The drop in neutrophils puts patients at risk of infections and may be due to primary causes (haematological malignancies) or secondary causes, most of which are drug-related toxicities.

TNF inhibitor drugs themselves and secondary morphological abnormalities in lymphocytes, such as LGLs, play a role in neutropenia associated with TNF inhibitor drugs and can suppress haematopoiesis, which may be part of an initial myelodysplastic syndrome.[1–4]

LGLs comprise a subgroup of T-lymphocytes within natural killer cells which appear normally in 10%–15% of peripheral blood.[2,3]

They may be of monoclonal origin as in LGL leukaemia, myelodysplastic syndromes, or of non-monoclonal origin secondary to viral infections, haematological disorders such as lymphoma or autoimmune disorders.

Studies from clinical trials in inflammatory bowel disease (IBD) and rheumatoid arthritis have established an incidence of neutropenia (count <1000) of 0.6%–0.9% for ADA and 1.1%–5.7% for infliximab. Despite this, 81% of patients stayed on the same treatment whereas all others switched to TNF inhibitor drugs; however, 62.5% had to suspend them due to recurrent neutropenia.[1]

In severe neutropenia (count <500), it is recommended that the drug be suspended and that secondary causes such as haematological disorders be investigated.

With these data, transient or persistent neutropenia associated with TNF inhibitor drugs is known to be underestimated with reports only in the form of case series.

Owing to the immunosuppressed conditions associated with TNF inhibitor drugs, such as neutropenia and LGLs, the risk of infections (both primary infections and reactivations), especially viral infections such as Epstein–Barr virus (EBV) infection may also induce changes in B- and T-lymphocyte cell differentiation, which may precipitate persistent myelodysplastic syndromes.[1,5]

Therefore, there are two concomitant phenomena inducing both neutropenia and LGLs. Our case featured both phenomena (ADA and suspected viral reactivation) as well as lymphocyte abnormalities. The question of the root cause warrants some reflection. It is recognised that EBV reactivation can induce changes in cytomegalovirus (CMV) serology results, as in our patient, and also that viral reactivations in immunosuppressed patients may have few symptoms.[4,5] Viral loads were negative on laboratory testing, whereas serological changes persisted, probably because the event was asymptomatic.

Following suspension of the medication, the patient's peripheral blood morphology returned to normal within a few days, whereas her serological abnormalities remained abnormal; hence, it appears that the presence of LGLs was due to the TNF inhibitor drug and this led to a viral reactivation.

In summary, both TNF inhibitor drugs causing changes in the bone marrow, such as LGLs, and the risk of reactivation of infections, mainly EBV infection, may induce associated myelodysplastic syndromes.

For IBD, this risk has yet to be evaluated, since monitoring guidelines do not include regular serology testing and most studies and case series reported have been in patients with rheumatic diseases.

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Tuberculous peritonitis mimicking carcinomatosis: a case report☆

Tuberculosis peritoneal que simula una carcinomatosis: a propósito de un caso

Peritoneal tuberculosis is the most common form of abdominal tuberculosis and a common cause of ascites in endemic countries. Its incidence has increased in recent decades, as it is associated with states of immunosuppression. It may simulate spread to the peritoneum of advanced cancer in any location, which may result in extensive, unnecessary surgery.[1]

A 49-year-old woman originally from Cuba with a history of posterior uveitis and a good response to treatment with adalidumab, currently stable, was admitted for the second time in two months due to signs and symptoms of fever and right subcostal pain. Antibiotic treatment and naproxen were started; with that, the patient's fever resolved.

Physical examination revealed a cushinoid phenotype and pain on palpation of the right hypochondrium. Laboratory testing showed a normal liver panel and bilirubin;

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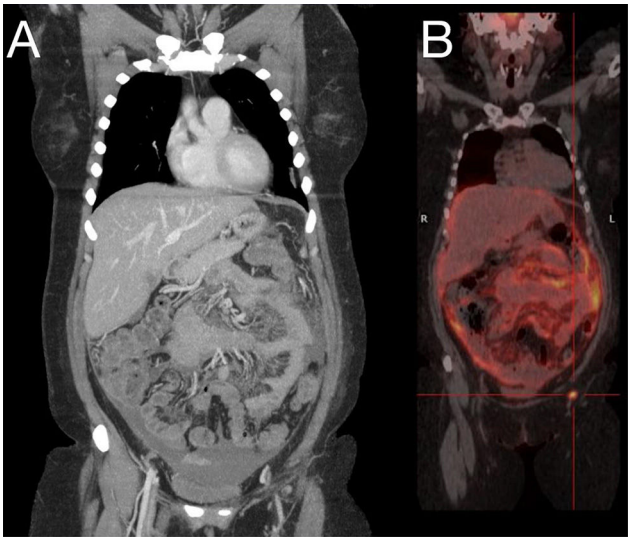

