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EDITORIAL

Thrombosis and COVID-19 vaccines

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Vaccines against COVID-19 from Moderna Biotech Spain, SL (COVID-19 Vaccine Moderna – mRNA technology), AstraZeneca (Oxford/Astrazeneca Vaccine - ChAdOx1 - adenovirus vector technology) and Janssen-Cilag International NV (COVID-19 Vaccine) Janssen - Ad.26.COV2.S - adenovirus vector technology) used in Europe, the United States, and Brazil has presented severe thrombotic adverse reactions. The reported thrombosis occurred in unusual sites, such as the sagittal venous sinus[1,2].

The first reports were described in Austria, Italy, and the Nordic countries. An unusual number of cerebral venous sinus thrombosis associated with thrombocytopenia and bleeding has been reported in Germany. This association was found in 7 cases as of March 15, 2021, with a temporal association consistent with the AstraZeneca vaccination. The seven affected individuals were women aged 20–50 years; 6 had cerebral venous sinus thrombosis, occurring 4-16 days after vaccination; 3 died[1].

In early April, an 18-year-old woman died from thrombosis after administering the first dose of the Oxford/AstraZeneca vaccine. Thus, there was a change in the Italian vaccine calendar caused by an intense emotional wave. Nevertheless, recently, the Italian scientific committee limited the use of this vaccine to people over 60 years old[3].

The European Medicine Agency (EMA) compared the clinical picture to similar heparin-induced thrombocytopenia, and two recently published case series have confirmed this similarity. All patients in each series had high levels of antibodies against platelet factor 4 (PF4) antigen complexes, as seen in heparin-induced thrombocytopenia (HIT). The authors coined the term vaccine-induced thrombotic thrombocytopenia (VITT) for this condition. Potential treatment options include high-dose immunoglobulins and certain non-heparin anticoagulants[3,4].

Regulatory agencies in the United Kingdom had received 79 reports of thrombosis associated with thrombocytopenia as of March 31, of which 44 were cavernous sinus thrombosis[5]. Of these 79 cases, 51 (13 fatal) were in women and 28 (six fatal) in men. The risk was most significant in the younger age groups, with 1.1/100,000 people immunized among those aged 20-29 years and 0.2/100,000 among those aged 60—69. For comparison, in women taking hormonal contraceptives, the risk of thrombosis is around 60/100,000

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people/year[6]. Another important point that should be mentioned is that risk factors such as previous venous thrombosis, thrombophilia, the presence of cancer, or prolonged immobilization should not be considered risk factors for developing this type of complication, considering that the pathophysiological mechanism of the process is different[3].

On May 7, 2021, Fiocruz, the Oxford/AstraZeneca/Fiocruz vaccine manufacturer, was notified to ANVISA of the suspected severe adverse event of hemorrhagic stroke with thrombocytopenia in pregnant women with fetal death.ANVISA immediately began evaluating the case. After this event, ANVISA strongly recommended to the Ministry of Health the suspension of vaccination of pregnant women with the Oxford/Astra Zeneca/Fiocruz vaccine as a precautionary measure and based on the insufficiency of data related to the safety of use by pregnant women available so far. In most adult age groups, the benefits of the AstraZeneca vaccine far outweigh the risks[8].

In summary, it can be assumed that VITT is a severe condition, which appears more frequently in young women, starting one to two weeks after the first dose of the vaccine, with fatality rates of up to 60%.

Critical in handling these cases:

1. Individuals with persistent symptoms (> 3 days), including severe headache, dizziness, focal neurological symptoms, visual disturbances, dyspnea, abdominal, chest, or extremity pain arising 5—20 days after vaccination with AstraZeneca COVID-19 vaccine, should be urgently investigated by laboratory tests (complete blood count, D-dimer, and fibrinogen levels, activated partial thromboplastin time, prothrombin time) and image-based screening (i.e., depending on symptoms, cranial MRI, ultrasound or CT scan chest/abdomen).
2. In case of thrombosis or thrombocytopenia (< 150,000/mm^3), a request for a screening enzyme for HIT, based on immunological detection of antibodies against PF4, is mandatory. In case of positivity for the HIT ELISA, it should be performed as a functional confirmatory test for VITT.
3. Until VITT is ruled out, anticoagulation with unfractionated heparin (UFH) or low molecular weight heparin (LMWH) should be avoided. Choose an alternative use of non-heparin anticoagulants (i.e., fondaparinux, danaparoid, argatroban) or direct oral anticoagulants (DOACs), which are safe for treating HIT and do not require initial therapy with heparin[7].
4. Platelet concentrates should not be transfused.
5. In patients with confirmed VITT, administration of high-dose intravenous immunoglobulin (IVIg, 1 g/kg per day for two consecutive days) or dexamethasone (40 mg per day for four days) may be helpful to interrupt the prothrombotic mechanism[1].

It remains clear that the benefits of the AstraZeneca vaccine far outweigh the risks for all adult age groups. When offered, people should accept vaccination but seek medical advice if they develop symptoms related to this rare complication (intense headache, accompanied by nausea, vomiting, syncope, persistent chest or abdominal pain)[5]. If this problem delays the distribution of vaccines or prevents some people from accepting vaccination, many more preventable deaths can occur. The risk of having thrombosis in the presence of COVID is greater than the risk of manifesting unusual thrombosis as a side effect of the vaccine. The best COVID-19 vaccine available is the one you can get today.

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