Case Report

Carbamazepine Induced Drug Reaction with Eosinophilia and Systemic Symptoms Syndrome

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Article history: Received 1 October 2022, Reviewed 8 December 2022, Accepted for publication 14 December 2022

Abstract

Background: Drug reaction with eosinophilia and systemic symptoms syndrome is a rare adverse, life threatening drug reaction caused by several drugs including Carbamazepine. The objective of this report is to create awareness of this life threatening reaction to a commonly prescribed drug for seizure disorders.

Methods: This is a case report of drug eosinophilia syndrome in a 33-year old female following clinical and laboratory evaluation at the skin clinic for generalized erythematous rashes following the use of Carbamazepine.

Results: She was found to have generalized, scaly, erythematous papules, patches and plagues. Laboratory results included blood eosinophilia, elevated liver enzymes and histopathology report of spongiotic dermatitis with eosinophilic infiltrates.

Conclusion: Drug reaction with eosinophilia and systemic symptoms syndrome can be caused by Carbamazepine. A diagnosis of this rare life threatening drug reaction should be suspected in patients presenting with generalized erythematous rashes following the use of Carbamazepine.

Keywords: DRESS, Carbamazepine, eosinophilia, drug reaction

Introduction

Drug reaction with eosinophilia and systemic symptoms syndrome (DRESS) a rare multi-systemic adverse drug reaction[1-3]. Several drugs are implicated in DRESS, and these include antibiotics especially Vancomycin, rifampicin, linezolid: anticonvulsants drugs like carbamazepine, and sulphonamides[4,5]. This rare life-threatening adverse drug reaction is characterized by fever, generalized maculopapular rashes, haematologic abnormalities, lymph node enlargement and the involvement of internal organs[5-7]. DRESS occurring following the use of carbamazepine is reported to have a genetic influence with individuals who have the **HLA-B*58:01** and **HLA-A*31:01** being more susceptible[1,8].

Case Summary

A 33-year-old female with a two-week history of generalized rash was attended to at our facility. She gave an initial history of fever with associated rigors. At the time of clinic attendance fever had resolved but the rash was pruritic, she felt unwell, cold, the skin felt peppery and she had generalized body swelling. She gave a history of having been prescribed Carbamazepine two months prior to the onset of the rashes for a neurological disease (specific diagnosis was not known by the patient). Carbamazepine had been discontinued by the patient 2 weeks prior to clinic attendance.

Examination findings included a generalized mix of erythematous and hyperpigmented scaly macules, papules, patches, plaques and xerosis (figures 1). Additional findings were facial swelling, excoriation marks and no peripheral lymphadenopathy.

A provisional diagnosis of drug induced erythroderma to exclude drug eosinophilia syndrome (DRESS) secondary to Carbamazepine was made. A skin biopsy, liver function test, complete blood count, electrolyte urea, viral screening (hepatitis B and C, retroviral) and creatinine were ordered for. Results of complete blood count, liver function test, viral screen and skin biopsy ordered are as follows.

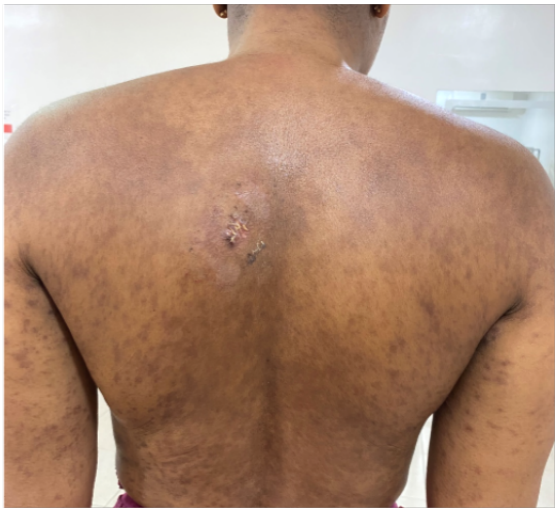

Figure 1: Generalised Erythematous Maculopapular Rashes

Complete blood count revealed a haemoglobin concentration of 11.1 g/dl (11.5-18.0), total white cell count of 8.58 x 10^9/L (4.0-11.0), a low platelet count of 33x10^9/L (150-450) and a high eosinophil percentage of 11.1% (0-6). Liver function test showed a slight increase in enzyme levels. Glutamyl transferase of 67IU/L (0-64), Alanine tranferase of 72 IU/L (<40), Aspartate transferase of 46 IU/L (15-40). Viral screen was negative, electrolyte, urea and creatinine was normal.

Skin biopsy report of subacute spongiotic diseases possibly drug induced was made based on observed hyperkeratosis, serum crust, parakeratosis, acanthosis with spongiosis. Superficial and mid-dermal dense perivascular and periadnexal lymphohistiocytic infiltrates with rare oesinophils around the sebaceous glands (figures 2A).

