with Gardner's syndrome, they are not specific to the disease and have been associated with other conditions like *MUTYH*-associated adenomatous polyposis (germline mutations) and with somatic mutations in the catenin beta 1 gene (*CTNNB1*).[5] Familial adenomatous polyposis associated with *MUTYH* mutations is an autosomal recessive disorder characterised by the appearance in adult age of multiple adenomatous polyps with an increased risk of developing colorectal cancer. In the event of histological findings consistent with pilomatricoma in a patient with multiple adenomatous polyps, the differential diagnosis should include more conditions than just Gardner's syndrome, and potentially test for genetic mutations responsible for attenuated polyposis syndromes, like the *MUTYH* gene, and not exclusively associated with the *APC* gene.

In conclusion, the identification of shadow cells in cutaneous epidermoid cysts may be the first finding to generate suspicion of polyposis syndromes like Gardner's syndrome. In our patient, the detection of shadow cells inside a removed cutaneous cyst guided us to this potential diagnosis. Although it ultimately did not meet the characteristic endoscopic or genetic criteria for this syndrome, these findings led to a colonoscopy being requested, which identified colorectal cancer. The onset of post-colonoscopy appendicitis led to the diagnosis of an appendiceal goblet cell tumour.

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Irene García de la Filia Molina[a,*], Laura Crespo Pérez[a], Raquel Ríos León[a], Ana Barbado Cano[b], Carmen Moreno García del Real[c], Ander Aburto Bernardo[d], Alexandre Figueroa Tubio[a], Carolina González Olivares[a], Rubén Sánchez Aldehuelo[a], Agustín Albillos Martínez[a]

[a] *Servicio de Gastroenterología y Hepatología, Hospital Universitario Ramón y Cajal, Madrid, Spain*
[b] *Servicio de Aparato Digestivo, Hospital Universitario La Paz, Madrid, Spain*
[c] *Servicio de Anatomía Patológica, Hospital Universitario Ramón y Cajal, Madrid, Spain*
[d] *Servicio de Cirugía Plástica, Estética y Reparadora, Hospital Universitario Ramón y Cajal, Madrid, Spain*

* Corresponding author.
E-mail address: irenegarciadelafilia@gmail.com
(I. García de la Filia Molina).
2444-3824/

Pulmonary aspergillosis in a Crohn's disease patient receiving adalimumab and steroid therapy☆

Paciente con enfermedad de Crohn en tratamiento con adalimumab y esteroides que desarrolla aspergilosis pulmonar

We present the case of a 41-year-old male patient diagnosed with ileocolic Crohn's disease (CD) in 1999 (A2 L3 B1+p), with ileocaecal resection in 2006, on treatment with mercaptopurine for prevention of recurrence. He subsequently developed a complex perianal fistula, which was initially treated with infliximab before switching to adalimumab in 2013 due to a sensitivity reaction, with good response and withdrawal of mercaptopurine. In 2016, adalimumab (80–80–80 mg/week) was reintroduced due to loss of response with perianal and luminal activity. Due to the patient's lack of improvement, steroids were added (1 mg/kg = 80 mg). One month after starting the treatment, the patient reported a three-day history of weight loss, cough and expectoration. The chest X-ray revealed several cavitated nodular images in both lung fields consistent with pulmonary tuberculosis. The study was broadened to include CT scan, blood panel, Mantoux test and bronchoscopy. The chest CT scan (Fig. 1) showed bilateral cavitated nodular images, the Mantoux test was negative and the blood tests only revealed a slight increase in CRP (15 mg/l) and fibrinogen (520 mg/dl). The bronchoscopy was normal, samples were taken for culture and bronchoalveolar lavage was performed. The microbiological study for mycobacteria was negative (AAFB and culture in Löwenstein medium). The microbiological study was broadened and multiple *Aspergillus* spp. colonies were isolated. Adalimumab was withdrawn and treatment with intravenous voriconazole, imipenem and cilastatin was started. After three months of treatment, the patient had no pulmonary or intestinal symptoms, together with radiological improvement, so adalimumab was reintroduced.

