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Letter to the Editor

SARS-CoV-2 detection in the pericardial fluid of a patient with cardiac tamponade

To The Editor

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is a novel coronavirus first identified in Wuhan, China, at the end of 2019. Since then it has caused more than 1700,000 confirmed cases of Coronavirus Disease 2019 (COVID-19) worldwide and almost 110,000 deaths [1]. It is responsible for a respiratory syndrome ranging from mild flu-like symptoms to severe respiratory failure (due to acute respiratory distress syndrome), shock, multiorgan failure and death. [2]. SARS-CoV-2 has been first identified in a bronchoalveolar-lavage fluid collected from patients with pneumonia admitted in a hospital of Wuhan on late December [3] and a real-time reverse transcriptase–polymerase chain reaction (rRT-PCR) of nasopharyngeal swabs is currently used to confirm the clinical diagnosis [4]. From its isolation, SARS-CoV-2 has been detected in the respiratory tract, in feces, conjunctiva and in blood [5, 6] but its localization in other sites has not been reported so far. We report here the first isolation of SARS-CoV-2 in the pericardial fluid of a patient affected with COVID19 and cardiac tamponade undergoing pericardiocentesis.

On February 15, 2020, a 59- year old man was admitted to our Emergency Department for acute chest pain. Non-ST Elevation Acute Coronary Syndrome was diagnosed with coronary angiography showing multivessel disease. The following day the patient underwent coronary artery bypass surgery with left internal mammary artery to the left anterior descending, right internal mammary artery to first obtuse marginal and left radial artery to right coronary. He was extubated on the third day and echocardiography showed mild pericardial effusion without hemodynamic impairment. On March 5, the patient complained of fever; blood and urine culture were performed resulting negative. After three days, a new episode of fever associated with dyspnea occurred; considering the increasing number of cases affected with COVID19 at our hospital, a nose-pharyngeal swab for SARS-CoV-2 research was performed with positive result; at the same time serological tests for Mycoplasma Pneumoniae and Chlamydia Pneumoniae, A/B Influenza viruses research on respiratory specimens, urinary antigens for Legionella Pneumophila and Streptococcus Pneumoniae were performed and all resulted negative. Patient underwent high-resolution lung CT scan showing “ground glass” areas with “crazy paving” pattern in both lungs, especially in the left lung, suggesting COVID19-related interstitial pneumonia. Therapy with lopinavir/ritonavir and hydroxychloroquine was started. Blood samples trend showed increasing inflammatory markers (C-reactive protein and fibrinogen), lactic dehydrogenase and D-dimer (Table 1); in the light of emerging evidence that suggested a role for low-molecular-weight-heparin (LMWH) to decrease mortality in COVID19 patients with markedly elevated D-dimer, enoxaparin was also started [7]. In the subsequent days, the patient was treated with helmet c-PAP for hypoxic respiratory insufficiency with a favourable clinical response. On March 17, we started antibiotic therapy with ampicillin and ceftriaxone because of a second blood culture showing the presence of Enterococcus Faecalis. After some days, global clinical conditions improved with progressive reduction in inflammatory markers (Table 1). On March 31, he complained of dyspnea and chest pain: temperature was 36.5 °C, blood pressure 100/65 mmHg, the pulse 130 beats per minute, the respiratory rate 24 beats per minute and the oxygen saturation 98% while he was breathing room air. An echocardiography was performed and documented severe circumferential pericardial effusion conditioning collapse of the right heart sections. As shown in Table 1, high sensitivity Troponin-I elevation was minimal. An echo-guided pericardiocentesis from subcostal approach was performed, draining 250 cc of sero-haemorragic fluid; a sample was sent to our laboratory for physico-chemical, cytological, microbiological and molecular analysis. A second nasopharyngeal swab and a blood sample for viral RNA detection were performed. Pericardial drainage was maintained in situ for two days and a total of 400 cc of fluid was aspired. Given the progressive improvement of clinical conditions and laboratory results, patient was discharged on April, 6, in fiduciary isolation.

