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The other biotherapeutic potential of colchicine

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Introduction

Colchicine is a classic and powerful anti-inflammatory agent, which also has an antiproliferative effect by acting as a destabilizer of microtubule polymerization through tubulin-binding and, thus, suppressing cell division and leading to apoptosis [1-3]. This antimitotic action of colchicine, demonstrated even at low doses, has been explored for its potential antitumor activity in several studies [1]. The low cost and long-standing prescription experience are additional factors that increase the interest as an alternative therapeutic agent for different types of cancer.

Case Report

A 50-year-old obese and type 2 diabetic woman presented with a 2-week history of epigastric pain, diarrhea and abdominal distention. Initial blood tests indicated isolated increase in C-reactive protein levels. An abdominal computed tomography (CT) scan showed moderate ascites and thickening of the stomach, peritoneum and large epiploon. The peritoneal fluid analysis revealed a mononuclear exudate associated with a serum albumin ascites gradient <1.1 g/dL, negative for bacterial, fungal and mycobacterial infections; anatomopathological exam showed scarce mesothelial cells with discrete nuclear atypia. Endoscopic studies with tissue biopsy excluded neoplastic lesions and tissue biopsy was negative for malignant cells. A diffusion weighted magnetic resonance revealed a high intensity micronodule in the peritoneal posterior recess. Positron emission tomography (PET)/CT scan showed a diffuse 18fluorine-fluorodeoxyglucose (^{18}F-FDG) uptake over abdominal fat, peritoneal effusion and abdominopelvic adenopathies (Figure 1). The patient underwent a diagnostic laparoscopy and biopsies were taken from the peritoneum, whose histopathological result showed chronic xanthomatous histiocytic inflammatory process; the histology was reviewed by an external laboratory, which concluded that specimen's features were compatible with cytosteatonecrosis and inflammation associated with mesothelial proliferation, with some small nodules of mesothelial cells showing atypia and an immunohistochemical profile (p53 and epithelial membrane antigen (EMA) positive, desmin negative) suggestive of a mesothelial neoplastic process, but not otherwise proven. Infectious (including tuberculosis), autoimmune and lysosomal diseases were excluded. Due to

family history of ascitic liver disease and the absence of unequivocal evidence of neoplastic etiology, an autoinflammatory condition was hypothesized and a colchicine 1 mg/day course was started. An unexpected symptomatic remission and regression of imaging findings were apparent in subsequent PET/CT (Figure 2). Despite a negative genetic study, diagnostic criteria for Mediterranean Family Fever were fulfilled; hence, the strategy was sustained. About seven months later, clinical relapse was observed. CT showed gastric thickening associated with perigastric adenopathies, ascites and peritoneal nodules. Upper endoscopy revealed a gastric mucosa densely infiltrated, with histological confirmation of diffuse/undifferentiated signet ring cell carcinoma; pelvic nodule core-biopsy suggested synchronous ovarian tumor. The patient received palliative chemotherapy, but she died of tumor progression a year after the onset of the disease.

