REPORT OF A CASE OF MALIGNANT TUMOR-LIKE GASTRIC LESION BY CANDIDA IN A DIABETIC PATIENT TREATED WITH CYCLOSPORINE FOR PSORIASIS AND REVIEW OF THE LITERATURE

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Gruppo editoriale
Archivio Siciliano di Medicina e Chirurgia (3)

ISSN 0393-6384

ACTA MEDICA MEDITERRANEA

ESTRATTO

VOLUME 27, N. 1 2011

Acta Medica Mediterranea, 2011, 27: 17

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[Lesione gastrica simil-maligna causata da candida in paziente diabetica trattata con ciclosporina per psoriasi. Revisione della letteratura]

SUMMARY

Mycotic infection of the alimentary canal are rare and usually involve the upper digestive tract. Mycetes, especially of Candida family, are habitual saprophytes in the digestive tract of healthy individuals. Under certain conditions, fungal flora may overgrowth, resulting in lesions of the digestive mucosa, which, rarely, might evolve to local diffusion and/or systemic lympho-hematogenous spreading. In the stomach, sometimes, mycotic infections may appear like benign gastric ulcers. We described a case of a woman, aged 64, affected by psoriasis, in chronic treatment with cyclosporine and type 2 diabetes mellitus, a well-known immunosoppressive condition, with endoscopic evidence of ulcerated vegetating gastric lesion, strongly suggestive for malignancy, due to Candida albicans infection, and completely healed after cyclosporine withdrawal and administration of oral antifungal drugs.

Key words: Candidiasis, mycotic infection of the gastrointestinal tract, submucosal tumor

RIASSUNTO

Le infezioni micotiche del canale alimentare sono rare e di solito coinvolgono il tratto superiore dell'apparato digerente. I miceti, specialmente della famiglia Candida, sono saprofiti abituali del tratto digestivo di individui sani. In determinate condizioni, però, la flora fungina può crescere eccessivamente, causando lesioni della mucosa dell'apparato digerente, che, raramente, possono evolvere verso la diffusione locale e/o sistemica per via linfo-ematogena. Nello stomaco, a volte, le infezioni micotiche possono manifestarsi come ulcere gastriche benigne. Nel lavoro descriviamo il caso di una donna di 64 anni, affetta da psoriasi, in trattamento cronico con ciclosporina, e diabete mellito tipo 2, una ben nota condizione immunodepressoria, con evidenza endoscopica di una lesione gastrica vegetante ed ulcerata, fortemente suggestiva per malignità, causata da Candida albicans e completamente guarita dopo la sospensione della ciclosporina e la somministrazione di farmaci antifungini per via orale.

Parole chiave: *Candidiasi, infezione micotica del tratto gastrointestinale, tumore sottomucoso*

Introduction

Hundres of saprophytes colonize the human gastrointestinal tract of healthy individuals: mycetes, especially Candida species, represent the common ones[1,2].

Rarely mycotic infection affect the digestive tract, but, under certain conditions, fungal flora may overgrowth, resulting in lesions of the digestive mucosa. The most affected district is the upper digestive tract. Sometimes mucosal lesions may evolve into a framework of local diffusion and/or systemic lympho-hematogenous spreading. The most important risk factors are smoking, systemic diseases, such as tuberculosis and polyarteritis nodosa, gastrointestinal diseases, such as eosinophilic gastritis, cancer (i.e. lymphoma), Zollinger-Ellison syndrome and Crohn's disease, and, finally, administration of antibiotics, steroids, immunosuppressive and anticancer drugs.

Mycotic infections of the stomach might, sometimes, look like benign gastric ulcers. Litterature reports several cases concerning this relathionship, but there are still no strong evidences[3,4].

We described the case of a woman, aged 64, affected by psoriasis, in treatment with immunosuppressive agents (cyclosporine), and diabetes mellitus, with endoscopic evidence of ulcerated vegetating gastric lesion, strongly suggestive for malignancy, due to Candida albicans infection, and completely healed after cyclosporine withdrawal and administration of oral antifungal drugs.

Case report

On August 2010 a 64-year-old woman was admitted in our Department for epigastralgia, melena, anorexia, and weight loss of 5 Kg over the last 3 months. Anamnesticaly she reporte d diagnosis of psoriasis (1990), treated with cyclosporine since 2003, type 2 diabetes mellitus, treated with metformin, mixed dyslipidemia, treated with fibrates and surgery for anal fissure (1995). She, also, refered single episode of paroxysmal atrial fibrillation (1997) and Transient Ischemic Attack (1998), in treatment with ASA, hypertensive heart disease and reactive depression since 2000.

