl alcohol, propylene glycol, sodium lauryl sulfate, stearyl alcohol, methylparaben, propylparaben, butylparaben). The baby improved over a period of 2 weeks and steroids were tapered and eventually stopped.

DISCUSSION

Epilepsy is a chronic neurological disease, which affects about 1% of the human population. There are 50 million patients in the world suffering from this disease and 2 million new cases per year are observed. The necessary treatment with antiepileptic drugs (AEDs) increases the risk of adverse reactions. Cutaneous reactions like maculopapular or erythematous pruritic rash may appear within 4 weeks of initiating therapy with AEDs in 15% of the recipients.

Among AEDs, PHB was the first effective aromatic organic anti-seizure agent. It has relatively low toxicity, is inexpensive and is still one of the more effective and widely used drugs. The World Health Organization recommends PHB as a first-line medication for partial and generalized tonic-clonic seizures in developing countries.[2] PHB inhibits seizures by potentiation of synaptic inhibition through an action on the $GABA_A$ receptor.

AEDs like carbamazepine, phenytoin and PHB are the most common causes for drug induced erythroderma. The incriminating drug, PHB was immediately withdrawn and symptomatic treatment was started. The case had a good prognosis.

Erythroderma or exfoliative dermatitis is an inflammatory skin disorder in which there is an involvement of total or near total body surface with erythema and scaling. It can be both acute (few days duration) or chronic. The mechanism is unclear, but there is the rise in adhesion molecule expression. Currently, it is believed that the condition is secondary to an intricate interaction of cytokines and cellular adhesion molecules, including interleukins 1, 2 and 8, intercellular adhesion molecule 1 and tumor necrosis factor.[4,5] It is one of the most severe patterns of cutaneous drug reaction. It is a non-specific disease pattern induced by different diseases or medications. It could be a potentially life-threatening condition.

The incidence of drug-induced erythroderma is 21% and PHB accounts for 9.5%.[6] The incidence of such occurrence is extremely small when compared with a number of patients receiving PHB, but it is gravely significant since it is mostly accompanied by systemic manifestations. The skin reactions differ in severity and range from a mild maculopapular erythema to exfoliative dermatitis.[7] This was attributed to unavoidable prescriptions for epilepsy in the pediatric age group with drugs like carbamazepine, phenytoin, phenobarbitone and lamotrigine. Other medicines such as sulfonamides, sulfones, allopurinol,[8] NSAIDs, antimalarials, and penicillins have also been associated with the occurrence of erythroderma. In a retrospective study of papuloerythroderma irrespective of causes, there were 14 male and 3 female patients (male/female ratio 4.7:1).[9]

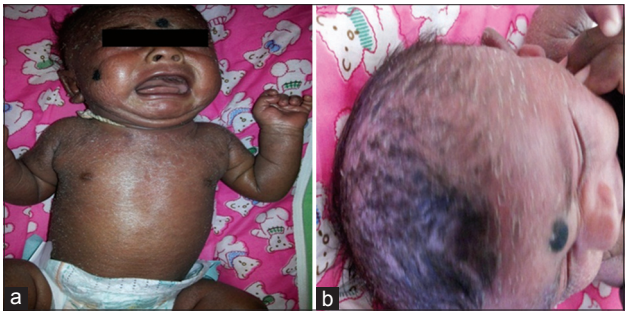

Figure 1: (a and b) Phenobarbital induced generalized erythroderma.

In this case, occurrence of erythroderma following ingestion of PHB and prompt resolution after withdrawal supports the diagnosis of PHB induced erythroderma. Drug induced erythroderma has the best prognosis of all the causes of erythroderma often resolving in 2-6 weeks. The causality was assessed using the Naranjo's adverse drug reaction probability scale. The association was probable with score of 6. It is a type B adverse drug reaction with moderate severity.

Erythroderma could be a potentially life-threatening condition, especially in the neonatal and infantile period. The severe complications that can occur are septicemic infections, hypoalbuminemia, hyperpyrexia and hypernatremic dehydration, which if not managed timely could lead to increased mortality. In the French study, the mortality was quite high (16%) and attributed to primary dermatosis or the complications.[10] However, proper diagnosis of this condition, treatment and careful monitoring of the patient would improve the final outcome.

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