Patients with inflammatory bowel disease (IBD) are particularly susceptible to opportunistic infections thanks to the use of immunosuppressants, particularly if several

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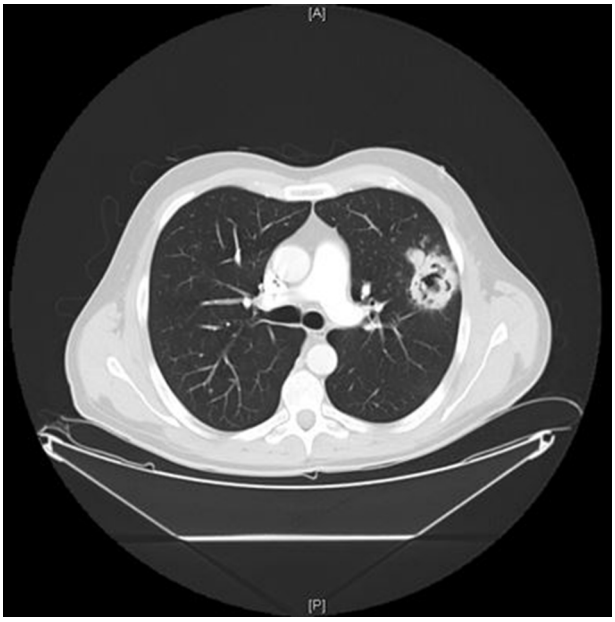

Figure 1 Lung CT scan.

are used in combination (steroids, immunomodulators and biologicals). The overall risk is minimal, particularly in monotherapy, and steroids are most associated with high risk and onset of infection. In our case, the addition of corticosteroids probably played a key role. Age is an independent factor, with older patients at greater risk. As such, the risk/benefit ratio of combination therapy should be carefully assessed in these patients, together with closer monitoring. Fungal infections are rare, but morbidity and mortality is high (50%).[1] Clinical suspicion is vital in order to make an early diagnosis and to administer the appropriate treatment to prevent complications. *Aspergillus fumigatus* is the most common species to cause infection (90%). There are very few published cases of mycosis associated with treatment with adalimumab in patients with IBD.[2,3] Invasive aspergillosis primarily affects the lungs and the symptoms are nonspecific (cough, chest pain and dyspnoea). It is difficult to diagnose as it requires the combination of consistent radiological findings and mycological criteria (histological evidence of invasive hyphae or positive culture of a normally sterile medium such as pleural fluid are consistent with invasive fungal disease). In this case study, granulomatous CT images were observed that are not specific to mycosis, with multiple negative microbiological studies. As a result, a pleural fluid culture was performed, which was positive, thereby confirming the diagnosis. In clinical practice, antifungal treatment is started early, even before a confirmatory positive culture, because of the risk of not treating it and its complications.[4] The drug of choice is voriconazole. Combination therapy with caspofungin is used in patients with serious conditions or a poor prognosis. The optimal duration of treatment is unknown. For pulmonary aspergillosis, at least 6–12 weeks are generally recommended. In immunosuppressed patients, treatment should continue for the duration of immunosuppression and until resolution of the lesions.[5] The optimal time to re-introduce biological therapy has also not been definitively established and will depend on the patient's characteristics, but in any case it should not be restarted until the lesions have resolved or improved. The European Crohn's and Colitis Organisation (ECCO) guidelines provide no guidance in this respect.[1] Experience with lung transplants reported by pulmonologists suggests that biological therapy could be reintroduced once antifungal treatment has been initiated.

In conclusion, patients with IBD treated with several immunosuppressants (steroids, biologicals or immunomodulators) are more susceptible to infection.

Invasive fungal infections are becoming increasingly common in immunocompromised patients (HIV, cancer patients, transplant patients, IBD, older patients and patients on steroids).

Invasive aspergillosis is complicated to diagnose. It requires the combination of clinical symptoms, consistent radiological findings and mycological criteria (histological evidence of invasive hyphae or positive culture).

Voriconazole is the treatment of choice for aspergillosis. Duration of treatment has not been well defined as it depends on the extent of the disease and on the patient's immune system.

At least 6–12 weeks of treatment are generally recommended. In immunosuppressed patients, treatment should continue for the duration of immunosuppression and until resolution of the lesions.

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Isabel Ferrer Bradley*, Nuria Maroto Arce, María Mora Escrig, Joaquín Hinojosa del Val

Unidad de Enfermedad Inflamatoria Intestinal, Departamento de Gastroenterología, Hospital de Manises, Manises, Valencia, Spain

* Corresponding author.
E-mail addresses: ifebrad@gmail.com, iferrerb@hospitalmanises.es (I. Ferrer Bradley).
2444-3824/