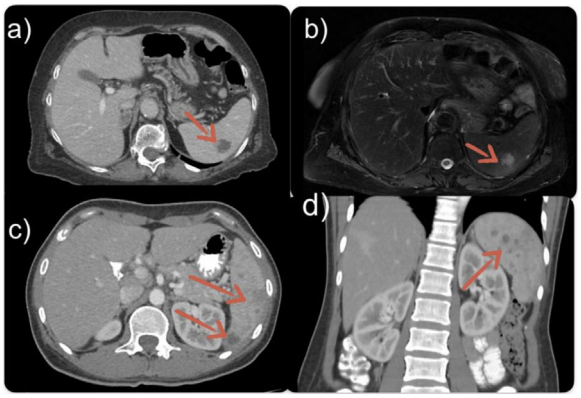


**Figure 1.** a) Case 1: Abdominal computerised tomography (CT), sagittal section. Hypodense splenic lesion; b) Case 1: Abdominal magnetic resonance imaging, T2-weighted sequence. Hyperintense splenic lesions with perilesional oedema; c) Case 2: Abdominal CT, sagittal section. Hypodense and heterogeneous splenic lesions; d) Case 2: Abdominal CT, coronal section. Hypodense and heterogeneous splenic lesions.

parenchyma with multiple focal lesions and bilateral periportal and axillary lymphadenopathy (Fig. 1). These were suspected to be splenic abscesses, but without being able to rule out lymphoproliferative syndrome. The imaging study was completed with echocardiogram, which revealed no vegetations. A core needle biopsy of the right axillary lymph node revealed epithelioid granulomatous lymphadenitis with focal necrosis, without evidence of lymphoma. Serology showed positive anti-*Bartonella henselae* IgM and nonspecific IgG antibodies, and the patient was started on treatment with rifampicin and azithromycin for two weeks. The follow-up CT scan after three months showed a notable decrease in the volume of the axillary lymphadenopathy with radiological improvement of the splenic lesions both in number and size and a decrease in the overall volume of the spleen.

The main reservoir of *B. henselae* is animals, particularly cats and their fleas.[1] Hepatosplenic involvement is rare, accounting for 5–25% of cases. Persistent fever, abdominal pain and weight loss are some of the main clinical manifestations of visceral involvement.[1] This condition should be considered within the differential diagnosis of fever of unknown origin.[2,3] It is common for blood tests to show abnormal liver function tests and elevated CRP.[2] In microbiological tests, serology is the technique that offers the best results with high sensitivity and specificity.[2,3] There is a possibility of cross-reactivity between *Bartonella*species, as well as with other microorganisms (*Treponema* spp, *Chlamydia* spp., *Mycoplasma* spp., *Coxiella* spp.). Identification would require culture or molecular techniques, which were not performed in the cases presented here, and *B. henselae* was assumed to be the most likely cause of the condition. Imaging tests show multiple focal lesions,[2,4] which, if biopsied, would correspond to necrotising granulomas.[1,2,5] With regard to treatment, although there is no clear consensus, azithromycin is usually recommended for five days.[6] However, in a clinical trial comparing azithromycin with placebo, no differences in clinical response were observed in the two groups.[7] Long courses, aminoglycosides or combinations are reserved for cases of endocarditis or involvement of other organs.[1,3,6]

## Conflicts of interest

The authors declare that they have no conflicts of interest.

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## Probable breakthrough fungal infection in immunocompromised patient with isolation of an infrequent species

### *Probable infección fúngica de brecha en paciente inmunodeprimido con aislamiento de una especie infrecuente*

This was a 70-year-old male patient diagnosed with R-ISS III light chain multiple myeloma with 1q gain in August 2021 after investigation of acute renal failure. He was started on first-line treatment with the bortezomib-lenalidomide-dexamethasone (VRd) regimen with lenalidomide adjusted to renal function for six cycles, achieving a very good partial response. After completing the six cycles, in May 2022 he received a melphalan-conditioned (140 mg/m$^2$) autologous haematopoietic stem cell transplant (AHSCT) as consolidation. Subsequently, maintenance therapy with VRd was prescribed starting in September 2022 and aciclovir as prophylaxis with periodic outpatient follow-up.

