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An Acute Exacerbation of Idiopathic Pulmonary Fibrosis After BNT162b2 mRNA COVID-19 Vaccination

A Case Report



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Idiopathic pulmonary fibrosis (IPF) is a fatal interstitial lung disease characterized by progressive scar tissue formation. An acute exacerbation of IPF (AE-IPF) is a clinically significant respiratory decompensation that accounts for a significant proportion of IPF-related morbidity and mortality. AE-IPF can be idiopathic or associated with pulmonary embolism, infection, aspiration, surgery, and drug toxicity. In this novel case report, we describe a potential association between AE-IPF and BNT162b2 mRNA COVID-19 vaccination that was successfully treated with a short course of glucocorticoids. While our aim is to raise awareness for this yet-to-be-described adverse event, immunization against vaccine-preventable disease remains widely recommended in vulnerable patients with chronic lung disease such as IPF.

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KEY WORDS: acute exacerbation; BNT162b2 mRNA COVID-19 vaccine; COVID-19; idiopathic pulmonary fibrosis; interstitial lung disease

Idiopathic pulmonary fibrosis (IPF) is a fatal interstitial lung disease (ILD) characterized by progressive scar tissue formation.¹ An acute exacerbation of IPF (AE-IPF) is a clinically significant respiratory decompensation defined by radiographic evidence of new-onset diffuse alveolar abnormalities that accounts for a significant proportion of IPF-related morbidity and death.² AE-IPF can be idiopathic or associated with pulmonary embolism, infection, aspiration, surgery, and drug toxicity.^{1,3} In this novel case report, we are the first to describe a potential association between AE-IPF and BNT162b2 mRNA COVID-19 vaccination.

Case Report

A 72-year-old gentleman with a medical history significant for IPF of 8 years duration that had been treated with nintedanib presented with progressive dyspnea over 1 week. Two weeks earlier, he had received his first dose of the BNT162b2 mRNA COVID-19 vaccine. One week after vaccination, he experienced worsening dyspnea, an increasing, nonproductive cough, fevers, and chills. He denied any sick contacts or recent travel. He was fully adherent to masking and social distancing. He denied any chest pains, palpitations, or lower extremity edema. He denied any episodes of difficulty swallowing, aspiration, or gastroesophageal reflux symptoms. He had not undergone any recent

ABBREVIATIONS: AE-IPF = acute exacerbation of IPF; DI=ILD = drug-induced ILD; ILD = interstitial lung disease; IPF = idiopathic pulmonary fibrosis; SAE = serious adverse event

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surgeries, blood transfusions, or medication changes. Three days before presentation he had a negative COVID-19 nasopharyngeal swab. On presentation, he was in acute hypoxemic respiratory failure (arterial blood gas, 7.49; PCO₂, 32 mm Hg; PAO₂, 68 mm Hg; HCO₃, 24 mEq/L) requiring 4 liters of oxygen. His laboratory data were significant for an elevated lactic acid, lactate dehydrogenase, erythrocyte sedimentation rate, C-reactive protein, and D-dimer; his troponin and brain natriuretic peptide levels were normal. His chest radiograph revealed worsening pulmonary infiltrates.

Despite his recent vaccination and negative test, he was placed on airborne isolation and a nasopharyngeal swab for COVID-19; a complete respiratory viral panel was performed. These tests, including two repeated COVID-19 swabs, were negative. CT angiography was negative for pulmonary embolism but showed new findings of diffuse ground-glass opacities (Fig 1). Broad-spectrum antibiotics were discontinued once his blood, sputum, and urine cultures results were negative. An echocardiogram revealed normal cardiac function.

Because no cause for his respiratory deterioration was identified, he was diagnosed with AE-IPF, possibly related to his recent vaccination. He received methylprednisolone 125 mg IV then transitioned to a 3-week prednisone taper. After steroid treatment, supplemental oxygen was weaned; the lactic acid, lactate dehydrogenase, erythrocyte sedimentation rate,

C-reactive protein, and D-dimer levels normalized, and he was discharged home.

Discussion

Diagnostic criteria for AE-IPF includes a diagnosis of IPF, worsening or new onset dyspnea within 1 month, new CT findings of bilateral ground-glass opacities and/or consolidation superimposed on a background pattern of usual interstitial pneumonia, and clinical deterioration not fully explained by acute heart failure or volume overload.² AE-IPF has been shown to occur in patients with stable disease and well-preserved lung function,² which describes the clinical profile for this patient because he had a slowly progressive IPF phenotype over the preceding 8 years; this was his first episode of AE-IPF.

