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Scientific letters

Reinfection confirmed by SARS-CoV-2 in a healthcare professional detected by an in-hospital infection control program

Reinfección confirmada por SARS-Cov-2 en profesional sanitario detectada mediante un programa de control de la infección intrahospitalaria

We present a case with solid evidence of SARS-COV-2 reinfection. The extensive monitoring of hospital workers during the SARS-COV-2 pandemic played a key role in identifying this suspicion of reinfection confirmed by sequencing. It should be noted that both infections were diagnosed from the contact study carried out among workers when cases of COVID-19 were identified in hospitalised patients without COVID-19. The first infection occurred during the first spike in the pandemic in April 2020. The worker was asymptomatic, and on 13/04/2020 she underwent a nasopharyngeal nucleic acid amplification test in the context of an occupational contact study regarding a positive patient. The RT-PCR result was positive with a Ct of 23.55 (<35). The positive test was followed by mild symptoms (headache, anosmia and ageusia). Thirty-seven (37) days after diagnosis, the RT-PCR was negative and an immune response was identified (IgG index value 3.98; positive >1.6; COVID-19 VIRCLIA® IgG monotest, VIRCELL).

In the following months, as mandated by the hospital-acquired infection control programme, several RT-PCR tests were performed with negative results (Fig. 1). Eight (8) months later, IgG levels had decreased significantly (IgG 1.55). Most people have an immune response after infection with antibodies,[1] and although they tend to decrease during the following months, many studies indicate that the neutralising activity is maintained for up to six or eight months.[2,3] This immune response is associated with protection against reinfection, at least in the short term.[4]

The second infection was also detected by contact study. It was diagnosed on 15/01/2021 by RT-PCR. The worker presented mild symptoms (cough and itchy throat) which she had not reported. We believe that although the early detection programme for SARS-COV-2 infection among workers was known and correctly implemented, since she had already had the infection and she was aware of her immune response, she did not suspect SARS-COV-2 infection and therefore did not notify the occupational health department. Moreover, a few days previously (11/01/21) she had received the first dose of the Pfizer vaccine. In this case, we know that the reinfection occurred after the 07/01/21, since an RT-PCR was obtained on that day with a negative result. We believe that the worker must have already been infected on the day of the vaccination, since on 15/01/21 she already had symptoms and the average incubation period is 5 to si6x days. In addition, 4 days after diagnosis, she underwent an RT-PCR and determination of IgG of the S1 subunit of SARS-CoV-2 (anti-S), in which low viral load (Ct >35) and very high immune response levels (>150) were detected. The dynamics of the immune response in humans has been described. It is possible to detect total antibodies, IgM and IgG, with increasing sensitivity over the course of the infection, which is greater than 90% in the second week after the onset of symptoms.[5,6] In our case, the fact that such high anti-S IgG levels were detected a few days after the onset of symptoms leads us to consider a possible *booster* effect, mainly associated with the vaccine, although the anti-N IgG are not available. The inoculation of a single dose of the mRNA vaccines in an individual who has had the infection is known to give rise to an exponential increase in the immune response.[7] Another publication[8] describes that a single dose of mRNA vaccine produces an immediate immune response in seropositive people, with post-vaccination antibody titres similar to or higher than seronegative people with two doses of the vaccine.

Sequencing is required to confirm reinfection and differentiate it from persistent RT-PCR. There are sporadic cases of reinfection confirmed by sequencing around the world.[9,10] In our case, the opportunity to sequence the two samples confirmed reinfection by showing different lineages. The sequencing technology used was Illumina (MiSeq platform) GISAID for the first infection EPI_ISL_1595836 and GISAID for the reinfection EPI_ISL_1595838. In the case of samples with low viral loads, the laboratory increases the amount of RNA extract to have sufficient material available for sequencing. The first infection corresponded to a member of Clade 20B (B.1.1 lineage) and the second corresponded to Clade 20E (B.1.177 lineage). The lineage of the second sample began to circulate in Spain as of the summer of 2020.