The patient was admitted in month +10 post-AHSCT in March 2023 with symptoms of dry cough, fever, chest pain and dyspnoea of several days' duration with a radiological diagnosis of bronchopneumonia. The analyses showed an increase in C-reactive protein (CRP) with a value of 22.77 mg/dl, creatinine of 2.4 mg/dl and

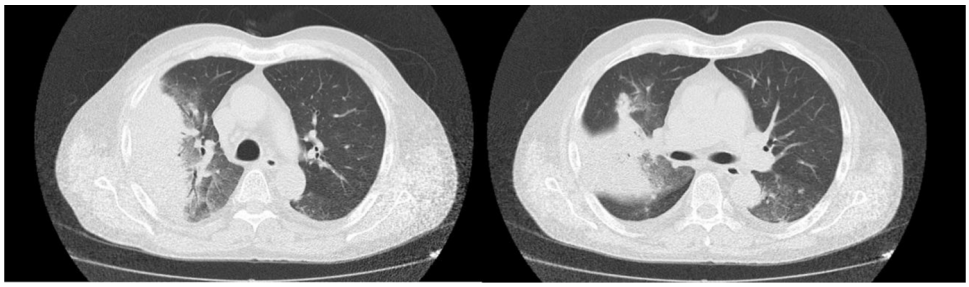

**Figure 1.** CT with evidence of extensive lung consolidation in the right upper lobe (RUL), accompanied by peripheral ground-glass opacities, and other subsegmental lung consolidations in the left lower lobe (LLL) with bronchial inflammatory signs, all suggestive of airway invasive aspergillosis.

neutrophils $2{,}000 \times 10^3/\mu$l. Broad-spectrum empirical antibiotic therapy was started given the absence of documented microorganism growth (negative blood cultures, urine cultures and urinary antigens) with good clinical and analytical progress. After seven days in hospital, he had a new episode of fever. New samples were requested with weakly positive detection of galactomannan in serum with a value of 0.56 using the Platelia™ Aspergillus Ag kit (BIO-RAD) and a CT scan was performed with findings consistent with a possible pulmonary invasive fungal infection (IFI) (Fig. 1).[1] An oral azole antifungal was added to the treatment (voriconazole, loading dose 400 mg/12 h for 24 h followed by 200 mg/12 h) with progressive improvement of respiratory symptoms. Treatment was continued on an outpatient basis without monitoring voriconazole plasma levels after discharge, as the levels had remained within range during admission.

The oral antifungal treatment was maintained until the patient was admitted again in July 2023 due to fever and pain in his right side. Due to the persistence of fever, a new CT scan was requested, which showed progression of pulmonary infiltrates, and a bronchoscopy with alveolar lavage was also ordered for microbiological study. He was then started on intravenous liposomal amphotericin B 3 mg/kg/24 h with a good clinical response. After his condition worsened once again 10 days later, it was decided to add an intravenous echinocandin (caspofungin 50 mg/24 h), with good clinical and radiological response 48 h after starting the dual antifungal treatment. The new samples with detection of galactomannan in serum and the rest of the microbiological cultures during admission were negative. After eight days, the patient was discharged from hospital with oral isavuconazole 200 mg/24 h and intravenous liposomal amphotericin B 3 mg/kg/48 h.

In the bronchial aspirate culture, a fungus was isolated and identified by MALDI-TOF (Bruker®) as *Aspergillus montevidensis* with *a score* of 1.4 repeated four times. An antifungal test was performed using a commercial microdilution technique (Sensititre Yeast-One®) with the following results: amphotericin B = 2; itraconazole = 0.03; posaconazole = 0.03; voriconazole = 0.03; and isavuconazole = 0.008. Based on these findings, a breakthrough pulmonary IFI was considered likely and that the patient was not achieving adequate plasma voriconazole levels, as the *in vitro* activity of voriconazole was good.

The patient is currently in good general health. Twice-yearly radiological monitoring by CT has been put in place due to the slow resolution of the previously identified lung consolidation. The last check-up, carried out in June 2024, showed the presence of residual lesions in both upper lobes, so the patient shall continue on treatment with isavuconazole 200 mg/day until the radiological abnormalities are resolved.

*A. montevidensis*, belonging to the *A. chevalieri* complex previously known as *A. amstelodami*, is a rare *Aspergillus* species associated with farmer's lung and used in the production of fermented foods under high osmotic conditions.[2] This is a slow-growing and slow-sporulating species, so laboratory identification can delay clinical diagnosis and, also therefore, patient treatment.

IFI is a serious infectious complication that can occur in immunocompromised patients.[3] It is one of the causes of high morbidity and mortality rates in transplant patients, although knowledge of the risk factors and groups, the introduction of early diagnosis techniques and the availability of antifungal drugs for prophylaxis and treatment have changed the prognosis.[4,5] Plasma voriconazole concentrations show high interindividual variability, so it is important to measure plasma levels to ensure good therapeutic management.

Appropriate selection, prescribing and monitoring of antifungal agents is crucial to prevent breakthrough infections in immunocompromised patients, as shown in this case, where lack of adequate monitoring of voriconazole may have contributed to the probable breakthrough pulmonary IFI.

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