LETTERS TO THE EDITOR

Nicorandil: A curable cause of anal ulceration to be known...

Le nicorandil : une cause curable d’ulcération anale à connaître...

Introduction

Aetiological diagnosis of anal ulcerations can be difficult because of the wide variety of possible causes ranging from anal fissure, tumour and haematological malignancies, Crohn’s disease, infection, specific dermatitis, trauma or systemic diseases to iatrogenic lesions. The latter occur rarely and have been described above all with drugs administered as suppositories [1]. However, nicorandil, a vasodilator administered orally for the prophylactic management of attacks of exertional angina, has recently been incriminated in the occurrence of anal ulceration [2–5] and we have been confronted with several patients in whom the diagnosis had not been considered previously. We are therefore reporting a particularly characteristic case of this iatrogenic pathology still poorly recognised but nevertheless reversible.

Case report

A 74-year-old man consulted in April 2009 for anal pain which had developed over a period of at least 6 months, associated with bleeding and seepage staining his underclothes. He was being treated for arterial hypertension and ischaemic heart disease. He had moreover undergone sclerosis and elastic ligature several times for a haemorrhoidal condition more than ten years before. He had stopped smoking several years previously. He was being treated medically with Adancor® (nicorandil 40 mg/d), Tenormine® (atenolol), Bi-Tildiem® (diltiazem), Lipanthyl® (fenofibrate) and Kardegic® (lysine acetylsalicylate).

On examination, he had ulceration of the posterior pole of the anus, with a clean base and non-indurated borders extending into the anal canal as far as the pectinate line (Fig. 1). Furthermore, there were haemorrhoidal tabs and internal haemorrhoids with no unusual features. The rest of the cutaneous and mucosal examination was normal.

A diagnosis of iatrogenic ulceration related to nicorandil was suspected and the treatment interrupted with the agreement of the cardiologist. The condition then evolved favourably with complete healing of the ulceration in a little over four months (Figs. 2 and 3).
Figure 3 Complete healing 5 months after cessation of therapy.

Discussion

Nicorandil is a nicotinamide ester marketed in France since the beginning of the 1990s under the trade names of Adancor® and Ikorel®. Oral mucosal ulceration related to the use of this product has been described since 1997 [6]. The first cases of anal lesions were reported in 2002 [2]. The largest series of anal lesions (24 patients) dates from 2005 [3] and, at the present time, more than 60 cases have already been published. Other digestive lesions have been described, particularly in the colon [7] and ileum [5]. The incidence today of ulceration induced by nicorandil, in any location, is estimated to be approximately 1 for 1500 prescriptions [3].

This iatrogenic anal ulceration appears in the months following the start of treatment in patients who, in general, have no particular history of digestive problems. It may occur in the anal canal, the anal margin or the peri-anal skin, and become apparent above all through pain. There may be a single or multiple instances of ulceration of varying sizes, extending and excavating progressively, even destructively. Analysis of their pathological anatomy is not specific. Other concomitant lesions, particularly in the mouth, are possible. Surgical treatment, without interrupting nicorandil administration, is ineffective. On the other hand, healing occurs within a few months of discontinuing administration [2–5].

The physiopathological mechanism of these ulcerations has not been elucidated. The hypotheses have been suggested of a vascular steal phenomenon and/or a toxic type of reaction. The effect seems to be dose-dependent since the ulcerations can sometimes heal simply by reducing the dose. It is probably the result of systemic passage since faecal excretion of nicorandil is slight, purely cutaneous lesions have been described and anal ulceration recurred after reintroducing the product in a patient who, in the meantime, had had a diverting colostomy. Whatever the mechanism, no factor encouraging the occurrence of this undesirable effect has been identified [3–5].

Conflict of interest statement

None.

References


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Chronic anemia resistant to erythropoietin in a patient treated with gemcitabine showing a hemolytic uremic syndrome (HUS)

Anémie chronique résistante à l’érythropoïétine chez un patient traité par gemcitabine révélant un syndrome hémolytique et urémique (SHU)

Hemolytic uremic syndrome (HUS) has been described for the first time by Gasser et al. in 1955 [1]. It involves several etiologies [2] with infections, connective tissue disease, some treatment (quinine, interferon, clopidogrel, etc.) and cancers. The first cases with cancer chemotherapy have been reported about 30 years ago with mitomycin C and 5-fluorouracil [1,2]. The use of gemcitabine nucleotide analog derivative from cytarabine [2,3] is rarely complicated by HUS. HUS typically results in thrombocytopenia, hemolytic anemia and renal failure [1–4]. The appearance of hypertension or worsening of figures in a patient treated with gemcitabine experienced hypertension are among the warning signs [4]. We report a case of HUS...