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.

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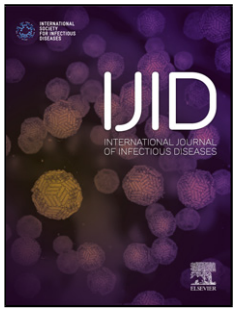

Acute respiratory distress syndrome due to SARS-CoV-2 and Influenza A co-infection in an Italian patient: mini-review of the literature

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Title

Acute respiratory distress syndrome due to SARS-CoV-2 and Influenza A co-infection in an Italian patient: mini-review of the literature.

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Highligths

- Acute respiratory distress syndrome due to SARS-CoV-2 and Influenza A co-infection
- Challenging in co-infection cases identification
- Improvement of preventive measures and patients' clinical outcome

Abstract

A case of acute respiratory distress syndrome due to SARS-CoV-2 and Influenza A co-infection and a mini-review of the literature is reported. Even in COVID-19 epidemics, the early identification of concurrent respiratory pathogens is important to improve etiological diagnosis, preventive measures and patients' clinical management and outcome.

Keywords

Acute respiratory distress syndrome; SARS-CoV-2; Influenza A, COVID-19 Epidemic

Introduction

In December 2019, a novel coronavirus, the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) which causes a human disease named coronavirus disease (COVID-19) was identified in the pneumonia outbreaks in Wuhan, China, in December 2019 (Chan et al, 2020). It is currently expanding rapidly to several countries all-around the word, on February 21 the first person-to-person transmission in Italy was reported (Spina et al, 2020). Here, we report a case of SARS-CoV-2 and Influenza A co-infection and a mini-review of the literature.

Case Presentation

A 56 year-old male general surgeon was admitted to the Lazzaro Spallanzani National Institute for

Infectious Diseases in Rome, Italy, on March 6, 2020. He was a smoker, within the overweight range (29-body mass index), with a history of two episodes of acute myocardial infarction treated with coronary angioplasty and stenting, For 4 days, he had been complaining of fever, diarrhea and asthenia after winter ski week in Northern Italy. Two days after the onset of symptoms, a nasopharyngeal swab was positive for SARS-CoV-2 (genes E and S) and Influenza A. On March 6, a chest computed tomography (CT) scan revealed bilateral and multiples peripheral ground glass opacities. Blood tests showed lymphopenia (lymphocyte and monocyte cell count: 0.67 and 0.09×10^9/L respectively), C- reactive protein and serum fibrinogen levels were increased (43.3 g/L and 7980 g/L respectively). An arterial oxygen tension (PaO_2)/ fractional inspired oxygen (FiO_2) P/F Ratio was 320. Oral oseltamivir (75 mg twice per day for 5 days) and lopinavir/ritonavir (400/100 mg twice per days for 14 days) were started together with antibiotic therapy (intravenous ceftriaxone 2 gr and oral azithromycin 500 mg per day) and intravenous methylprednisolone (40 mg twice daily for 5 days with tapered discontinuation). On day eight of hospitalization, he developed respiratory failure (P/F Ratio dropped to 202) and a second chest CT scan showed a worsening of the bilateral ground-glass opacities with fibrotic consolidation in both lower pulmonary lobes (Fig1a). At that time, nasopharyngeal swabs were positive for SARS-CoV-2, only. The patient was transferred to the Intensive Care Unit (ICU) and non-invasive ventilation through continuous positive airway pressure (C-PAP) mask was started with positive end-expiratory pressure (PEEP) 7.5 mmHg and FiO2 40%. After three days, he was re-admitted to the High Isolation Unit and discharged in good clinical conditions with persistently negative nasopharyngeal swabs. A SARS-CoV-2 serology by an in house indirect immunofluorescence assay (IgA 1:1280, IgM 1:320 and IgG 1:80) was positive (Colavita et al, 2019). During the following week, low-grade fever re-occurred with nocturnal sweats, a third CT scan showed a reduction of the ground glass areas with residual interstitial damage (Fig1b) and a further nasopharyngeal swab was negative. Symptoms healed spontaneously few days later.

Discussion

Previous cases of viral pneumonia SARS-CoV-2 and influenza coinfection have been reported in literature. During the new coronavirus epidemic, a total number of 37 cases were described. Table1 summarizes the characteristics of the coinfected patients. Fourteen cases belonged to epidemiological studies and clinical data were not available. All patients had a similar clinical presentation (fever, cough and shortness of breath) and 9 of them (9/37, 24.3%) presented a progressive worsening with ARDS. Furthermore, six patients needed ICU monitoring and were subsequently discharged in good clinical conditions with the exception of three patients who died.