Figure 1 A: CT scan of the chest, abdomen and pelvis: peritoneal carcinomatosis, moderate intra-abdominal ascites, pathological lymphadenopathy in the right cardiophrenic angle and bilateral pulmonary micronodules. B: PET/CT scan: peritoneal and hepatic pericapsular carcinomatosis with multiple instances of supra- and sub-diaphragmatic lymphadenopathy and probable pleural implants.

leukopenia (3100 leukocytes/dl); elevated tumour markers; beta-2 microglobulin 3.68 mg/l; Ca 125 528.2 U/mL; and neuron-specific enolase 24.6 ng/m. A computed tomography (CT) scan of the chest, abdomen and pelvis was ordered. This scan found peritoneal carcinomatosis, moderate intra-abdominal ascites, pathological lymphadenopathy in the right cardiophrenic angle and countless bilateral lung micronodules. These findings were suggestive of tumour spread of an unknown primary neoplasm (Fig. 1A). The study was complemented and a PET/CT scan was performed, which confirmed the findings of peritoneal and hepatic pericapsular carcinomatosis with multiple instances of supra- and sub-diaphragmatic lymphadenopathy and probable pleural implants (Fig. 1B). A diagnostic paracentesis was performed and a sample was taken for ascitic fluid testing which was negative for malignant cells. A fine-needle aspiration biopsy (FNAB) of a right subphrenic lymphadenopathy also was performed and also came back negative for malignancy. To attempt to identify the possible primary neoplasm, a gastroscopy and colonoscopy were performed. These revealed no significant abnormalities. A gynaecological examination and a mammogram were also done and yielded normal results.

Given the negative results of the examinations, a decision was made to perform an exploratory laparoscopy. This found a complete omental block with friable adhesions to the parietal peritoneum and the bowel, complicating dissection and causing bleeding when grazed. A full omental patch dissection was performed and the specimen was sent as a biopsy. Pathology confirmed findings of necrotising granulomatous peritonitis with acid–alcohol-fast bacilli, consistent with tuberculous disease.

The patient started treatment with isoniazid, rifampicin, pyrazinamide and ethambutol, and a *Mycobacterium tuberculosis* (MT) antibiogram revealed that the bacteria was resistant to these drugs. The patient's antibiotic treatment was adjusted and treatment was started with levofloxacin, ethambutol, linezolid and capreomycin. After that, the patient reported improved pain and followed a favourable clinical course with subsequent follow-up for a year, with no onset of any new symptoms or relapses.

Tuberculosis has a global incidence of 2%, whereas the incidence of peritoneal tuberculosis ranges from 0.1% to 0.7%[2] and is higher in developing countries. It generally develops as a result of haematogenous spread of a pulmonary focus or direct spread from adjacent organs, such as the bowel. Cirrhosis, peritoneal dialysis, diabetes mellitus, human immunodeficiency virus (HIV) and use of immunosuppressants, especially TNF inhibitor drugs, are risk factors for peritoneal tuberculosis.[3]

Clinical symptoms and radiological findings in peritoneal tuberculosis are highly variable and non-specific, and they overlap with other diseases with very different prognoses and treatments, such as peritoneal carcinomatosis and Crohn's disease. Hence, strong diagnostic suspicion is required.

Clinically, it is an insidious, disease with a long clinical course in which the most common signs and symptoms are fever, ascites, abdominal pain and weight loss.[4]

Most studies have suggested that CT does not distinguish between tuberculosis and peritoneal carcinomatosis,[5] as in our case. Images such as peritoneal thickening and ascites are usually useful for diagnosis but may also overlap with other diseases.

Ascitic fluid testing is one of the diagnostic tests available for peritoneal tuberculosis. Ascitic fluid is usually an exudate, with lymphocytosis, but acid–alcohol-fast bacilli (AAFB) are detected in the culture in only 25% of cases. Adenosine desaminase (ADA) is the most commonly used biomarker to diagnose tuberculosis. A diagnosis of tuberculosis is generally accepted and, as a result, empirical antituberculous treatment is started in patients with consistent signs and symptoms. In this case, it was not tested, since this possibility was not clinically suspected.

