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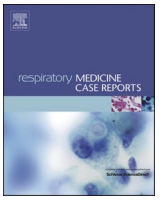

Case report

Combination of acute exacerbation of idiopathic nonspecific interstitial pneumonia and pulmonary embolism after booster anti-COVID-19 vaccination

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ABSTRACT

Coronavirus disease-2019 (COVID-19) is a systemic disorder with the lung and the vasculature being the preferred targets. Patients with interstitial lung diseases represent a category at high risk of progression in the case of Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV)-2 infection, and as such deserve special attention. We first describe the combination of acute exacerbation and pulmonary embolism in an elderly ILD patient after booster anti-COVID-19 mRNA vaccination. Vaccines availability had significantly and safety impacted COVID-19 morbidity and mortality worldwide. Immunization against COVID-19 is indisputable but must not be separated from the awareness of potential adverse effects in *fragile* patients.

1. Introduction

The Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV-2) pandemic has dramatically challenged the daily life of all societies with enormous public health and economic repercussions. Different vaccines, either approved by Regulatory Authorities or for emergency use, have been utilized worldwide to protect populations from severe and potentially lethal forms of its related disease, i.e. Coronavirus disease-2019 (COVID-19). Overall, these vaccines have achieved estimated protection ranging from 50 to 83.5% with a fairly good safety profile [1,2]. As the efficacy of vaccines may partly be affected by virus variants, vaccination has been extended as much as possible in parallel with boosting implementation.

Herein we first describe the combination of acute exacerbation (AE) and pulmonary embolism in an 82-yr old female patient affected by idiopathic nonspecific interstitial pneumonia (iNSIP) after booster anti-COVID-19 mRNA vaccination.

2. Case presentation

An 82-yr old female never smoker patient affected by clinically stable iNSIP for three years presented to our observation with a 3-

Abbreviations: COVID-19, Coronavirus disease 2019; ILD, interstitial lung disease; SARS-CoV-2, Severe Acute Respiratory Syndrome Coronavirus-2; AE, acute exacerbation; iNSIP, idiopathic nonspecific interstitial pneumonia; HRCT, high-resolution computed tomography; GGO, ground glass opacity; IPF, idiopathic pulmonary fibrosis; MIP, maximum intensity projection.

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day history of acute dyspnea. Two days before she had received the booster dose of an anti-SARS-CoV-2 mRNA vaccine (BNT162b2 BioNTech/Pfizer, the same as the first two received in March 2021). She took an influenza vaccine annually with no adverse events, denied any allergy, and reported no lifestyle changes. Blood gases analysis at rest in ambient air showed severe hypoxemia (paO_2 31 mmHg) on hospital admission. Laboratory findings revealed an increase of total white blood cells, with a neutrophils/lymphocytes ratio of 27. Additional alterations concerned C-reactive protein (16.2 mg/dL), D-Dimer (10,728 ng/mL), interleukin-6 (94.3 pg/mL), and pro-BNP (12,406 pg/mL). Chest X-ray showed a widespread reticulation with multiple small opacities in the lower lung zones. Chest high-resolution computed tomography (HRCT), confirmed the presence of ground-glass opacities (GGO) and areas of consolidations mainly in the lower lobes (Fig. 1). Integrated CT-angiography revealed the concomitance of bilateral endoluminal thromboembolic defects at the segmentary/sub-segmentary level (Fig. 2). Serological tests and cultures of sputum and blood samples showed no evidence of infection and SARS-CoV-2 nasal swabs were negative. Fiber-bronchoscopy was not performed due to the severe patient's conditions. No endo-cavitary clots were revealed by echocardiography. Estimated systolic pulmonary arterial pressure was 55 mmHg. Deep vein thrombosis and vaccine-induced immune thrombotic thrombocytopenia were excluded. Treatment with methylprednisolone, fondaparinux, and wide-spectrum antimicrobial agents was early started. Respiratory failure rapidly progressed despite the use of various devices of ventilatory support. Paroxysmal atrial fibrillation ultimately led to hemodynamic imbalance, multiorgan failure, and death.