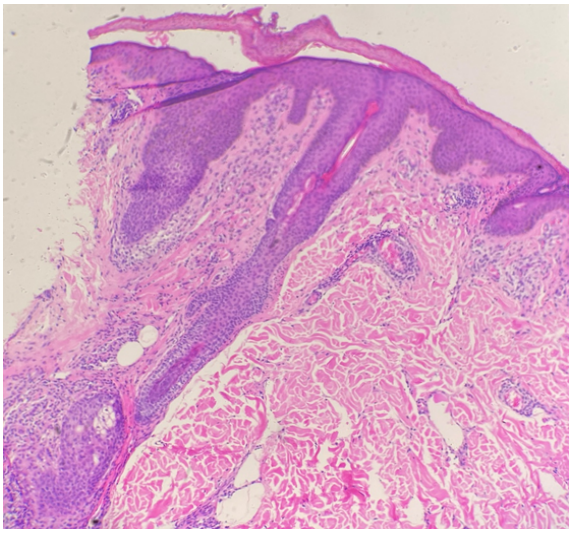

Figure 2: H & E Photomicrograph of DRESS showing superficial and deep perivascular and periadnexal lymphocytic infiltrates. X 10 magnification

She was managed with tablets Loratidine 20 mg daily, polytar shampoo three times per week, tablets prednisolone 30 mg daily for 2 weeks, glycerin in bath water and moisturizers. A final diagnosis of Carbamazepine induced DRESS was made following the results of investigations.
Review at two weeks revealed a remarkable improvement in skin appearance with residual hyperpigmentation, resolution of malaise and body swelling.

Discussion

Drug reaction with eosinophilia and systemic symptoms syndrome (DRESS) is a rare multi-systemic adverse drug reaction that occurs irrespective of age and gender[1,3,6,9,10]. The incidence is reported to be 2.18/100,000 persons and so most reports are case reports and case series like this report[5-7,8]. Several classes of drugs are reported to cause DRESS including anticonvulsants and carbamazepine is the most implicated anticonvulsant[4,5,7].
The pathogenesis of DRESS remains unclear[2,3,10]. DRESS is however, said to occur following a complex interplay between human herpes virus-6 (HHV-6) reactivation, antiviral and anti-drug immune response, drug detoxification pathways and slow drug acetylation[2,10]. DRESS being a type IV hypersensitivity reaction is mediated by T-Cells which through the release of cytokines and chemokines lead to the activation and recruitment of eosinophils[2,10]. This

cascade is thought to occur following the reactivation of HHV-6 and concurrent drug hypersensitity[2,10].

Genetic susceptibility to DRESS following the use of carbamazepine is reported in individuals who have the HLA-B*58:01 and HLA-A*31:01 genes[1,8]. HLA-A*31:01 induced susceptibility to DRESS following the use of carbamazepine is common in Europeans, the Japanese, the Chinese and it has been reported in a few North Africans[8]. We were unable to conduct HLA studies in this patient. Investigations for these HLAs is advocated in order to predict those who would have DRESS when carbamazepine is prescribed[1].

The diagnostic criteria for DRESS includes fever with temperature >38℃, an acute generalized maculopapular rashes, hospitalization, a reaction suspected to be drug induced, at least one haematologic abnormality (low platelet count, leukocytosis or leukopaenia, atypical lymphocytes and oosinophilia), lymph node enlargement (more than 2 sites), prolonged clinical symptoms (over 2 weeks) following drug discontinuation and the involvement of more than one internal organ (liver with high liver enzyme values, kidney)[2,3,5-7]. The index patient had 5 of the criteria.

Clinically, facial oedema, maculopapular rashes involving more than 50% of the body surface area like in this patient is documented in the Spanish guideline for DRESS[2]. DRESS occurs four to six weeks after the intake of carbamazepine and this patient developed DRESS 8 weeks after commencing the medication[6,7,9]. At 2 weeks, body and facial swelling had regressed and the skin lesions had significantly resolved with residual hyperpigmentation in the patient. Typically, DRESS resolves two weeks following drug withdrawal as occurred in the index patient[9].

The histopathology of DRESS includes lichenoid dermatitis and a non-specific pattern of dermatitis with a basket weave hyperkeratosis, diffuse and perivascular lymphocytic infiltrates[2]. Eosinophils may or may not be present[2]. The index patients's histopathology report is in keeping with what has been described with oesinophils.

Systemic corticosteroids are the gold standard for management[2,3]. The patient was prescribed prednisolone and antihistamines with significant resolution of symptoms.

This report was limited by the inability to ascertain the neurological disorder for which carbamazepine was prescribed and the inability to conduct HLA studies in the patient**.**

The author recommends caution in the routine prescription of carbamazepine for various indications. Patients who develop a skin rash following the use of Carbamazepine should be evaluated for DRESS. In addition, the author recommends studies of the implicated human leukocyte antigen alleles responsible for Carbamazepine induced DRESS as this will serve as a guide in the choice of patients who can be safely prescribed Carbamzapine.

Conclusion

DRESS although rare should be suspected in any patient who develops a severe adverse drug reaction following the use carbamazepine.

Acknowledgement: The patient is acknowledged for the opportunity to have this report.

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