When she was admitted clinical examination showed severe pain in epigastrium, psoriatic lesions (sacrum and nails) and singol enlarged lymph node in the right supraclavicular fossa, with benign characteristics.

Laboratory assays showed hypochromic microcytic anemia (hemoglobin concentration 8.3g/dl), with hyposideremia (3μg/ml) and hypoferritinemia (7ng/ml), and positive occult blood in feces. Endoscopic examination of the upper digestive tract revealed a multi-ulcerated vegetating lesion, with circumferential pattern, size more than 5cm, on the posterior wall of the stomach body, that affected the progression of peristaltic waves (Figure 1).

Figure 1: endoscopic appearance of multi-ulcerated vegetating lesion, with circumferential pattern, size more than 5cm, on the posterior wall of the stomach body. Ulcers presented with irregular margins and fibrinous bottoms.

Ulcers appeared with mamelon margins and fibrinous bottoms. Neverthless these findings had a strong clinical evidence of malignant gastric lesion, the biopsies of ulcers and vegetating lesion excluded this one, revealing, only, marked chronic inflammatory infiltrate, at moderate activity, associated with degenerative-necrotic phenomena. We prescribed proton pumps inhibitors (PIPs), then discharged the patient recommendig endoscophical and byoptical follow-up.

Soon after, September 2010, the patient, presenting the same symptoms, was re-admitted to our Department and underwent to another upper digestive tract endoscopy, that showed, easily bleeding, unchanged ulcerated vegetating lesion on the posterior wall of the stomach body. Biopsies showed chronic gastritis with moderate activity, locally severe, with areas of foveolar hyperplasia. CT of chest and abdomen, using contrast material, revealed nodular lesion, sizeing 7mm, in the medial segment of the right middle lung lobe of unknown origin, and irregular thickening, partially mammelonated, of the posterior wall of the stomach body, associated with hyperplastic lymph nodes along lesser curvature of the stomach, liver hilum, and celiac, portacaval, and interaortocaval level, and, finally, splenomegaly (Figure 2).

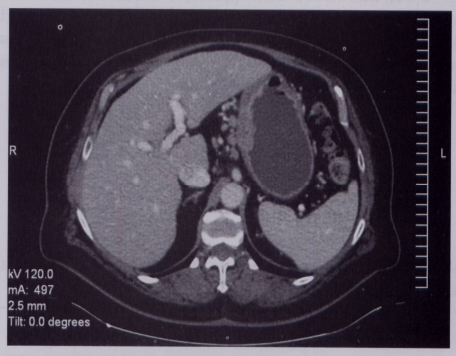

Figure 2: CT appearance of irregular thickening, partially mammelonated, of the posterior wall of the stomach body, associated with hyperplastic lymph nodes along lesser curvature of the stomach, liver hilum, and celiac, portacaval, and interaortocaval level, and splenomegaly.

The patient was assigned to the Surgery Department of our Hospital, where she underwent further upper digestive tract endoscopy, with evidence of the same lesion, extended to stomach body and antrum (Figure 3), and multiple deep gastric lesion biopsy specimens.

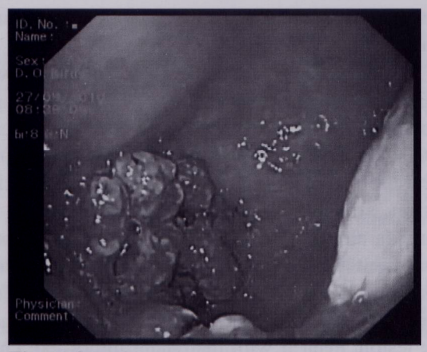

Figure 3: endoscopic appearance of easily bleeding, unchanged ulcerated vegetating lesion on the posterior wall of the stomach body and antrum.

Biopsies showed chronic gastritis, with moderate activity and degenerative-necrotic phenomena, and a lot of hyphae of Candida albicans in the inflammatory exudates (Figure 4).

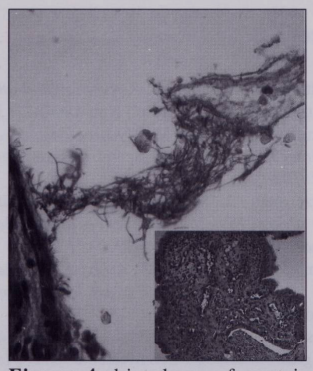

Figure 4: histology of gastric lesion, showing chronic gastritis, with moderate activity and degenerative-necrotic phenomena (hematoxylin and eosin staining), and a lot of hyphae of Candida albicans, positive for Alcian Blue and Periodic Acid-Schiff (PAS) staining, in the inflammatory exudate.