3. Discussion

The interaction of SARS-CoV-2 with the lung is rather delicate due to the possible repercussions of the infection beyond acute interstitial pneumonia. Concerning the expected long-term COVID-19 *sequelae*, it has been hypothesized that a not negligible proportion of patients can develop pulmonary fibrosis with persistent organ damage [3,4]. In light of this dreadful consideration, patients with chronic lung diseases, particularly those affected by interstitial lung diseases (ILDs), have caused concern due to their high risk of rapid worsening in case of SARS-CoV-2 infection [5]. AEs are unpredictable events that can precipitate the natural history of any ILD inexorably. They can occur either *sine causa* or in response to known triggers in the absence of really effective treatments [6]. In 2010, Umeda Y et al. reported a case of AE in a 57-yr old male patient affected by idiopathic pulmonary fibrosis (IPF) after two days from influenza (H1N1) vaccination [7]. Similarly, a potential association of AE and the first dose of an mRNA COVID-19 vaccination has recently been observed in a 72-yr old male IPF patient successfully treated with glucocorticoids [8]. This association has further been confirmed by the case of a 84-yr old male patient affected by f-ILD after receiving the second of an mRNA vaccine [9]. In line with these previous observations, our findings reinforce the triggering role of anti-COVID-19 vaccination on ILD progression suggesting that such an adverse event may occur even later and despite the patient well tolerated the first two doses of immunization. Unfortunately, in our case the clinical course was unfavorable as the patient experienced a sudden progression refractory to any treatment. This happened despite she was suffering from an ILD less aggressive than IPF. In addition, and as a novelty of our case in comparison with the previous ones, contextual bilateral pulmonary embolism further aggravated the clinical picture. After exclusion of immune-mediated thrombosis [10], this scenario recalls a peculiar feature of SARS-CoV-2 which may affect the systemic vasculature [11,12], with the lung being the preferred target [13]. In our opinion, since the patient well tolerated the first two vaccine doses, it is highly conceivable that the reinforced immune stimulation of the booster dose has triggered a cytokine storm as it happens in severe COVID-19 pneumonia [14]. This hypothesis is supported by the high levels of inflammation and pro-coagulation markers and marked blood lymphopenia, all correlated with COVID-19 mortality [15].

The need to protect ILD patients in the ongoing pandemic is indisputable. However, the eventuality, albeit remote, of vaccine-induced acute deterioration should be kept in mind. ILD patients are *fragile* subjects placed between the anvil and the hammer, and as such merit special attention.

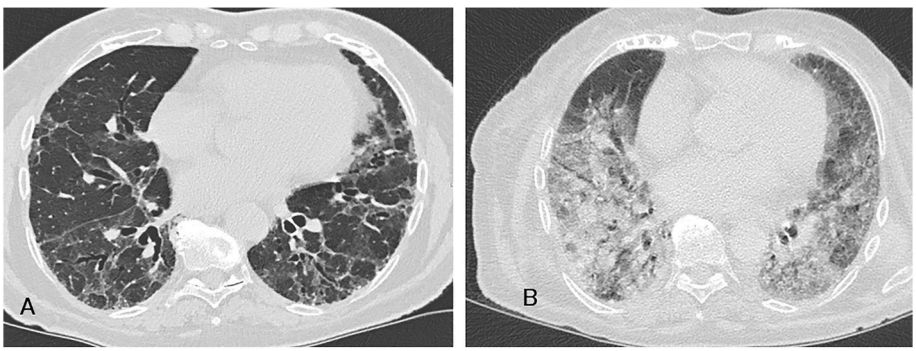

Fig. 1. Representative HRCT of the chest before and after booster mRNA anti-COVID-19 vaccination. A) Comparison CT scan performed 18 months before anti-COVID-19 vaccination showing extended patchy areas of GGO along with traction bronchiectasis and bronchiolectasis in the lower lobes with left predominance suggestive for a fibrotic NSIP pattern. B) After the third dose of vaccination, chest HRCT revealed the presence of new areas of diffuse and severe GGO over-imposed on the NSIP pattern as for acute exacerbation.

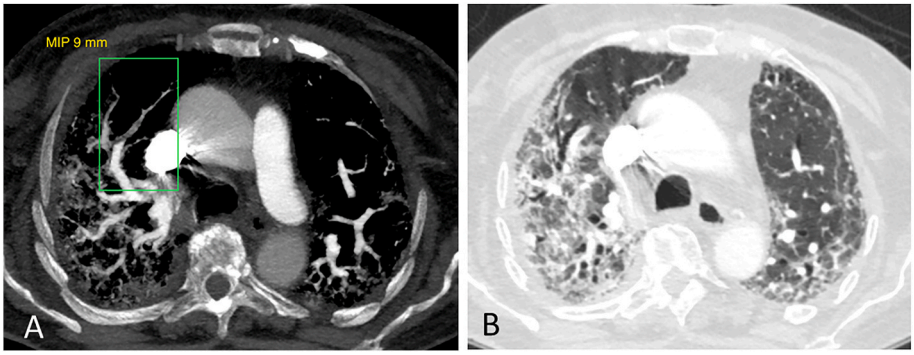

Fig. 2. A) Representative lung CT angiography images after booster mRNA anti-COVID-19 vaccination. Evidence of a hypodense embolic defect in an anterior segmental vessel of the right pulmonary artery is appreciable in the ipsilateral upper lobe, suggestive for pulmonary embolism, as shown in the mediastinal window with a 9 mm MIP (Maximum Intensity Projection) reconstruction. B) Contextual evidence of GGO alterations as for NSIP acute exacerbation is detectable in the lung window.