Even during a pandemic scenario, several respiratory pathogens should be considered in the diagnostic algorithm, for an early etiological identification and appropriate treatment. SARS-CoV-2 and influenza viruses share common route of transmission, same season occurrence and overlapping clinical features (Lai et al, 2020, Chow et al, 2019). Indeed, SARS-CoV-2 exhibits prevalent human-to-human transmission through close contact with an estimated R0 of 3.28 and a median of 2.79 with IQR of 1.6 (Liu et al, 2020).

Respiratory symptoms are always the initial manifestations of both SARS-CoV-2 and influenza infections which could progress towards ARDS. Recently, ground-glass opacities and a higher median PaO2/FIO2 (198.2 vs 107.0) were observed in COVID-19-induced ARDS rather than H1N1 patients (Tang et al, 2020).

Nevertheless, a timely identification of the two co-infections is needed in relation to difference in treatments and prognosis. Antiviral therapy is currently available for influenza infection (i.e. oseltamivir, zanamivir, and peramivir) while experimental off-label drugs (i.e. lopinavir/ritonavir, chloroquine, and hydroxychloroquine) have been commonly used in COVID-19 treatment. In particular, the boosted

protease inhibitor lopinavir/ritonavir has been previously associated with significantly fewer adverse clinical outcomes for the treatment of SARS and furthermore, in association with the Interferon Beta-1b, it has been demonstrated to be beneficial in animal studies against the Middle East Respiratory Syndrome(Chu et al, 2004, Chan et al 2015). Considering the severity of the clinical picture and the prompt availability of lopinavir/ritonavir in our Institute, clinicians opted for this treatment although the antiviral effects remain to be determined (Cao et al, 2020).

Despite a recent report on beneficial effect of steroids treatment in COVID-19 patients who develop ARDS, its routinely use remains controversial with lack of an accurate assessment of the harm/benefit balance (Wu et al, 2020).

The epidemiological situation in Italy in February 2020 and the recommendations in use at that time allowed a timely identification of our patient with a prompt hospitalization and subsequent diagnostic investigations. Therefore, the early antiviral treatments of both influenza and SARS-CoV-2, together with a brief steroid course and oxygen supplementation, had an impact on the patient's outcome avoiding the progressive worsening and the evolution towards the severe ARDS phase. In conclusion, even in epidemic setting, the early and prompt identification of concurrent respiratory pathogens is important in order to improve etiological diagnosis, preventive measures and patients' clinical management and outcome. Further studies are needed to better understand the pathogenic role of viral coinfections in respiratory diseases.

Declaration of interests

The 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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Ethical approval

This study was approved by the Spallanzani Institute Ethical Board and patient's written informed consent for publication was collected

Conflict of interest

All authors have no conflict of interest to declare.

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Figure Legend

Title

Chest computer tomography scan at patient's worsening and recovery

Legend

(a) bilateral ground-glass opacities with fibrotic consolidation in both lower pulmonary lobes (b) reduction of the ground glass areas with residual interstitial damage.

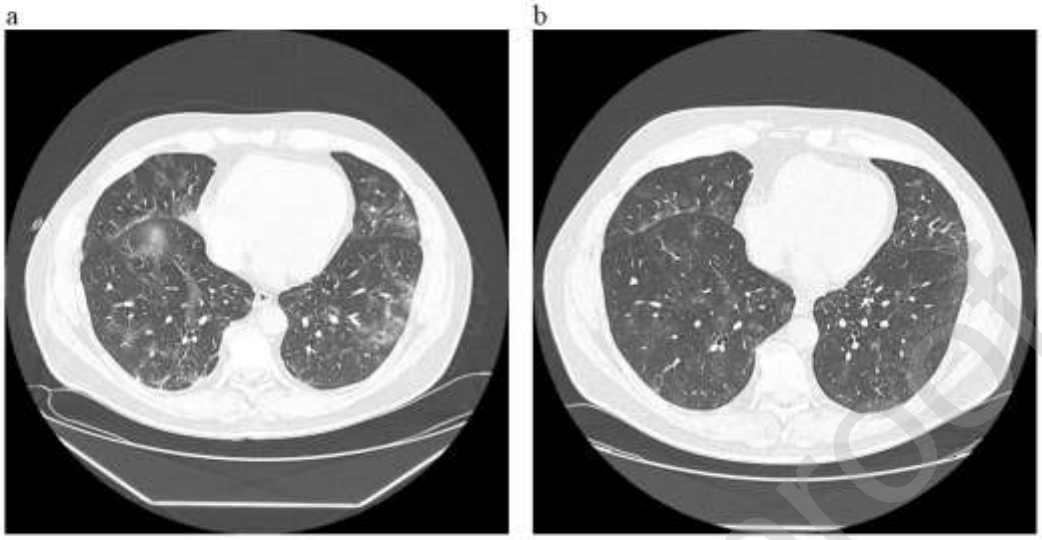

Table. Clinical Characteristics of SARS-CoV-2 and Influenza Coinfection, COVID-19 Epidemic

