Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

tion showed a discrete oxygenation anomaly (baseline Sat. O_2 92%), very significant neutrophilic leukopenia with lymphocytosis; CRP 19.6 mg/dL, ESR 86 mg/dL; ferritin 2,512 ng/mL; increased transaminases > 3 x LSN; CKD-EPI 68 mL/min and the ions at the limit of normal. The X-ray showed a bilateral low intensity pulmonary focus suggestive of viral infection and the PCR-SARS-CoV2 confirmed the positive result. Treatment was maintained with hydroxychloroquine 200 mg/12 h, azithromycin 500 mg/24 h and paracetamol 1 g/8 h, and was supplemented with enoxaparin sodium 60 mg/day, fluid therapy and oxygen therapy through nasal prongs at 3 L/min.

On 31 March the patient was still suffering from severe symptoms with dyspnoea and abnormal laboratory values: Hb 12 g/dL; leukopenia with very significant lymphocytosis; elevated transaminases and alkaline phosphatase; D-dimer 307 μg/L (<230 Ref.), ferritin 2,283 ng/mL and CRP 9.5 mg/dL. Computed tomography (CT) showed a new ground glass peripheral bronchopneumonic image at the base of the upper lobe of the left lung and persistence of peripheral involvement of the right lung parenchyma and vascular thickenings, more evident than in previous radiographs.

Given that our research team has extensive experience in cell therapy, on 2nd April, with prior authorization and under the control of the Spanish Agency of Medicines and Medical Devices, we infused intravenously a dose of 80 × 10 E6MSC of allogeneic bone marrow (1 × 10 E6MSC/kg of weight) in suspension of 100 cc saline solution administered at a rate of 40 drops/min. The MSCs were isolated and cultured under the correct manufacturing standards for clinical application (GMP) at the Institute of Molecular Biology and Genetics of Valladolid.

We did not experience any complications or adverse effects. At 24 hours, the patient was afebrile with generalized improvement in symptoms and biochemical values, with persistent difficulties in intake due to hyposmia and hypogeusia, but which improved notably after 48 hours. From the fifth day all biochemical parameters were within normal range and the clinical symptoms related to the coronavirus had disappeared, maintaining the loss of appetite and tiredness. CT showed a clear improvement in the right pulmonary focus and the left lung abnormality. Hospital discharge was granted on 8th April, maintaining anticoagulant treatment for one month.

PCR-SARS-CoV-2 became negative as of 6th April and after a month the leukocyte formula and the rest of laboratory values were normal, showing negative IgM antibodies (0.7) and positive IgG (8.5 +++) against SARS-CoV-2. Lung CT scan was almost normal (see CT Fig. 1) and complete lung function tests were strictly normal: FVC 4.35 L (97% ref.), FEV_1 3.64 L (105% ref.), index 70%, TLC 6.10 L (90% ref.), DLCO 25.7 mL/min/mmHg (95% ref.).

Even assuming the role that natural immunity might have played, with the beneficial effects of hydroxychloroquine being disputed, we speculate that the immunomodulatory and pro-regenerative effect of intravenous administration of high-dose expanded MSC may have been primarily responsible for the favourable clinical, biological and radiological course of the case. The clinical trials already underway should provide quality data that allow us to advance in the knowledge of this innovative therapeutic proposal.

Authorization of treatment with Cell Therapy

Authorization for Compassionate Use from the Spanish Agency of Medicines and Medical Devices (AEMPS).

Informed consent

Informed consent was obtained from the patient.

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SARS-CoV-2 and EBV coinfection☆

Coinfección por SARS-CoV-2 y virus Epstein-Barr

Dear Editor:

Co-infection by two or more pathogens is a common finding in infectology. However, the simultaneous infection by two viruses such as the Epstein-Barr virus (EBV) and the severe acute respiratory syndrome coronavirus-2 (SARS CoV-2) has not been reported to date. In the context of a coronavirus pandemic (COVID-19), any infectious clinical condition is suspected of COVID-19. The lockdown of the population sometimes makes us forget that other pathogens can also be transmitted and manifest themselves.

A 19-year-old French woman, with no relevant history, came to the emergency department with a two-day history of fever, bilateral eyelid oedema, and right hemifacial swelling. In addition to the skin manifestations, the physical examination showed bilateral cervical lymphadenopathy, non-suppurative pharyngotonsillitis, and splenomegaly.