This evidence suggested to withdraw cyclosporine and undertake oral itraconazole therapy (100mg b.i.d. for 15 days, then repeated after 15 days of suspension). After 6 weeks, the patient's symptoms disappeared, body weight increased (about 3 Kg), and anemia improved (hemoglobin concentration 10.8g/dl). She underwent endoscopic follow-up, after 2 months, which showed significant volume reduction of stomach vegetant and ulcerated lesion (Figure 5), whereas CT of chest and abdomen, with contrast material, showed the complete disappearance of the gastric thickening, the abdominal lymph nodes and the lung nodular immage. Further upper digestive tract endoscopy, after 6 months, showed the complete disappearance of the lesion.

Figure 5: endoscopic appearance of significant volume reduction of stomach vegetant and ulcerated lesion.

Discussion

Fungal infection of the gastroenteric system are usually rare, even thought some risk factors allow this pathologycal event. Candidiasis represent more pervasive one. Candida has been described in oropharynx, jejunum, ileum and stools samples[5]. Althought immunocomprimised patients are the most affected, apparently healthy subjects may be affected too[6]. Esophagus is the most involved and occur with odynophagia, dysphagia and bleeding. Stomach, despite the extremely acid environment, may be affected too, showing diffuse mucosal involvement, or, occasionally, focal invasion and colonization of benign gastric ulcers[7,8].

Autoptic studies are the best way to assess prevalence of gastrointestinal fungal infection. These weighted fungal infection prevalence in 4% of patients who died from cancer. Esophageal localization has been appraised in 2.5-7.3% of patients who had undergone endoscopy, and presence of a fungal infection in 16% of benign gastric ulcers and in 18% of resected stomach for gastric ulcer. These data suggested not uncommon association between benign gastric ulcer and overlyng Candida infection[3,5,9,10].

Decreased immunological competence and increased incidence of systemic diseases (especially diabetes mellitus and malignancies), as well as by increased use of anti-H2 receptors or PPIs, which, altering gastric acid environment, may promote overgrowth of the physiological mycotic flora, could explain the high prevalence of gastrointestinal fungal infections[11]. The stomach fundus, being the most common site of benign gastric ulcers, is mainly affected by infected benign gastric ulcers. Endoscopic findings of Candida-infected gastric ulcers vary from ulcerated lesions, with irregular borders, to submucosal tumor-like lesions, bezoar-like images, gastric foreign body, and very large lesions (> 2cm)[12,13].

Therapy should be undertaken as soon as possible being reported few cases of bleeding or perforation caused by Candida infected gastric ulcers[14]. Treatment include anti-H2 receptors or PPIs, or antifungal drugs, or a combination of both, but a well-defined guideline has not yet been established. Evidences show antifungal treatment is unecessary in young patients without severe underlying diseases, cause most of these recovered without specific treatment. Antifungal drugs may be considered either in colonized ulcers unresponsive to treatment with anti-H2 receptors and PPIs or in systemic spreading of mycetes, or in high-risk patients (advanced age, use of immunosuppressive drugs, malignancy), in which elevated fungal proliferation may cause local complications (bleeding and/or perforation)[15,16].

To our knowledge, this is the first report of a ulcerated vegetating gastric lesion, strongly suggestive of malignancy, whose Candida etiology is clearly prooved by the failure of standard therapy with anti-H2 receptors and PPIs, and the complete response to the suspension of the immunosuppressive drug and to the antifungal therapy. As described in litterature, the infection occurred in an adult high-risk immunosoppressed patient, affected by psoriasis, in chronic treatment with cyclosporine, and by type 2 diabetes mellitus, a well-known immunosoppressive condition[3,4].

Inflammation and cellular infiltration in the deep mucosal layer, completely healed after antifungal treatment, could explain the macroscopic malignant tumor-like characteristics of the lesion, as the hemorrhagic complication of the lesion (iron deficiency and sideropenic anemia, with positive occult blood in feces) and his locoregional (circumferential gastric wall involvement plus abdominal lymph nodes colonization) and probably systemic (pulmonary) diffusion.

In conclusion, gastric lesions, appearing with different endoscopic and radiologic feedings, should be suspected of Candida infection in patients with abdominal pain, and predisposing conditions. We report a case of gastric ulcerated vegetating lesion, strongly suggestive for malignancy, by Candida albicans, in a diabetic woman, in chronic treatment with cyclosporine for psoriasis, and described its endoscopic and radiologic (CT) features. The case suggests that the presence of a gastric lesion, even if with malignant tumor-like characteristics, in a high risk patient for fungal infections, may indicate the possibility of an alternative diagnosis of Candida infection and a specific antifungal treatment.

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