

Idiopathic oesophageal ulcers in a woman who is HIV+: Thalidomide therapy

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Abstract

We present a case of an HIV+ woman with idiopathic esophageal ulcers with an excellent response to thalidomide therapy, which also induced the remission of a concomitant febrile syndrome. The mechanism of action of thalidomide in this situation is unknown

although it can be related with the effects of the drug on the immune system, or to a direct anti-retroviral effect.

Key words: thalidomide, HIV, AIDS, idiopathic oesophageal ulcers, idiopathic oesophagitis.

Introduction

The esophagus is often a site of opportunist infections in HIV positive patients, which are most commonly manifested as dysphagia and odynophagia, often with severe consequences on the patient's feeding and nutritional state. The microorganism most frequently responsible is *Candida albicans*, but cases are also described of oesophagitis by cytomegalovirus (CMV), the herpes simplex virus, the Epstein-Barr virus and mycobacterium.¹⁻³ Besides infectious oesophagitis, cases of esophageal ulcers are also described in this population, in which it is not possible to identify the microorganisms responsible, and which it is speculated may be directly caused by the HIV.⁴ The treatment of these situations is controversial; the drugs most commonly used are corticoids which, besides being problematic due to their side effects and immunosuppressant action, are also associated with frequent recurrences.⁵ Thalidomide, the efficacy of which has been demonstrated in the treatment of oral idiopathic ulcers in HIV+ patients,^{6,7} has been used successfully in some cases of idiopathic esophagitis.⁸⁻¹²

Case report

Patient aged 25 years, female, drug dependant, admitted with productive cough, asthenia and extreme fatigue, weight loss (± 10 Kg), odynophagia and upper dysphagia, with around two months of

evolution. Objectively, she was cachectic, apyretic, pale and dehydrated, with exuberant oropharyngeal thrush, generalized microadenopathy and slightly enlarged liver.

The laboratory tests revealed severe normocytic anemia, with Hb of 5.7 gr/dL. Serology for HIV (by Western Blot) was positive for HIV 1, and serology for the hepatitis C virus was also positive. The lymphocyte counts were 107 CD4/mm³ and 730 CD8/mm³. The antigen p24 was "weakly positive" (68.4 pg/mm³).

Chest telerradiography showed a heterogeneous condensation at the base of the right lung which, in the computed axial tomography of the chest, proved to be pneumonia of the middle lung lobe. Direct study of acid-alcohol resistant bacilli in the expectoration and bronchial lavage and Mantoux were negative. However, given the high probability that it was pulmonary tuberculosis, in clinical and epidemiological terms, therapy was instituted with isoniazid, rifampicin and pyrazinamide, resulting in rapid clinical and radiological improvement, and improvement of the anemia.

The lesions of the oral candidiasis also disappeared, as well as the dysphagia and odynophagia, under therapy with fluconazole. However, around two weeks later (still under fluconazole), the onset of very marked dysphagia occurred (located in the lower third of the esophagus) and retrosternal pain, with high fever several days later.

Upper digestive endoscopy was carried, showing three irregular surface ulcers, with hyperemiated base, in the upper and middle thirds of the esophagus; histological exam revealed "grade IV oesophagitis", with no infectious agent being isolated. Ten days of thera-

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py with acyclovir iv were administered without any response, therefore it was decided, with the patient's informed consent, to start thalidomide (100 mg p.o./day for 14 days), with rapid and total regression of the oesophagitis and of the fever. She was discharged without symptoms, with significant weight gain, and no side effects of the thalidomide. She was readmitted around seven months later with miliary tuberculosis (the therapy was abandoned soon after discharge), and she later died. In the meantime, there was no recurrence of any of the esophageal symptoms.

Comments

Thalidomide, a drug whose tragic history led to it being practically abandoned, has seen a resurgence in recent years for the treatment of various complaints, predominantly those affecting the skin or mucosae,¹³⁻¹⁷ including in oral idiopathic ulcers in HIV+ individuals;^{6,7} by extension, their use has been tried in other idiopathic ulcerations of the mucosa in these patients (esophageal and others), with good results in the few cases published.^{8-12,18-20} In our patient, the efficacy was dramatic, improving, within a few days, from a situation of near incapacity to ingest foods to total regression of the symptoms and disappearance of the fever 24 hours after the start of therapy.

The exact mechanisms of action of thalidomide have yet to be clarified. Some works speculate on the possibility of a direct antiretroviral effect.²¹ But complex effects on the immune system are also described, in particular, the decrease in serum levels of tumor necrosis factor (TNF- α),^{22,23} which it is admitted is the basis of its effect on the weight loss syndrome and diarrhea by microsporidia in HIV+ patients, which is currently the subject of study.^{24,25} Knowing that TNF- α is one of the principal intrinsic pyrogenic cytokines, it can be speculated that this mechanism was the basis of the action in reducing fever in our patient. It is noted, incidentally, that we find reference to a further two cases in which simultaneous remission of fever and esophageal ulcers was observed under therapy with thalidomide.^{9,11}

Thalidomide is, therefore, going through a process of rediscovery, and we present this case as a call to attention for new indications of a drug that, despite its severe potential and side effects, has proven to be of great usefulness, particularly in HIV+ patients, for whom any addition to the therapeutic arsenal is welcomed. ■

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