European Journal of Internal Medicine 91 (2021) 90–92

Contents lists available at ScienceDirect

European Journal of Internal Medicine

journal homepage: www.elsevier.com/locate/ejim

Letter to the editor

Primary adrenal insufficiency associated with Oxford-AstraZeneca ChAdOx1 nCoV-19 vaccine-induced immune thrombotic thrombocytopenia (VITT)

ARTICLE INFO

Keywords
AstraZeneca COVID-19 vaccination
ChAdOx1 nCoV-19 Vaccine
Immune thrombotic thrombocytopenia
Adrenal insufficiency
Adrenal hemorrhage

Dear editor,

In the setting of coronavirus disease 2019 (COVID-19) vaccination a very uncommon cause for adrenal insufficiency was observed in a 47-year-old man without previous relevant disease who was admitted for bilateral segmentary pulmonary embolism (without hemodynamic compromise) 10 days after receiving adenoviral (ChAdOx1) vector-based COVID-19 vaccine. Therapy with low-molecular-weight-heparin (LMWH) was initiated and 24 h later the patient began to develop neurological symptoms (headache, somnolence, and mild confusion). Physical examination showed normal vital signs (blood pressure: 139/93 mmHg, pulse-oxygen saturation: 96%, afebrile), slow mental activity, negative meningeal signs, and absence of focal neurological deficit. Laboratory tests showed a substantial increase in D-dimer (20,506 ng/ml) and thrombocytopenia (51,000/μl; previous: 103,000/μl) as main findings. In cranial CT/MRI, findings of cerebral venous thrombosis were detected in several locations (Fig. 1a and 1b). With clinical diagnosis of vaccine-induced immune thrombotic thrombocytopenia (VITT), LMWH was discontinued and treatment with intravenous immunoglobulins and subcutaneous fondaparinux was started. Platelet-factor-4 (PF4) antibody testing was positive. Ten days later, the patient had a completely normal level of consciousness and mental status, and control cranial MRI was performed (Fig. 2), showing partial revascularization of the superior sagittal cerebral venous sinus. However, he started to develop arterial hypotensive tendency and progressive abdominal discomfort. Mild hyponatremia was detected (natraemia:130 mmol/L; previous levels: 138–140 mmol/L). Abdominal MR image showed bilateral adrenal nodular enlargement with hyperintense peripheral halo and hypointense center, corresponding to ongoing subacute bilateral adrenal hemorrhage (Fig. 3). In hormonal laboratory testing, low levels of cortisol (3.8μg/dL; range values:4.8–19.5), DHEA (0.3 ng/mL;1.1–10.6 ng/mL) and aldosterone (42.2pg/mL;70–300), and high ACTH levels (345 pg/mL;7–63) confirmed primary adrenal insufficiency. Hormone replacement therapy with hydrocortisone was started, achieving disappearance of abdominal pain and rapid normalization of natraemia levels. Finally, the patient was discharged with the diagnosis of non-massive pulmonary embolism, cerebral venous thrombosis and primary adrenal insufficiency due to bilateral adrenal hemorrhage in the setting of vaccine-induced immune thrombotic thrombocytopenia (VITT).

Adrenal insufficiency is an infrequent entity, mainly caused by autoimmune adrenalitis (up to 90% of the cases). Among the remaining etiologies, bilateral adrenal hemorrhage has been described in association with heparin-induced thrombocytopenia [1] and, more recently, with sporadic cases of ChAdOx1 nCoV-19 vaccine-induced immune thrombotic thrombocytopenia (VITT) [2,3], as expression of thrombosis in unusual sites including cerebral, splanchnic and adrenal veins. However, symptomatic adrenal insufficiency has rarely been described.

VITT is caused by antibodies that recognize platelet factor 4 and induce platelet activation with a significant stimulation of the coagulation system, leading to clinically relevant thromboembolic events [4, 5, 6]. In this setting, when thrombosis affects adrenal veins, an adrenal hemorrhagic infarction develops, and in bilateral involvement, adrenal insufficiency may be clinically manifested. Nevertheless, in large population-based cohorts and randomized clinical trials reporting cardiovascular and hemostatic events with Oxford-AstraZeneca ChAdOx1 nCoV-19 [7, 8], adrenal bleeding has scarcely been described and adrenal insufficiency has not been reported.

Clinical manifestations of adrenal insufficiency are nonspecific and include fatigue, gastrointestinal complaints (nausea, vomiting, abdominal pain) and postural hypotension, while most common laboratory findings include hyponatremia and hyperkalemia [9]. In cases of intercurrent severe stress an adrenal crisis (entity associated with high lethality) may be precipitated.

In conclusion, due to its nonspecific clinical manifestations and its potentially fatal course, it is very important to have a high index of suspicion for adrenal insufficiency in the setting of hypercoagulable states such as vaccine-induced immune thrombotic thrombocytopenia.

https://doi.org/10.1016/j.ejim.2021.06.025
Received 7 June 2021; Received in revised form 18 June 2021; Accepted 22 June 2021
Available online 10 July 2021