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Table 1
Lab and serological results.

Lab parameters	Units	Result	Normal values
Leukocytes	10^9cel/L,	11,8	3,89–9,23
Neutrophils	10^9cel/L (%)	1,58 (13)	1.49–4.67 (45–75)
Lymphocytes	10^9cel/L (%)	8.46 (71)	1.24–3.05 (20–50)
Monocytes	10^9cel/L (%)	1.61 (13.6)	0.29–0.72 (2–9)
Transaminases	UI/L		
Aspartate transaminase		239	≤32
Alanine transaminase		264	≤33
Gamma-glutamyltransferase		89	≤40
Alkaline phosphatase	UI/L	306	35–104
Ferritin	ng/mL	243,8	15–150
D-dimer	ng/mL	2950	150–500
C-reactive protein	mg/dL	0,95	≤0.5

Serology	IgM (Index)	IgG (Index)
EBV (CLIA)	+, (6.1)	+, (1.6)
Mumps (CLIA)	+, (5,6)	+, (3.9)
Rubella (Elecsys Rube test)	–	+, 159 IU/mL
Measles (CLIA)	+, (1,2)	+, (2.9)
CMV (Enzyme Immunoassay)	–	–
Parvovirus B19 (CLIA)	–	+, (7.5)
HIV (ELISA)	–	–

The results of the lab tests and the serological study are summarized in Table 1. The presence of SARS-CoV-2 RNA was detected in the reverse transcriptase polymerase chain reaction (RT-PCR) of the sample obtained by oronasopharyngeal swab. The presence of EBV was also detected by PCR in blood (4700 copies/mL) and plasma (9600 copies/mL). The mumps virus could not be detected in the saliva cell culture. An anteroposterior chest radiograph and a computed tomography (CT) scan of the chest and abdomen showed splenomegaly (diameter greater than 16 cm) in the absence of pulmonary pathological findings. With a diagnosis of infectious mononucleosis (IM) mimicking mumps and asymptomatic Covid-19, in the absence of other complications, exclusively symptomatic and supportive treatment was recommended. The patient experienced a significant clinical improvement after two weeks of follow-up.

IM is a clinical syndrome characterized by fever, weakness, bilateral cervical lymphadenopathy, pharyngotonsillitis, and splenomegaly. The pathogen responsible for most cases is herpesvirus 4 or EBV and to a lesser extent, cytomegalovirus (CMV). Other pathogens that cause mononucleosis syndromes are hepatitis viruses, coxsackie A, parvovirus B-19, and HIV, but not coronaviruses. The patient had common laboratory abnormalities in IM, such as lymphocytosis or hypertransaminasemia, although abnormally high ferritin or D-dimer lab values were simultaneously observed, typical of COVID-19. Although fever is common in both COVID-19 and IM, splenomegaly and cervical lymphadenopathy are not common symptoms of SARS-CoV-2 infection.[1]

Mumps or parotitis is not common in Spain since the introduction of the MMR vaccine (measles, mumps and rubella) in the vaccination schedule in 1981, although outbreaks have been reported in recent years in universities and student residences in young people born between the years 1990 and 2000.[2] We were able to verify that the patient was immunized in France with the MMR vaccine at 12 and 16 months in 2002. The different clinical manifestations of IM include bilateral eyelid oedema and facial swelling mimicking mumps. In this case, and in the absence of the virus in the saliva sample, we interpret the elevation of the anti-mumps IgM antibody titre as a false positive. This serological cross reaction has been previously reported and attributed to EBV.[3] On the contrary, serological cross-reaction with measles is not so common in EBV, so we cannot rule out that SARS-CoV-2 was also involved in this case. SARS-CoV-2 shares morphostructural similarities with paramyxoviruses and they all express class I membrane fusion proteins.[4] Our patient did not present pulmonary abnormalities in the CT scan performed, showing exclusively laboratory abnormalities attributable to COVID-19, despite the immunosuppression that IM can induce. Some authors suggest that the stimulation or training of the innate immune response induced by other infections and vaccines would favour the early synthesis of interferon and *Toll-like* receptors, which could explain the benign course of COVID-19 infection in children and young adults.[5]

In conclusion, we consider it important not to ignore other pathogens in febrile syndromes during this pandemic, not being tempted to attribute new, previously unreported clinical manifestations, to SARS-CoV-2.

Conflicts of interest

The authors declare no conflict of interest.

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