

CASE REPORT

Iran J Allergy Asthma Immunol
December 2014; 13(6):453-455.

Phenobarbital-Induced DRESS: A Lichenoid Picture

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Received: 13 November 2013; Received in revised form: 17 January 2014; Accepted: 16 February 2014

ABSTRACT

We describe, the first case of phenobarbital-induced DRESS syndrome presenting as a lichenoid eruption.

A 49-year-old man had received phenobarbital for a cerebral metastasis. Twenty-five days later, he developed a purplish skin eruption, odynophagia, oral mucosal erosion and fever. Physical examination revealed a cervical lymphadenopathy and facial edema associated to a diffuse violaceous maculo-papular itchy rash. Laboratory findings showed a $1200/\text{mm}^3$ eosinophil's cell count. Alanine aminotransferase was 169 IU/l. Lactate dehydrogenase and creatinine phosphokinase were at 768 and 90 IU/l, respectively. All symptoms resolved completely five weeks after phenobarbital withdrawal. Few days later, the patient died because of a cardio-respiratory arrest.

Keywords: DRESS; Lichenoid eruption; Phenobarbital

INTRODUCTION

Drug reaction with eosinophilia and systemic symptoms, known as "DRESS" is a rare and severe adverse drug reaction.¹ The main drugs implicated are aromatic anticonvulsant agents.^{1,2} However, phenobarbital has been more rarely described.¹⁻³ The skin eruption picture in DRESS is variable; exanthema being the most reported one.^{1,4} Lichenoid eruption has been rarely observed in patients with DRESS.^{1,5-7} Phenobarbital has never been reported to induce such an eruption in the context of DRESS or other illnesses. We described the first case of phenobarbital-induced DRESS presenting as a lichenoid eruption.

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CASE REPORT

A 49-year-old man with a one-year history of small cell lung cancer treated by systemic chemotherapy (courses of cisplatin and etoposide) and radiotherapy has been admitted to the pneumology department due to an intracranial hypertension induced by a cerebral metastasis. He was treated with phenobarbital, hydrocortisone and mannitol. The last chemotherapy course had been undertaken five months prior to the study. Twenty-five days after phenobarbital initiation, the patient developed a purplish skin eruption, odynophagia, oral mucosal erosion and fever. The physical examination revealed a body temperature of 38.5°C , a cervical lymphadenopathy and marked facial edema with labial and jugal mucosal erosion, associated with a diffuse and confluent erythematous to violaceous maculopapular rash (Figure 1). The laboratory findings showed a white cell count of $11000/\text{mm}^3$ with $1200/\text{mm}^3$ of eosinophils (11%).



Figure 1. Confluent erythematous and violaceous maculopapular rash.

Table 1. The patient Kardaun score's

Item	Score
Fever $\geq 38.5^{\circ}\text{C}$	0
Enlarged lymph nodes	1
Eosinophilia	1
Atypical lymphocytes	0
Skin rash extent	1
Skin rash suggesting DRESS	1
Organ involvement (liver)	1
Resolution ≥ 15 days	0
Evaluation of other potential causes	0
Total score	5

≤ 2 : unlikely); 2-3: possible; 4-5: probable; >5 : definite.

Alanine aminotransferase (ALT) was 169 IU/l, aspartate aminotransferase (AST) was 49 IU/l. Lactate dehydrogenase (LDH) and the creatinine phosphokinase (CPK) plasmatic levels were at 768 IU/l and 90 IU/l, respectively. C-reactive-protein (CRP) was at 27 mg/dl. The platelet count and renal function were normal and no atypical lymphocytes were found.

The symptoms were thought to result from a hypersensitive reaction and phenobarbital was withdrawn. All other drugs were continued. The skin biopsy specimen revealed an epidermal parakeratosis without acanthosis associated with a lichenoid inflammatory infiltrate in the upper dermis with a vacuolar degeneration and melanin incontinence in the basal cells. These findings were in accordance with a lichenoid eruption. The clinical and biological symptoms resolved completely two and five weeks after phenobarbital withdrawal, respectively. A few days later, the patient died of a sudden cardio-respiratory arrest (Table 1).

DISCUSSION

In our case, the clinical, biological and histological data are in accordance with DRESS diagnosis criteria. According to the scoring system established by Kardaun et al.,⁸ our case deserved a score of 5. Thus, the patient's scoring was of probable type.

We believe that phenobarbital was the culprit drug in view of a clear temporal relationship between phenobarbital administration and the symptoms onset (25 days, typically 2 to 6 weeks), as well as the regression of the clinical and biological disorders some weeks after phenobarbital withdrawal. Such chronology is in accordance with the literature data since the full recovery from this condition has been reported to be long lasting and to vary from several weeks to months.² Thus, based on the Naranjo algorithm,⁹ it is probable that this systemic reaction was due to phenobarbital. Anticonvulsant agents are the most implicated drugs inducing DRESS.^{3,10} Phenobarbital seems to be rarely involved. Indeed, according to different case series reported in the PubMed database, the frequency of phenobarbital-induced DRESS did not exceed 6% among all implicated drugs and varied from 10 to 28% among anticonvulsant agents.^{1-3,10}

In addition to DRESS, phenobarbital is known to induce several other cutaneous eruptions.¹¹ However, no previous cases of phenobarbital-induced lichenoid eruption has been reported.

Originally, our case describes a phenobarbital-induced DRESS presenting as a lichenoid eruption and confirmed by histological findings.

Several skin eruption have been described with DRESS.^{1,4,12} However, DRESS presenting as a lichenoid eruption has been rarely reported since the PubMed database reports only six cases and there were no phenobarbital-induced cases.^{1,5-7}

CONCLUSION

We report the first case of phenobarbital-induced DRESS presenting as a lichenoid eruption. Physicians should be aware of this syndrome because the skin eruption feature is rather nonspecific and may be highly variable.

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Phenobarbital-Induced DRESS

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