AE-IPF represents an intrinsic acceleration of underlying fibrotic injury in response to external stimuli.² Although a bronchoscopy with BAL and biopsy can be informative, it is of limited utility for AE-IPF and not widely recommended.^{2,4} Thus, a bronchoscopy was deferred, and we surmise that the patient experienced a yet-to-be-reported serious adverse event (SAE) to the BNT162b2 mRNA COVID-19 vaccine in a form of drug-induced ILD (DI-ILD). DI-ILD is an exclusionary diagnosis characterized by a nonspecific radio histopathologic pattern of diffuse lung parenchymal changes after a drug exposure.⁵ Patients with IPF are more susceptible to external insults because of the biologic dysfunction present in the fibrotic lung.² Although a contrast-enhanced CT scan can overstate the

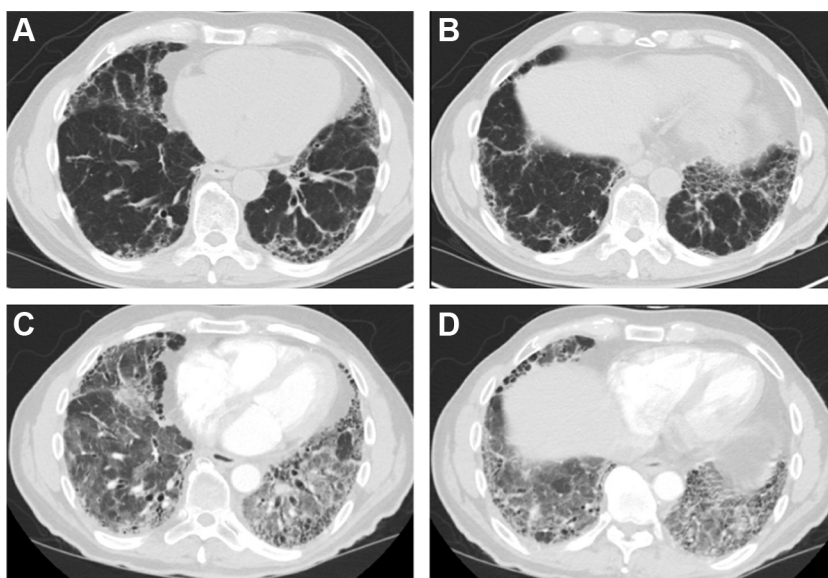


Figure 1 – A-D, Representative CT images before and after BNT162b2 mRNA COVID-19 vaccination. A and B, Baseline high-resolution CT scan performed 6 weeks before the BNT162b2 mRNA COVID-19 vaccine was given was definite for usual interstitial pneumonia. C and D, After the vaccination, the CT angiography was negative for pulmonary embolism but revealed new areas of diffuse ground-glass opacities with background interstitial pneumonia.

significance of ground-glass opacities, the overall clinical picture of this patient's acute onset chronic hypoxemia suggested that they were beyond an artifactual finding. Moreover, given the temporal relationship between vaccination and symptoms and the presence of elevated inflammatory biomarkers, which have been associated with various instances of DI-ILD,⁶ we believe he experienced a steroid-responsive episode of AE-IPF that was likely triggered by the vaccine.

In one large cohort of vaccinated patients, the most common adverse events included local and benign systemic reactions; SAEs were exceedingly rare.⁷ Interestingly, this cohort included 1,478 individuals with chronic lung disease, although rates of SAEs among this group were unavailable.⁷ In this case, although the patient's respiratory deterioration cannot be attributed definitively to the vaccine, the temporal association between vaccination and symptoms and the exclusion of identifiable triggers of AE-IPF suggests a potential relationship. Ultimately, immunization against vaccine-preventable disease is supported widely in chronic lung disease,^{8,9} including IPF.¹ Thus, for vulnerable populations during this global pandemic, the benefits of vaccination far outweigh the risks.

AE-IPF practice guidelines provide a weak recommendation for treatment with steroids, with no specific dose or duration.² Although an occult infection remains a possibility in this case because no lung biopsy was performed, his response to a short course of corticosteroids lends further support that his acute

disease process represented sterile inflammation. Presently, he remains off oxygen and participates in pulmonary rehabilitation.

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