DEAR EDITOR, mRNA-based novel vaccines have been playing a critical role in controlling the burden of the coronavirus disease 2019 pandemic on healthcare systems. Despite concerns regarding their effects on the immune system, whether that be reactivation or emergence of a new autoimmune disorder, vaccines are generally well tolerated in this population. Data on this subject have been accumulating as case reports and case series in the literature [1, 2]. We present the first case of a major organ flare following mRNA vaccination in a Behçet’s syndrome (BS) patient on immunosuppression.

A 31-year-old male with a BS diagnosis was admitted with dyspnoea, chest tightness and pleuritic chest pain in August 2021. Previous medical history revealed that he had been using AZA and ciclosporin for panuveitis for 2 years, between 2017 and 2019. However, it was learned that he did not use medication and was not followed up until he applied to us. He had not been vaccinated against or infected by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Physical examination showed mild sinus tachycardia with normal oxygen saturation and absent breath sounds in the lower lobe of the left lung. Laboratory investigations exhibited increased acute phase parameters. A SARS-CoV-2 PCR test was negative and other infectious causes were ruled out. Chest CT showed a ground-glass appearance and pleural effusion in the left lung, suggesting small-sized pulmonary vasculitis, and a hypoechogenic lesion of 9 × 10 mm originated from the interventricular septum, consistent with thrombus formation in the right ventricle (Fig. 1A, B). There was no evidence of pulmonary artery aneurysm (PAA), pulmonary artery in situ thrombosis or caval vein thrombosis. Serum ANCA, antinuclear antibodies and lupus anticoagulant were negative. Hereditary thrombophilias were excluded. The patient was diagnosed with BS-related small-sized pulmonary vasculitis and intracardiac thrombosis. Because the patient is opposed to CYC induction due to concerns about adverse effects, he has begun a combination of AZA and high-dose methylprednisolone. Based on the absence of clinical symptoms and normal acute phase reactants and chest X-ray findings in November 2021, he was considered to be in clinical remission. As a result, the steroid was gradually reduced and eventually discontinued.

In December 2021 he presented with fever and chest tightness 2 weeks following the second dose of BNT162b2 (Pfizer-BioNTech) vaccine administration. Physical examination revealed decreased breath sounds in the right lower lung fields. Laboratory parameters were significant for marked elevation in CRP (172 mg/l, 0–5) and ESR (67 mm/h, 0–10), SARS-CoV-2 PCR was negative and no infectious foci were detected. Chest CT demonstrated a ground-glass appearance, in situ thrombosis of the right pulmonary artery branches and a thrombus of 14 × 13 mm adjacent to the cardiac septum (Fig. 1C, D). No evidence of PAA and thrombosis in the caval veins were found. Echocardiography showed a thrombus formation of 15 × 12 mm originating from the interventricular septum. Based on the history and clinical findings, the possibility of vaccine-induced reactivation of BS affecting the pulmonary and cardiac systems was considered. With the patient’s permission, a combination of CYC and high-dose methylprednisolone was initiated.

The occurrence of BS flares after vaccination has previously been documented in the literature, specifically with the use of the 23-valent polysaccharide pneumococcal vaccine [3, 4]. In our case, based on normal acute phase reactants and chest X-ray without any clinical symptoms, the patient was considered in clinical remission on AZA and steroid was successfully ended at the last outpatient visit. The new clinical presentation emerged 2 weeks after the second BNT162b2 vaccination, and the interval between two vaccine doses was only 3 weeks. Due to this temporal association, we assert that the vaccination remains the only inciting factor. Although there was no echocardiographic evaluation showing that the cardiac thrombus had shrunk or disappeared at the last visit, a relapse in pulmonary findings and an increase in the size of the cardiac thrombus can be attributed to vaccine-related reactivation. The absence of PAA in our patient does not rule out this possibility because vasculitis in segmental or subsegmental small pulmonary arteries can occur in the absence of central PAA and manifest as ground-glass opacities, haemorrhages and pleural fluid [5, 6]. Interestingly, Tagini et al. [7] recently described a case manifested as new onset of oral ulcers, genital lesions and pseudo-folliculitis following mRNA vaccination, consistent with a diagnosis of BS. In a clinical observation, all flares related to mRNA vaccination in BS patients were mucocutaneous, with no described major organ involvement [2].
To our knowledge, this is the first report in the literature of a flare affecting the lung and heart in BS after mRNA vaccination. Theoretically the main proposed pathogenic mechanisms are mRNA itself as an immunogen that directly stimulates the innate immune system and/or being served by the lipid nanoparticle carrier indirectly to the humoral immune system elements [8]. The unique aspect of this case is that it announces that vaccine-related reactivation can occur even with adequate immunosuppression, implying the potential role of yet unknown mechanisms.

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Data availability statement
Data are available upon reasonable request by any qualified researchers who engage in rigorous, independent scientific research, and will be provided following review and approval of a research proposal and Statistical Analysis Plan (SAP) and execution of a Data Sharing Agreement (DSA). All data relevant to the study are included in the article.

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