Catastrophic antiphospholipid syndrome triggered by mRNA COVID-19 vaccine

Sirs,

We report the case of a 27-year-old female patient with a previous history of selective immunoglobulin A deficiency and confirmed paucisymptomatic COVID-19 in March 2021. Unknown at the time of admission, the presence of anticardiolipin (aCL, 129.5 MPL IgM) and antibeta$_2$ glycoprotein I (aB2GP-1, 101.3 MPL IgM) antibodies had been identified in 2017; Lupus anticoagulant (LA) negative.

36 hours after receiving the first dose of BNT162b2 mRNA vaccine, she presented to the Emergency Department with fever, digital ischaemia and abdominal pain. She was rapidly admitted to the Intensive Care Unit due to haemodynamic instability, signs of hypoperfusion such as hyperlactataemia, acute renal failure and disseminated intravascular coagulation (DIC). A computerised tomography scan confirmed the absence of renal and suprarenal perfusion and free fluid in the pelvis. Surgical exploration during an emergency laparoscopy, for suspected septic shock of abdominal or gynaecological origin was normal, and all cultures were negative. After antibiotic coverage and haemodynamic stabilisation, during hospitalisation the patient continued to experience daily fever, elevation of acute phase reactants and established kidney failure requiring haemodialysis due to bilateral renal cortical necrosis. Additional tests confirmed complement consumption and positivity of aCL (52.6 IgM MPL), aB2GP-1 (32.3 IgM MPL) and anti-phosphatidyl-serine/prothrombin antibodies (38.1 IGM MPL) detected by ELISA, as well as the presence of lupus anticoagulant (2.34 diluted Russell viper venom time). An 18-FDG PET/CT scan confirmed the absence of neoplasms and other potential infection sources. Haematological or other organ involvement was absent and haemogram and coagulation tests normalised after supportive therapy in ICU. Antinuclear antibodies were negative.

Based on catastrophic antiphospholipid syndrome (CAPS) diagnosis, anticoagulation with low molecular weight heparin (LMWH) and three 500 mg methylprednisolone pulses were initiated. Despite rapid defervescence, together with clinical and analytical recovery, renal function did not improve. Unfortunately, a kidney biopsy could not be performed since the patient presented a suspected transfusion-related acute lung injury (TRALI) just before the procedure. Due to this complication, as well as to the high risk of bleeding expected with the extensive renal necrosis, the multidisciplinary team in charge decided not to carry out the intervention afterwards. In parallel, due to the lack of a clinically relevant improvement in renal function or vascular evidence supporting kidney recoverability, no additional therapy was used. The patient was discharged with low-dose prednisone, hydroxychloroquine, adjusted LMWH (after anti-Xa monitoring) and thrice-weekly haemodialysis. Arrangements were also made at discharge to place a peritoneal dialysis catheter as a bridge to future renal transplantation.

Widespread COVID-19 vaccination constitutes a quantum leap in the battle against the pandemic. However, certain conditions such as antiphospholipid syndrome (APS) have been excluded from clinical trials and therefore specific data regarding this population are still lacking (1). Initial studies suggested antiphospholipid antibodies as potential mediators in COVID-19 coagulopathy and thrombotic diathesis, but the evidence is inconclusive to date (2). Despite this uncertainty, other reports have shown that mRNA vaccines may not only trigger a type I IFN response and antiphospholipid antibodies production but could also intrinsically lead to the thrombosis that defines APS (3). In addition, Yu *et al*. recently showed that the SARS-CoV-2 spike protein, a key molecule

