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Letter to the Editor

Reinfection, reactivation or delayed complication of the initial SARS-CoV-2 infection[☆]



Reinfección, reactivación o complicación tardía de la infección inicial por SARS-CoV-2

Dear Editor,

As the months go by and the number of SARS-CoV-2 (COVID-19) infections increases, new and complex clinical situations are being identified and etiopathogenic responses are being sought. Thus, there are individuals who, having been infected with COVID-19 and showing improvement and negative microbiological tests, subsequently experience symptoms compatible with the same infection and positive laboratory tests.¹

While some authors argue that these are asymptomatic carriers of the virus, others believe that it is a residual effect of the initial infection in the lower respiratory tract which, through recurrent coughing, is transferred to the upper respiratory tract.² On the other hand, some believe that this situation represents late complications of the initial infection or that, especially in immunosuppressed and elderly patients, viral clearance may be slower, thus favouring the reactivation of the virus.³

A descriptive study of a series of six cases in which SARS-CoV-2 was isolated for the second time after confirmed COVID-19 by nasopharyngeal PCR between October and November 2020. A descriptive analysis of the main sociodemographic variables was carried out, as well as variables of clinical and epidemiological interest. The study was approved by the Clinical Research Ethics Committee of the reference Autonomous Community (CEImPA 2020.550).

Four women and two men were identified. The mean age was 68.5 years. In the first episode, four of the six patients had symptoms of varying intensity, from cough and runny nose to severe bilateral pneumonia. Four of the six patients had chronic diseases without immunosuppression and were exposed to polypharmacy. The number of copies of SARS-CoV-2 ranged from 17,864 to 66,988,460 copies.

In the second episode, all six patients had symptoms and the number of copies was much lower than the initial one. Four patients required hospital admission. One of them died 11 days after admission. **Table 1** shows detailed information on the clinical and epidemiological variables of the study.

The series includes elderly patients with *diabetes mellitus*, obesity, HBP and cancer, but also a younger person with no relevant history and a pregnant woman. Currently, there is no specific marker that is capable of predicting a new positive PCR result for coronavirus.⁴

The average time between initial detection and negative results was 15.1 days. The mean time between negative results and new positive results was 13.3 days. The new positive PCR has been identified in a range between 3 and 22 days, very similar to that observed in other series.^{2–5} It is believed that when positive results repeat in a short period of time it is due to intermittent and prolonged secretion of the virus in the nasopharynx or the detection of fragments of viral RNA that does not necessarily imply active infection or transmissibility. In these cases, the patients are asymptomatic or have mild symptoms. When the new positive PCR occurs over a longer time range, this is often associated with more severe symptomatology and even different symptoms to those of the first diagnosis, with late complication of the initial infection being the most plausible hypothesis.³

In view of the above, the authors consider that this situation corresponds to a series of late complications of the initial infection, rather than new infections, as mainly a short period of time between the two episodes, marked symptoms and hospitalisation are observed in most cases.

Finally, although most authors agree that these patients are not infectious, it seems appropriate to apply the precautionary measures, and that the management of these patients should be the same as that of individuals in whom the infection is detected for the first time. Finally, given that this is a very recent phenomenon, and its public health significance is unknown, it is of interest to carry out an exhaustive registry and follow-up of cases in order to increase knowledge of COVID-19 and, consequently, its prevention, control and treatment.

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Table 1
Clinical characteristics of the cases.

	Age	Sex	Medical history	Active drug therapy	First episode symptoms	First episode number of copies	First episode hospitalization (days stay)	First episode treatment	Time between PCR and PCR (first episode)	Time from first episode resolution (PCR-) to the start of the second episode (PCR+)	Second episode symptoms	Second episode number of copies	Second episode hospitalization (days stay)	Second episode treatment	Serology
Patient 1	83	M	Alcoholism, depression, vitamin deficiency	Paroxetine, folic acid, omeprazole, paracetamol	Cough and mucus	17,864 copies	No	Paracetamol	14	15	Fever and diarrhoea	579 copies	Yes (10 days) <i>Death</i>	Azithromycin, metronidazole, ciprofloxacin, enoxaparin	IgM-; IgG+
Patient 2	81	F	Endometrial cancer, type 2 DM, asthma, depression, cardiomyopathy	Lorazepam, folic acid, oral antidiabetic ipratropium bromide, salbutamol, trazodone, spironolactone, furosemide, acetylsalicylic acid, atorvastatin, ramipril	Asymptomatic	66,988,460 copies	No	Not specified	14	17	Fever and dyspnoea	272 copies	Yes (12 days)	Ceftriaxone, dexamethasone, salbutamol, ipratropium bromide, enoxaparin	Undetermined
Patient 3	82	F	HBP, type 2 DM, morbid obesity	Insulin, vildagliptin, enoxaparin, losartan, mirtazapine, furosemide, beclomethasone dipropionate/formoterol fumarate, tiotropium, haloperidol, brinzolamide/timolol maleate	Severe bilateral pneumonia	4,365,266 copies	Yes (14 days)	Ceftriaxone, dexamethasone, salbutamol, ipratropium bromide	15	22	Bilateral pneumonia	272 copies	Yes (7 days)	Piperacillin-tazobactam, enoxaparin	IgM+; IgG+
Patient 4	38	M	Chronic rhinitis	Desloratadine	Fever, asthenia, dyspnoea	66,988,460 copies	No	Paracetamol	20	10	Cough, asthenia	1150 copies	Yes (3 days)	Dexamethasone, colchicine, enoxaparin, azithromycin	IgM+; IgG+
Patient 5	91	F	HBP, breast cancer (2008), toxic multinodular goitre	Lorazepam, omeprazole, amiloride/hydrochlorothiazide, haloperidol	Asymptomatic	277,332 copies	No	Not specified	14	3	Prostration	579 copies	No	Not specified	IgM-; IgG+
Patient 6	36	F	Pregnant woman 23 weeks, migraines, herniated disc	Folic acid	Anosmia, cough, nasal congestion	33,728,730 copies	No	Paracetamol	14	13	Asthenia, palpitations	272 copies	No	Not specified	IgM+; IgG-

DM: diabetes mellitus; F: female; HBP: high blood pressure; IgM: immunoglobulin M; IgG: immunoglobulin G; M: male.

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Conflict of interests

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