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## LETTER TO THE EDITOR

**An unusual presentation of T-lymphoma in a Crohn's disease patient treated with combo therapy: We are willing to take a risk of serious adverse events for a doubtful benefit?**

Dear Sir,

It is still questioned the use of combination therapy with biologics and immunosuppressants in the management of severe or steroid-dependent Crohn's Disease (CD). The main concern is about the risk that a prolonged therapy may increase the incidence of lymphoproliferative disorders.<sup>1</sup>

A 46 year-old man with ileocolonic CD diagnosed at the age of twenty year-old was admitted, on January 2012, to our unit for the abrupt onset of obstructive jaundice, associated with weight loss. The previous clinical course of CD was indolent in the last 20 years, and the patient maintained long periods of remission after short courses of steroids and metronidazole up to 2004, when he moved to USA for work. In USA the patient was followed-up in outpatients' clinic and combo therapy was started with infliximab (5 mg/kg) and 6-mercaptopurine (1.5 mg/kg/die) because of the evidence of osteoporosis at the bone densitometry, despite clinical remission. This therapy was prolonged for six years. The patient came back to Italy after 8 years for holidays.

At the admission, on physical examination the patient presented with palpable gallbladder, associated with mild right upper abdominal tenderness, without any abdominal mass or peripheral lymphadenopathy; the Crohn's Disease Activity Index was inferior to 150.

Laboratory tests showed slight elevation of aminotransferases (AST/ALT 2,5/5 × upper normal limit [UNL],) and of cholestasis markers (alkaline phosphatase 1.5 × UNL, gamma-glutamyltransferase × 10 ULN, total bilirubin 11.13 mg%, with direct bilirubin 5.34 mg%). Erythrocyte sedimentation rate and C-reactive protein were normal.

An abdominal ultrasound showed an extrahepatic obstruction of the biliary tree, associated with gallbladder distension and intrahepatic biliar tract dilation, caused by a hypoechoic neof ormation of 3 centimeters, due to lymphadenopathy, which compressed circumferentially the distal tract of chole-docus (Fig. 1). To investigate the possibility of a lymphoproliferative disease, a chest and abdominal Computed Tomography scan was performed, showing a bulky mass in the thymic lodge, with multiple lymphadenopathy in the mediastinum and

significant pericardial and pleural effusion (Fig. 2), and confirming the distal obstruction of the biliary tree. An endoscopic retrograde cholangio-pancreatography was performed to place a stent, with resolution of the biliary obstruction. However, 2 days after, worsening dispnoea occurred, and a cardiac tamponade was diagnosed, thus the patient underwent to urgent therapeutic pericardiocentesis. In few days the patient showed a marked clinical improvement, thus he underwent a biopsy of the mediastinic mass; at the histology a lymphoblastic T-lymphoma was diagnosed.

The patient was treated with chemotherapy (Idarubicine, Vincristine, Asparaginase and corticosteroids), but unfortunately died 10 days after because of an Acinetobacter baumannii pneumonia.

Although recently the SONIC<sup>2</sup> study showed an advantage of combo therapy compared to monotherapy with azathioprine or infliximab in patient with active CD, the current european and Italian guidelines suggest that thiopurines could be add in the naive patient, but the long-term combination of azathioprine or 6-mercaptopurine and anti-TNF therapy is best avoided in young people because of the risk of hepatosplenic T-cell lymphoma.<sup>3,4</sup> In this case the indication to the combo therapy was not justified by the

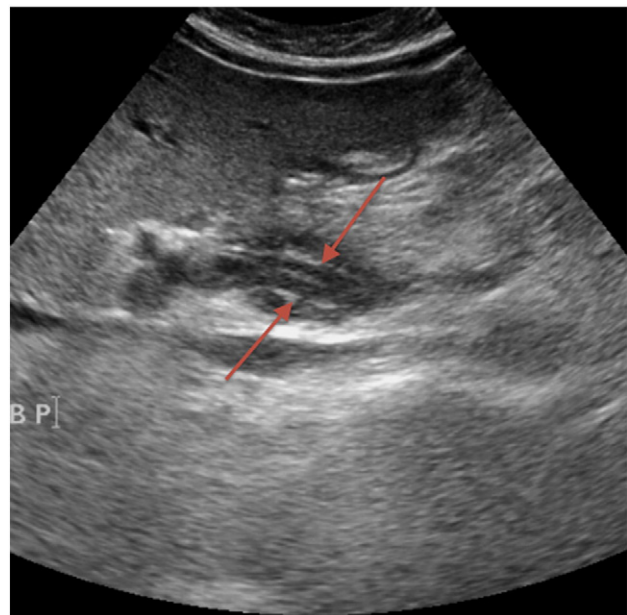


Figure 1.

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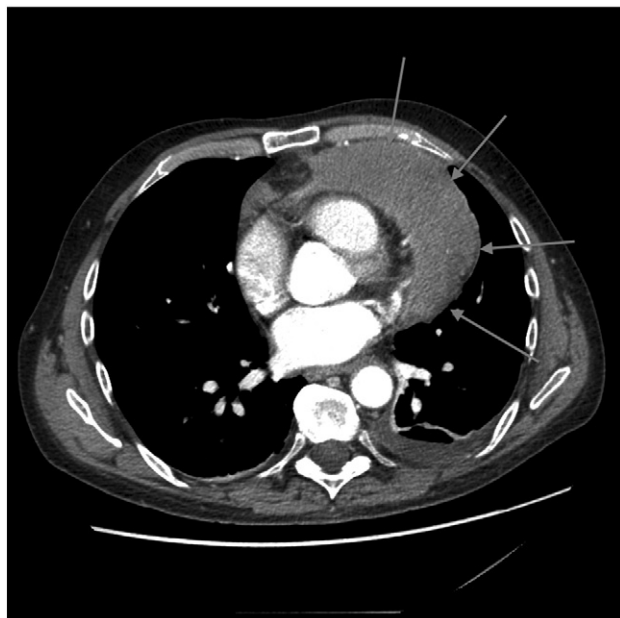


Figure 2.

clinical activity of CD, but only by the diagnosis of asymptomatic osteoporosis. Our opinion is that the combo therapy exposes to a risk of adverse events, and in any therapeutic decision the possible benefits must be weighted against possible risks, as in the case reported, where there was not a strong indication for this aggressive treatment.

Thus, when we decide to treat active CD with combo therapy we should consider if we are willing to take a risk of serious adverse events, although rare, for a doubtful benefit.

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