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LETTER TO THE EDITORS

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Vinca alkaloids and macrolides in human immunodeficiency virus-related malignancies: a safe association

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Sirs,

With regard to the recent report of serious side effects following the administration of vinblastine and erythromycin in cancer patients [3] and the warning about the risks of the above-mentioned association and its increasingly widespread use, we would like to report our personal experience in the management of patients infected with the human immunodeficiency virus (HIV) and treated for cancer.

It is well known that malignancies, above all Kaposi's sarcoma and non-Hodgkin's lymphoma, are acquired immunodeficiency syndrome (AIDS)-defining conditions, and their incidence is growing due to the prolonged survival of patients infected with HIV in developed countries. Importantly, these neoplasms often occur in the late stages of the disease, when the patients are heavily medicated with antiretrovirals and antibiotics for both therapy and prophylaxis. Moreover, HIV-positive subjects are peculiarly prone to develop unwanted side effects to drugs otherwise very well tolerated in the general population, e. g. life-threatening multisystem reactions to cotrimoxazole.

The drugs most commonly prescribed include zidovudine and its nucleoside analogues didanosine and zalcitabine; cotrimoxazole for therapy and prophylaxis of *Pneumocystis carinii* pneumonia and neurotoxoplasmosis; and multidrug regimens for pulmonary and extrapulmonary tuberculosis and for disseminated mycobacterial infections. The latter regimens often comprise associations of rifampicin or rifabutin with clarithromycin, all extensively interacting with cytochrome P-450 enzymes in the liver. With regard to erythromycin, though, clarithromycin and the cytochrome P-450 enzymes do not form complexes in vivo without prior induction with steroids [1, 2]. Due to the increased life span of severely immunodepressed patients, all these medications are likely to be consumed for very long periods.

Clarithromycin, alone or in association with fluoroquinolones, is widely prescribed in the immunocompromised host because of its high intracellular concentrations and peculiar range of activity, even in the case of fevers or respiratory tract infections other than the above-mentioned clinical entities. On the other hand, vinblastine and vincristine are frequently given to our patients both as single drugs for Kaposi's sarcoma and as components of chemotherapy regimens for lymphomas. As a rule, our patients receive full doses of all prescribed drugs. Withdrawal of concomitant antiretrovirals and administration of recombinant hematopoietic growth factors, while avoiding the risk of dangerous myelosuppression, allow us to comply with the principle of dose intensity, at least in the therapy of lymphomas.

For all these motives, the concomitant administration of standard doses of vinca alkaloids and clarithromycin and, possibly, rifabutin is very likely to occur in such subjects, and it did occur in at least half a dozen cases among our patients. Thus far, no side effect such as those described has been observed. Our patients are very closely followed during their antiblastic therapies with weekly blood counts and clinical assessments. On the whole, they are well aware of the nature of the possible unwanted side effects of their therapy and can be relied upon to report them at their first appearance. It is therefore highly unlikely that they have gone unreported or unnoticed.

We can conclude that in our patients the association between vinca alkaloids and clarithromycin has always proved safe. We therefore suggest that clarithromycin be taken into account whenever a macrolide is needed in patients treated with vinblastine or vincristine. Greater caution should perhaps be exercised when steroids or other drugs interacting with cytochrome P-450 enzymes are added, although in our experience the association of rifabutin with the above-mentioned drugs has been equally well tolerated.

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