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Short communication

Herpes simplex virus, *Candida albicans* and mouth ulcers in neutropenic patients with non-haematological malignancy

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Summary. Mouth ulcers are a frequent cause of morbidity in patients rendered neutropenic as a result of chemotherapy. We report here a series of 28 such patients from whom swabs were taken for viral isolation and mycological culture. In 13 patients, herpes simplex virus (type I) was isolated and in 17 patients *Candida albicans* was cultured. Both organisms were isolated in 9 patients. Our results suggest that both a viral and fungal element may be important in the aetiology of oral ulceration and that antiviral and antifungal agents may each have a role in the prophylaxis and treatment of such patients.

Introduction

Mouth ulcers are a problem for many patients receiving chemotherapy. Their frequent occurrence and associated morbidity, particularly in patients who are neutropenic as a result of treatment, has prompted an investigation into their aetiology. Oral ulceration is commonly associated with candidal infection, but antifungal treatment does not always lead to the resolution of the ulcers. Viral infections are frequent in patients with myeloproliferative and lymphoproliferative disorders [2, 3]. Herpes viruses have recently been incriminated in the opportunistic infections occurring in patients with acute leukaemias [5] and high-grade lymphomas [1] as well as other groups of immunosuppressed patients [4]. The aim of this study was to investigate whether herpes viruses were associated with oral ulceration in patients with solid tumours who were rendered neutropenic by chemotherapy.

Patients, methods and results

A total of 28 neutropenic patients with mouth ulcers who were receiving chemotherapy for solid tumours (8 with lung cancer, 14 with other cancers and 6 with lymphomas) were studied. Swabs were taken from the ulcers, the floor of the mouth and the nose and throat for virus isolation and mycological culture. Swabs for viral culture were submitted to the laboratory in viral transport medium and then inoculated into cell cultures of baboon kidney, HEp2 (human epithelial) and MRC5 (embryonic fibroblast) with standard antibiotic and antifungal agents.

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The cell cultures were examined at least twice weekly for any cytopathic effect. Suspicious cultures were then examined by the direct fluorescent antibody technique using monoclonal antibodies against herpes simplex virus (types I and II). Swabs from the ulcers and the floor of the mouth were submitted for mycological investigation. The swabs were broken off into *Trichomonas* medium (Oxoid). On their receipt in the laboratory, the swabs were used to inoculate petri dishes containing malt peptone agar. Plates were incubated for 48 h at 37° C and the yeasts identified.

The results obtained are shown in the following scheme:

	Site of swab:	
Virus isolated	*Ulcer*	*Nose and throat*
Herpes simplex virus (type I)	13/28 (46%)	12/28 (43%)
Fungus isolated	*Ulcer*	*Floor of mouth*
C. albicans	17/28 (61%)	17/28 (61%)

In eight patients (29%) yeasts were cultured in the absence of any viral growth; however, in four cases, two of whom had a solid cancer, herpes simplex virus (type I) was grown in the absence of fungal infection. Herpes simplex virus and *C. albicans* were both isolated in nine patients.

Comment

These results suggest that although *C. albicans* may frequently be associated with oral ulceration, the herpes simplex virus (type I) may also be an important aetiological agent in nearly half of such patients. Although the number of patients in this study was small, the results suggest a role for both antifungal and antiviral agents in the prophylaxis and treatment of oral ulceration in patients on chemotherapy for common solid cancers. Indeed, in a subsequent series of comparable patients, we were impressed by the responses seen when oral acyclovir (200 mg 5 times daily for 5 days) was given in addition to conventional antifungal agents such as nystatin.

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