As the yield of peritoneal fluid culture is usually low and MT grows slowly, the diagnosis generally requires a laparoscopic or laparotomic peritoneal biopsy.[3]

As part of the diagnostic study in patients with suspected peritoneal tuberculosis, surgical biopsy has a high diagnostic yield and in many cases is needed to hasten diagnosis, as well as treatment, thus reducing the disease's morbidity and mortality.

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Severe gastrointestinal bleeding due to synchronous herpes simplex virus and cytomegalovirus esophagitis☆

Hemorragia digestiva grave secundaria a esofagitis por virus del herpes simple y citomegalovirus

Infectious oesophagitis is the third most common cause of oesophagitis, after gastro-oesophageal reflux and eosinophilic oesophagitis.[1] The most commonly implicated micro-organism is *Candida*, followed by herpes simplex virus (HSV) and cytomegalovirus.[1] Concomitant infection with HSV and cytomegalovirus, though very uncommon, increases the risk of gastrointestinal bleeding and perforation.[2,3]

We report the case of a 65-year-old woman with a history of chronic alcoholism (more than 80 g of alcohol per day), type 2 diabetes mellitus, heart failure secondary to severe tricuspid insufficiency and persistent atrial fibrillation (being treated with apixaban). She was admitted to hospital for respiratory sepsis and decompensated heart failure and treated with piperacillin/tazobactam, intravenous corticosteroids and diuretics. Apixaban was replaced with low-molecular-weight heparin.

During her stay, the patient presented gradual development of anaemia (haemoglobin 12 mg/dl to 7 mg/dl; platelets 120×10^9/l; INR 1.2), melaena and an episode of haematemesis with no haemodynamic instability. A gastroscopy revealed multiple vesicles along the oesophagus measuring 10—20 mm (Fig. 1). In addition, the inferior third of the oesophagus presented ulcerated, friable mucosa with vesicles and fresh blood remnants (Image 1B). The oesophageal biopsies reported necrotic matter, calcifications and fibrinoleukocyte material. Given the simultaneous presence of ulcerated lesions in the oral cavity, empirical treatment was started with intravenous aciclovir. Seven days later, a repeat gastroscopy showed complete resolution of the lesions and a small varix in the distal third of the oesophagus. Subsequently, the results of the polymerase chain reaction (PCR) performed on the patient's blood at the onset of her signs and symptoms were received: the test was positive for cytomegalovirus. For the oesophageal samples, PCR was positive for cytomegalovirus and HSV type 1. An abdominal CT scan performed during the patient's stay revealed an irregular liver parenchyma with lobulated contours and ascites.

The patient was discharged after a stay of 69 days without presenting any new complications secondary to infectious oesophagitis. She is being followed up for her chronic liver disease.

The main risk factors for infectious oesophagitis are HIV, organ transplant and use of chemotherapy drugs, immunosuppressants and corticosteroids.[1,4]

The most common symptom is odynophagia; gastrointestinal bleeding is very uncommon.[1,5] However, concomitant infection with HSV and cytomegalovirus increases the risk of gastrointestinal bleeding and perforation.[2,3] This may be because the herpes infection is located in the epithelium of the oesophageal wall, whereas the cytomegalovirus infection affects mesenchymal cells, including the endothelial cells of the small blood vessels, in the deepest part of the oesophageal wall.[3]

In oesophagitis due to HSV, depending on the duration and severity of the infection, findings ranging from small vesicles on an erythematous base to multiple superficial or deep ulcers covered in yellowish exudate may be observed. Lesions are essentially located in the medial and distal oesophagus, and in immunosuppressed patients perforations secondary to necrotic oesophagitis may develop.[1,2,4]

Oesophageal ulcers due to cytomegalovirus are also located in the medial or inferior oesophagus. They are usually large and not very deep (though they sometimes have raised edges) and may be single or multiple.[1,4]

The diagnosis is made based on biopsies of oesophageal ulcers; the most sensitive method is PCR.[3]

Aciclovir, famciclovir or valaciclovir is used to treat oesophagitis due to HSV in immunosuppressed patients; ganciclovir, valganciclovir or foscarnet may be used to treat oesophagitis due to cytomegalovirus.[1] Our patient required no additional treatment for cytomegalovirus as her lesions resolved rapidly with aciclovir.

In conclusion, although infectious oesophagitis is an uncommon cause of gastrointestinal bleeding, it must always be suspected in immunosuppressed patients given its variable clinical and endoscopic presentation and the possibility of resolution with empirical treatment.

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