drugs exert their effects. On the other hand, medical and ethical considerations make it virtually impossible to obtain repeated biopsies of tumor tissues from the same patient and recent studies indicate the lymphocytes are a good surrogate for measuring AT levels and for investigating changes in the activity of this DNA repair enzyme induced by chemotherapeutic agents.[6]

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Safe administration of oral etoposide after hypersensitivity reaction to intravenous etoposide

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Introduction

Etoposide, a semi-synthetic derivative of podophyllotoxin, is commonly used in the treatment of malignant disease. It has been available clinically for over 20 years. A well known but rare toxicity is manifested by dyspnea, chest discomfort, hypotension, bronchospasm or skin flushing and is typical of a type I hypersensitivity reaction (HSR).[1] It has been variably suggested that this reaction may be due to either the active drug or the solvent.

We report for the first time the details of a patient who despite experiencing an anaphylactic reaction to intravenous etoposide, tolerated the subsequent use of oral etoposide without any allergic problems. We conclude that in this case at least, the solvent and not the active drug was responsible for this toxicity.

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Case report

A 76 year old female with limited small cell lung carcinoma was treated with intravenous etoposide (120 mg/m^2) and carboplatin (100 mg/m^2) daily for 3 days. The patient had a previous history of a penicillin allergy which occurred almost 20 years ago.

The etoposide infusion was prepared immediately prior to administration using standard aseptic techniques. The dose of etoposide (190 mg) was added to 500 ml of normal saline. Within minutes of the administration of etoposide, the patient complained of generalized discomfort, pruritus, shortness of breath, wheeze, erythema and was very distressed. The infusion was immediately stopped and intravenous hydrocortisone (100 mg) and promethazine (12.5 mg) were administered, along with nebulized salbutamol. After 1 h, the patient had markedly improved. Carboplatin was not administered. Treatment was changed to vincristine

1.4 mg/m^2, doxorubicin 50 mg/m^2 and cyclophosphamide 750 mg/m^2 once daily, repeated every 4 weeks. After four cycles of therapy the patient had stable disease. Five months later the patient represented with progressive disease. She was commenced on oral etoposide, 100 mg daily for 14 days. After 2 weeks of therapy the patient had not experienced any allergic reactions.

Discussion

HSRs to etoposide are rare.[1] Although isolated reports establish allergic reactions to etoposide as uncommon, one study observed HSRs in 33% of children treated for acute leukemia.[2] This study concluded that HSRs to epipodophyllotoxins in children are more common than reported, but rarely constitute dose-limiting toxicities. HSRs often occur whilst the drug is being infused, but can occur upto several hours after administration.[1] There are no known risk factors for sustaining a reaction and few patients have any history of drug allergy.

The mechanisms underlying such allergies to epipodophyllotoxins have not been elucidated. Typically, type I HSRs occur, although type II reactions have also been reported.[1,3,4] It has been suggested that the vehicle used to dissolve etoposide (benzyl alcohol and Tween 80) is responsible for these reactions, although the evidence supporting this presumption is not conclusive. In contrast, there have been no reports of HSRs induced by oral etoposide. The oral formulation contains citric acid, glycerin and polyethylene glycol.[1] The safety of oral etoposide following an allergic reaction to intravenous etoposide has never been reported. This case suggests that the vehicle (benzyl alcohol and Tween 80) and not the actual drug may be the critical factor in the etiology of type I HSRs.

The outcome of HSRs to etoposide is almost universally one of complete recovery, with only one report of a fatality.[5] Continued treatment with intravenous etoposide is often possible using premedication.[1] Alternatively, oral etoposide should be considered for patients who experience HSRs to intravenous etoposide.

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