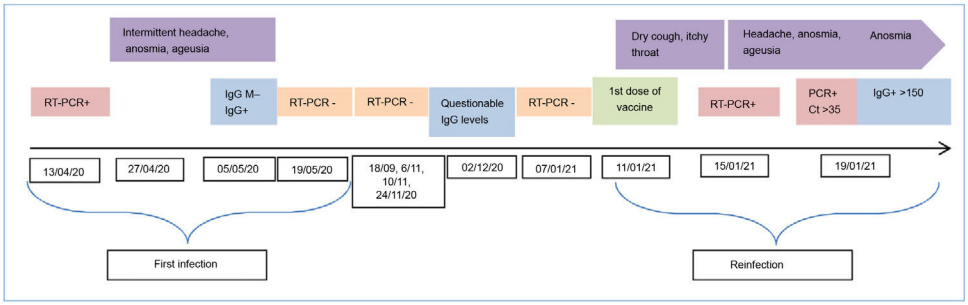

Figure 1. Chronology of the onset of symptoms, molecular diagnosis and serological follow-up.

The implementation of the comprehensive diagnostic and monitoring programme for workers during the COVID-19 pandemic in our centre allowed us to detect this case. We believe that this is important for the good control of hospital-acquired infection.

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Chromoblastomycosis due to *Cladophialophora immunda*: An emerging pathogen in immunocompromised patients?

Cromoblastomicosis por Cladophialophora immunda*: ¿un patógeno emergente en pacientes inmunocomprometidos?*

Chromoblastomycosis is a chronic granulomatous infection of the skin and subcutaneous tissue caused by traumatic inoculation of dematiaceous (pigmented) fungi present in soil, plants and decaying wood.[1] It is more common in tropical and subtropical climates, although autochthonous cases have been described in regions with a temperate climate.[2] The highest incidence is recorded in men between 20 and 60 years of age, probably due to greater occupational exposure, and it is responsible for 90% of cases.[1] Its diagnosis is fundamentally based on the identification in the tissue of thick-walled pigmented cellular structures known as Medlar bodies, sclerotic bodies or muriform cells, which represent the invasive form of the fungus and are pathognomonic of this entity.[3] In addition, culture is recommended and, for the identification of the species, the sequencing of internal transcribed spacer regions [ITS] of fungal ribosomal DNA (rDNA) is the most appropriate.[3] We present a case of chromoblastomycosis due to *Cladophialophora immunda*, a species recently identified in soils contaminated with hydrocarbons,[4,5] in a kidney transplant patient.

The case is a 56-year-old man originally from Guinea–Bissau, resident in Spain for 30 years, with a history of end-stage kidney disease secondary to interstitial uric acid nephropathy and who had undergone a kidney transplant from a cadaveric donor on immunosuppressive treatment with tacrolimus 4.75 mg/day, mycophenolic acid 180 mg/8 h and prednisone 5 mg/day. Ten months after the transplant, he attended a dermatology consultation due to a fast-growing multinodular exophytic tumor lesion in the external metatarsal area of his right foot (Fig. 1A). The patient denied previous trauma and had not travelled to his country of origin in the previous year. He did not report fever or other accompanying symptoms and nor did he present locoregional adenopathies. The serologies were negative and the blood count and blood biochemistry showed no significant findings. A skin biopsy of the main lesion was performed for histology and microbiology studies. The histology revealed pseudoepitheliomatous epidermal hyperplasia associated with an intense dermal inflammatory process comprised of suppurative granulomas and multinucleated giant cells. Both in the cytoplasm of these cells and among the neutrophils, numerous rounded brownish fungal structures were observed, sometimes clustered in chains, and haematoxylin and eosin (H&E) and Grocott staining revealed the presence of septa (muriform cells) (Fig. 2A–C). Direct examination with calcofluor white was negative for yeasts, hyphae or pseudohyphae. After three days of incubation, fungal growth was observed at 30°C in Sabouraud chloramphenicol gentamicin agar and potato dextrose agar with chloramphenicol, but not in media with cycloheximide. Macroscopically, the colonies were velvety, dark olive-grey in colour and black on the reverse side (Fig. 2D), with a maximum growth temperature of 37°C. Septate, branched, pale brown hyphae were observed microscopically, with poorly differentiated conidiophores producing ellipsoidal conidia forming long coherent chains, without dark scars (Fig. 2E and F). These characteristics permitted the identification of the genus *Cladophialophora.* Species identification was performed by sequencing ITS regions of the rDNA. The aligned sequence was a 99% match for *C. immunda*, CBS 126867, GenBank accession number MH864254.1. On further questioning, the patient said he had been working in a paint factory. With the diagnosis of chromoblastomycosis due to *Cladophialophora immunda*, treatment was initiated with terbinafine 250 mg/24 h for 4 weeks, with subsequent curettage and electrocoagulation of the residual lesion and a new histological and microbiological study that confirmed

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