Statement of ethics

The study of the case report was conducted according to the Declaration of Helsinki. The daughter of the patient provided written informed consent for publication (available upon request).

Ethical review board

NA.

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Author contribution

MB, AB, ADD, AAS contributed to collect clinical data and to patient assistance. GR and RL contributed to the imaging study. MB wrote the manuscript. All Authors critically revised the text and approved the final version.

Declaration of competing interest

The Authors have no conflict of interest to declare.

References

[1] T. Fiolet, Y. Kherabi, C.J. MacDonald, J. Ghosn, N. Peiffer-Smadja, Comparing COVID-19 vaccines for their characteristics, efficacy and effectiveness against SARS-CoV-2 and variants of concern: a narrative review, Clin. Microbiol. Infect. 28 (2) (2022) 202–221.
[2] W.H. Khan, Z. Hashmi, A. Goel, et al., COVID-19 pandemic and vaccines update on challenges and resolutions, Front. Cell. Infect. Microbiol. 11 (2021) 690621.
[3] A. Nalbandian, K. Sehgal, A. Gupta, et al., Post-acute COVID-19 syndrome, Nat. Med. 27 (4) (2021) 601–615.
[4] L.T. McDonald, Healing after COVID-19: are survivors at risk for pulmonary fibrosis? Am. J. Physiol. Lung Cell Mol. Physiol. 320 (2) (2021) L257–L265.
[5] Y. Kondoh, K. Kataoka, M. Ando, et al., COVID-19 and acute exacerbation of interstitial lung disease, Respir. Invest. 59 (5) (2021) 675–678.
[6] H.R. Collard, C.J. Ryerson, T.J. Corte, et al., Acute exacerbation of idiopathic pulmonary fibrosis. An international working group report, Am. J. Respir. Crit. Care Med. 194 (3) (2016) 265–275.
[7] Y. Umeda, M. Morikawa, M. Anzai, et al., Acute exacerbation of idiopathic pulmonary fibrosis after pandemic influenza A (H1N1) vaccination, Intern. Med. 49 (21) (2010) 2333–2336.
[8] A. Ghincea, C. Ryu, E.L. Herzog, An acute exacerbation of idiopathic pulmonary fibrosis after BNT162b2 mRNA COVID-19 vaccination: a case report, Chest 161 (2) (2022) e71–e73.
[9] T. Bando, R. Takei, Y. Mutoh, et al., Acute exacerbation of idiopathic pulmonary fibrosis after SARS-CoV-2 vaccination, Eur. Respir. J. 59 (3) (2022) 2102806, https://doi.org/10.1183/13993003.02806-2021.
[10] Z.M. Afshar, M. Barary, A. Babazadeh, et al., SARS-CoV-2-related and Covid-19 vaccine-induced thromboembolic events: a comparative review, Rev. Med. Virol. (2022) e2327.
[11] H.K. Siddiqi, P. Libby, P.M. Ridker, COVID-19 - a vascular disease, Trends Cardiovasc. Med. 31 (1) (2021) 1–5.
[12] T. Iba, J.H. Levy, M. Levi, J.M. Connors, J. Thachil, Coagulopathy of coronavirus disease 2019, Crit. Care Med. 48 (9) (2020) 1358–1364.
[13] G. Rea, F. Lassandro, R. Lieto, et al., Lesson by SARS-CoV-2 disease (COVID-19): whole-body CT angiography detection of "relevant" and "other/incidental" systemic vascular findings, Eur. Radiol. 31 (10) (2021) 7363–7370.
[14] B. Hu, S. Huang, L. Yin, The cytokine storm and COVID-19, J. Med. Virol. 93 (1) (2021) 250–256.
[15] B.M. Henry, M.H.S. de Oliveira, S. Benoit, M. Plebani, G. Lippi, Hematologic, biochemical and immune biomarker abnormalities associated with severe illness and mortality in coronavirus disease 2019 (COVID-19): a meta-analysis, Clin. Chem. Lab. Med. 58 (7) (2020) 1021–1028.