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Case Report

Carbamazepine induced anticonvulsant hypersensitivity syndrome

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ABSTRACT

Anticonvulsant hypersensitivity syndrome (AHS) is a potentially fatal drug-induced, multi-organ syndrome. The syndrome has been reported with anticonvulsants such as carbamazepine, phenytoin, phenobarbitone, and lamotrigine. A 17-year-old female who presented with papules and desquamation all over was diagnosed with AHS. She gave a history of fever, earache, peripheral edema, and erythematous papular eruptions 3 days prior. She gave a history of carbamazepine treatment since 15 days for generalized tonic-clonic seizures. On examination, there was cervical lymph node enlargement without tenderness. Investigations revealed elevated absolute eosinophil count at 550/mm^3 and positive C-reactive protein tests. Carbamazepine was immediately withdrawn. Symptomatic treatment was administered, and resolution of the symptoms was observed. In this case, causalty assessment using Naranjo adverse drug reaction probability scale showed that carbamazepine was a probable cause for the AHS (Score - 7).

Keywords: Anticonvulsant hypersensitivity syndrome, Anticonvulsants, Carbamazepine, Fever, Rash, Lymphadenopathy, Hepatitis, Absolute eosinophil count

INTRODUCTION

Anticonvulsant hypersensitivity syndrome (AHS) is a potentially fatal drug-induced, multi-organ syndrome. The syndrome has been reported with anticonvulsants such as carbamazepine, phenytoin, phenobarbitone, and lamotrigine. Medications such as sulfonamides, sulfones, allopurinol, and non-steroidal anti-inflammatory drugs have also caused a multi-organ hypersensitivity syndrome.[1-3]

AHS is characterized by the appearance of a triad of clinical features – Fever, rash, and internal organ involvement. The incidence of AHS is about 1 in 1000 to 1 in 10,000 of anticonvulsant recipients.[4]

Carbamazepine is used alone or in combination to control certain types of seizures in epileptics. It is also used to treat trigeminal neuralgia. Extended-release capsules are used to treat episodes of mania or mixed episodes in bipolar I disorder patients. Carbamazepine belongs to the class of anticonvulsants.[5]

CASE REPORT

A 17-year-old female presented with papules, scaling (desquamation), and itching all over her body. History revealed that she had fever, earache, peripheral edema, and erythematous papular eruptions all over 3 days back. The patient was a known epileptic since 2 years, but not on medication. She had an episode of generalized tonic-clonic seizure with loss of consciousness 15 days back. She started taking carbamazepine tablets after consultation in National Institute of Mental Health and Neuroscience. On examination, cervical lymph nodes were enlarged. Investigations revealed normal hemogram, normal urine analysis, normal serum calcium, negative widal test, absolute eosinophil count raised at 550/mm^3, negative for malarial parasite, normal liver function test, normal serum albumin, normal total serum protein, and positive C-reactive protein. A diagnosis of carbamazepine induced AHS was made.

Carbamazepine was withdrawn from treatment immediately. She was administered tablet hydroxyzine

1-0-1, tablet cetirizine 0-0-1, and calamine lotion for topical application.

DISCUSSION

Fever, rash, and hepatitis are the common clinical features. Each of these clinical features may have a variable onset, and this can cause confusion and a delay in diagnosis.[6]

Fever is the commonest feature occurring in 90-100% of the cases.[7,8] High spiking fevers are characteristic, and an intermittently elevated temperature may persist for weeks even after the offending drug is withdrawn.[8] The fever may be seen concurrently with or preceding the eruption.[7]

A rash is seen in 90% of the cases.[8] It is usually a macular erythema which becomes confluent and can get generalized in to erythroderma. Initially, the face, trunk, and upper limbs are involved followed later by the lower limbs. The face may be spared. Desquamation occurs during resolution (Figure 1). Facial and periorbital edema may be severe and is seen in 25% of the cases. Blistering could be seen over the edematous areas.[8] Anticonvulsants may cause a variety of cutaneous reactions, not related to AHS. These may be urticaria, purpura, erythema multiforme, and exfoliative dermatitis.[9] Toxic epidermal necrolysis which is uncommon usually occurs in patients who are re-exposed to or continue treatment with anticonvulsants even after hypersensitivity has occurred.[10]

Hepatitis is seen in 50% cases of AHS and is usually mild, sometimes severe.[8,11] The mortality rate could be 18-40% in the presence of hepatitis. Liver function tests may be significantly elevated and continue to rise after the offending agent has been withdrawn.[8] Return to normalcy may take a year. Local or generalized tender lymphadenopathy occurs in 70% of the cases. Splenomegaly may be present.[8]

Hematological abnormalities may be seen in 50% of patients with AHS. The most common seen abnormality is leucocytosis with atypical lymphocytes and eosinophilia.[3] Coagulopathy may occur.[8,12]

Some features of AHS suggest it is a form of allergic hypersensitivity.[1] Intermediate metabolites like arene oxides can contribute to the immunological response and even cause cell death.[13,14]

Evidence suggests that inability to detoxify arene oxides leads to AHS. A familial tendency in this regard has been reported.[13,15]

Treatment is largely symptomatic. The offending drug should be withdrawn immediately.[8] Topical steroids and antihistamines may be employed to control the rash associated symptoms. Systemic steroids, when used, appear to benefit the cutaneous but not systemic manifestations.[1]

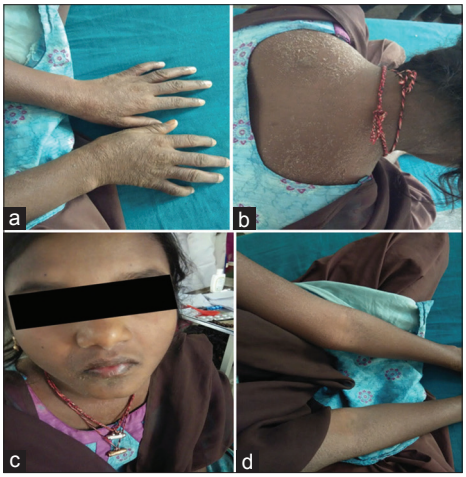

Figure 1: (a-d) Carbamazepine induced anticonvulsant hypersensitivity syndrome.

Monitoring of hematological, biochemical values is mandatory. Supportive care is also important. Relapse is common.[1]

A high rate of cross-reactivity is of concern as it limits treatment choices.[13,16]

In this case, causalty assessment using Naranjo adverse drug reaction probability scale showed that carbamazepine was a probable cause for the AHS (Score - 7).

CONCLUSION

Any patient developing fever, rash, or lymphadenopathy on treatment with phenytoin, carbamazepine, phenobarbitone, or lamotrigine should be suspected to have AHS. The offending drug should be immediately withdrawn pending investigation. Recognition is essential to avoid morbidity and possible mortality.

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