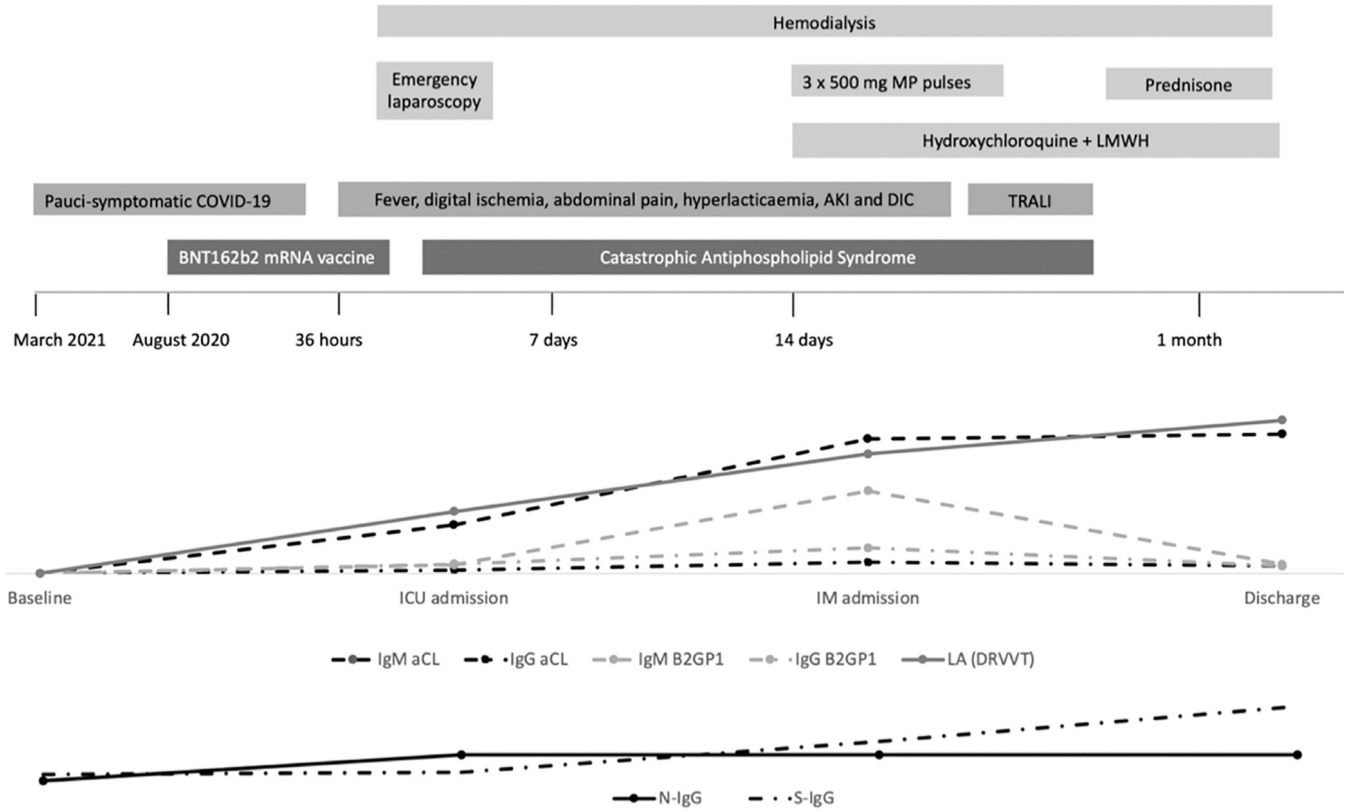

Fig 1. Chronological relationship between vaccination, main clinical events, therapies and antiphospholipid and antiSARS-CoV2 antibody titres.
AKI: acute kidney injury; DIC: disseminated intravascular coagulation; TRALI: transfusion-related acute lung injury; MP: methylprednisolone, LMWH: low molecular weight heparin; aCL: anticardiolipin antibodies; B2GP1: antibeta$_2$ glycoprotein I antibodies; LA: lupus anticoagulant; DRVVT: diluted Russel viper venom time; N-IgG: SARS-CoV-2 nucleocapsid IgG antibodies; S-IgG: SARS-CoV-2 spike Igg antibodies.

in COVID-19 mRNA vaccine immunogenicity, could be responsible for he thrombotic manifestations during COVID-19 disease since it directly activates the alternative complement cascade (4). Altogether, these data support that the mRNA vaccine could have been the "second-hit" triggering CAPS in our patient. While infections and other vaccines are well-known precipitating factors for CAPS, to our knowledge, this is the first case of APS after an mRNA COVID-19 vaccine (5). Strict APS population surveillance and the identification of other cases might clarify this issue.

Key message

mRNA COVID-19 vaccine can trigger CAPS in APS patients.

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