References	Sex	Age	Comorbidities	Coinfection	Oseltamivir	Antivirals	Glucorticoids	ARDS	ICU	NIV	IMV	Outcome
Azekawa S et al, 2020	F	78	Dyslipidemia, hypothyroidism	Influenza A	Yes	No	No	No	No	No	No	Survived
Blasco ML et al, 2020	NA	NA	NA	Influenza A and RSV	NA	NA	NA	NA	NA	NA	NA	NA
Cuadrado-Payán et al, 2020	M	53	ERSD	Influenza A	Yes	Yes	NA	Yes	Yes	No	Yes	Survived
	M	78	T2DM	Influenza A	Yes	Yes	NA	Yes	Yes	No	Yes	Survived
	M	56	T2DM	Influenza A and B	No	No	NA	No	No	No	No	Survived
	F	81	ERSD	Influenza B	Yes	Yes	NA	Yes	Yes	No	Yes	Survived
De Souza Luna et al, 2020	NA	36	NA	Influenza B	NA	NA	NA	NA	NA	NA	NA	NA
Ding et al., 2020	F	47	None	Influenza A	Yes	Yes	Yes	No	No	No	No	Survived
	M	50	Hypertension, cancer	Influenza A	Yes	Yes	Yes	Yes	No	Yes	No	Survived
	F	66	Hypertension, CVD, HBV	Influenza B	Yes	Yes	No	No	No	No	No	Survived
	M	39	HBV	Influenza B	Yes	Yes	Yes	No	No	No	No	Survived
	F	49	None	Influenza A	Yes	Yes	No	No	No	No	No	Survived
Garazzino S et al, 2020	NA	<17	NA	Influenza A	NA	NA	NA	NA	NA	NA	NA	NA
Hashemi SA et al, 2020	F	78	NA	Influenza A	Yes	Yes	NA	Yes	NA	NA	NA	Dead
	M	75	NA	Influenza A	Yes	Yes	NA	Yes	NA	NA	NA	Dead
Khodamoradi et al., 2020	F	74	Hypertension, CVD	Influenza A	Yes	Yes	No	No	No	No	No	Survived
	M	40	None	Influenza A	Yes	Yes	No	No	No	No	No	Survived
	M	64	None	Influenza A	Yes	Yes	No	No	No	No	No	Survived
	M	50	None	Influenza A	Yes	Yes	No	No	No	No	No	Survived
Kim D et al, 2020	NA	NA	NA	Influenza A	NA	NA	NA	NA	NA	NA	NA	NA
Konala VM et al, 2020	M	57	hypertension, T2DM, CVD, AICD	Influenza A	Yes	Yes	No	No	No	No	No	Survived
	F	35	sickle cell trait	Influenza A	Yes	Yes	No	No	No	No	No	Survived
	F	68	T2DM, hypertension, GERD	Influenza B	Yes	Yes	NA	Yes	Yes	No	Yes	Dead
Konala VM et al, 2020	F	66	T2DM, CVD, hypertension, CKD	Influenza A	Yes	Yes	NA	Yes	Yes	No	Yes	Survived
Nowak MD et al, 2020	NA	NA	NA	Influenza A	NA	NA	NA	NA	NA	NA	NA	NA
Pongpirul WA et al, 2020	M	61	None	Influenza A	Yes	No	No	No	No	No	No	Survived

Richardson S et al, 2020	NA	NA	NA	Influenza A	NA	NA	NA	NA	NA	NA	NA	NA
Wehl G et al, 2020	NA	4 months	None	Influenza A	Yes	No	No	No	No	No	No	Survived
Wu Q et al, 2020	NA	<17	NA	MP, Influenza A&B, RSV	NA	NA	NA	NA	NA	NA	NA	NA
Wu X et al, 2020	M	69	None	Influenza A	Yes	NA	NA	Yes	Yes	No	Yes	Survived
Zhu X et al, 2020	NA	NA	NA	2 pts Influenza A 5 pts Influenza B	NA	NA	NA	NA	NA	NA	NA	NA

Legend: SARS-CoV-2: severe acute respiratory syndrome coronavirus-2, COVID-19: coronavirus disease-19, CVD: cardiovascular disease, HBV: hepatitis B virus, NA: not available, ARDS; Acute Respiratory Distress Syndrome, ICU: Intensive Care Unit, NIV: non-invasive ventilation, IMV: invasive mechanical ventilation, T2DM: type 2 diabetes mellitus. AICD: automatic implantable cardioverter defibrillator. RSV: Respiratory syncytial virus. MP: Mycoplasma pneumonia. ESRD: end-stage kidney disease. CKD: chronic kidney disease. GERD: gastroesophageal reflux disease