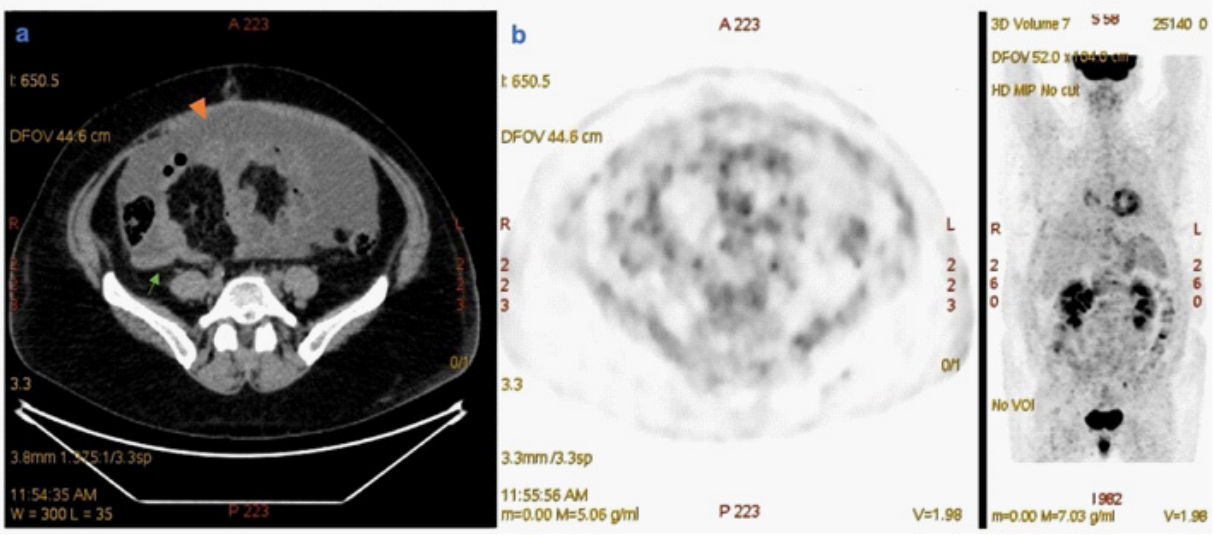

Figure 1: CT and 18F-FDG PET scans at baseline.
Axial CT (a) and 18F-FDG PET/CT scan (b; axial and coronal sections, respectively) showing generalized densification of abdominal fat (arrow), associated with large peritoneal effusion (arrow head), with heterogeneous 18F-FDG uptake.

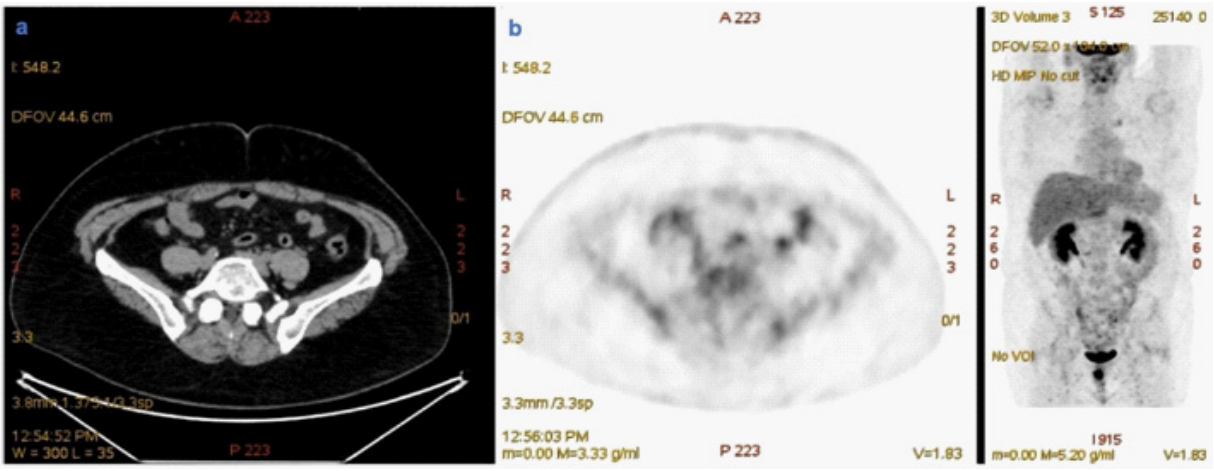

Figure 2: CT and 18F-FDG PET scans after 2 months of colchicine treatment.
Axial CT (a) and 18F-FDG PET/CT scan (b; axial and coronal sections, respectively) demonstrating marked reduction in the extent of mesenteric fat densification, which currently shows no 18F-FDG uptake, and the disappearance of peritoneal effusion.

Discussion

We hypothesize that neoplastic scenario was present from the beginning, but the diagnosis could not be established. The purpose of this case is to reflect on the cytomodulatory effect of colchicine and its possible application as an adjunctive treatment in certain oncological conditions.Despite being commonly used in clinical practice in safe dosage, more recent colchicine semi-synthetic derivatives are equipotent, but with less toxicity [4,5].

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