Pericardial fluid analysis

Chemical and cytological analysis of pericardial sample documented presence of inflammatory cells: erythrocyte, mononucleates elements and lymphocytes were predominant, neoplastic cells were not found. The presence of SARS-CoV-2 in pericardial fluid The presence of was detected by a rRT-PCR amplification of SARS-CoV-2 RNA through the GeneFinder COVID-19 PLUS RealAmp Kit (OSANG Healthcare Co, Ltd., Korea) on the ELITe InGenius platform (ELITech Group, Puteaux, France), which integrates extraction and amplification. The rRT-PCR kit detects in the same PCR reaction the presence of three SARS-CoV-2 targets: the envelope protein (E), the nucleocapsid protein (N) and RNA-dependent RNA polymerase (RdRp) genes. An endogenous internal control based on the amplification of human beta-globin gene allows to confirm the quality of the sample material extracted and the execution of the test. The rRT-PCR analysis revealed the presence of SARS-CoV-2 N gene with a cycle threshold (Ct) value of 37.07 (the test is considered positive if $Ct < 43$). No amplification was detected for the other two SARS-CoV-2 genes, thus suggesting the presence of a low viral load; the value of single positive target gene has already been

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Table 1
Laboratory Results.

Variable	Reference Range	February, 15	March, 11	March, 17	March, 23	March, 29	April, 5
Hemoglobin (g/dl)	14–18	13	11.9	12.5	12.2	11.8	11.3
Hematocrit (%)	42–50	40.6	36.5	38.7	39.4	38.3	35.6
Platelet Count (per mm^2)	150,000–400,000	150	106	202	460	324	215
White Cell Count (per mm^2)	4000–10,000	5.8	1.9	5.6	8.5	4.7	5.2
Absolute Neutrophil Count (per mm^2)	2000–7000	4.02	1.25	4.8	6.95	2.84	3.47
Absolute Lymphocyte Count (per mm^2)	1500–4000	0.95	0.5	0.35	0.6	0.86	0.83
C-Reactive Protein (mg/liter)	<1	1.34	2.43	11	4.76	0.58	2.76
Troponin I (ng/L)	<15	4580		<15	<15	22	20
D-dimer (ng/ml)	<400			1956	1966	4566	1607
Fibrinogen (mg/dl)	150–350				775		631
Sodium (mmol/ liter)	135,145	141	136		136	138	140
Potassium (mmol/liter)	3,5–5	3.8	4.3		4.2	4.1	4.4
Albumin (g/dl)	3.5–5.2			2.72	2.84		
Creatinine (mg/dl)	0.6–1.17	0.92	0.76	0.68	0.74	0.82	
NT-proBNP (ng/L)	<300			2705			
Glucose (mg/dl)	65–110	131	93		128	100	86
Aspartate aminotransferase (U/liter)	<35	65	31	34	37		36
Alanine aminotransferase (U/liter)	<45	27	25		65	53	68
Lactate dehydrogenase (U/liter)	125–250		204	648	264	206	162
Procalcitonin (ng/ml)	<0.49			0.10	0.11		

postulated in a suggestive clinical context [8]. Our patient had a previous nasopharyngeal swab positive for all three target genes and a suggestive lung CT scan; after about three weeks and a full course of antiviral therapy, the second nasopharyngeal swab and viral RNA research in the blood were both negative: this data are in agreement with the bland positivity in the pericardial sample. In our opinion the absence of viral RNA in blood and nasopharyngeal secretions and its presence in pericardial fluid could suggest a persistence site; whether this has pathogenic implications is still unknown.

COVID-19 pathogenesis is still being characterized. Until now, virus has been detected only in sites corresponding to clinical manifestations: respiratory, gastro-intestinal and ocular involvement are well known. However, although cardiac involvement has been described [9], pericardial and myocardial tropism of SARS-COV-2 was only assumed. The present data provide a new piece in the complex puzzle of this emerging disease, suggesting a possible direct virus involvement in cardiologic manifestations. Further studies in this direction are necessary.

Declaration of Competing Interest

All authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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