COVID-19 Evidence Digest 04/16/21

Thrombotic Thrombocytopenia after ChAdOx1 nCov-19 Vaccination (NEJM)

Bottom Line: The AstraZeneca ChAdOx1 nCov-19 vaccine may result in rare cases of thrombotic events or thrombocytopenia one to two week after administration.

Details: There have been several rare cases of thrombotic events (event causing blood clot) and thrombocytopenia (low blood platelet count) that developed after administration of the AstraZeneca (ChAdOx1 nCov-19) vaccine. This study examined the clinical and laboratory features of 11 patients who developed thrombosis (blood clot) or thrombocytopenia after receiving the AstraZeneca vaccine in Germany and Austria. This study tested the presence of platelet factor 4 (PF4)-heparin antibodies (these are antibodies that develop against heparin, which is a blood thinner, and may lead to development of thrombosis) using a standard enzyme-linked immunosorbent assay and platelet-activating antibodies using a PF4-enhanced platelet-activation test. Of the 11 patients, 9 were women with a median age of 36 years (range: 22 to 49). From 5 to 16 days after vaccination, 10 patients presented with thrombotic events while 1 patient presented with intracranial hemorrhage. These thrombotic events included: cerebral venous thrombosis (blood clot in the brain's venous sinuses; n = 9), splanchnic-vein thrombosis (blood clot in the abdominal veins; n = 3), pulmonary embolism (blood clot in the pulmonary arteries in your lungs; n = 3), and other thromboses (n = 4). Of these patients, 6 died. None of the patients had received heparin before onset of the symptoms, and all patients tested positive for antibodies against PF4-heparin. Vaccination with the ChAdOx1 nCov-19 can rarely result in thrombotic events that result from development of platelet activating antibodies against PF4.

Key Takeaways:

- Thrombosis and thrombocytopenia can rarely develop one to two weeks after receiving the AstraZeneca ChAdOx1 nCov-19 vaccine.
- Similar events have recently been reported with the Johnson & Johnson vaccine among six women and are being investigated. New York City has halted the administration of the Johnson & Johnson vaccine as a result beginning April 13th.

SARS-CoV-2–Specific Antibodies in Breast Milk after COVID-19 Vaccination of Breastfeeding Women (JAMA)

Bottom Line: This study found significant secretion of SARS-CoV-2 specific IgA and IgG antibodies in breast milk for six weeks after vaccination, suggesting that it can potentially protect infants against infection.

Details: This prospective cohort study of 84 breastfeeding women recruited in Israel between December 23, 2020 and January 15, 2021 explored if maternal immunization resulted in the secretion of SARS-CoV-2 antibodies into breast milk and noted potential adverse events among these women and their infants. Patients received two doses of the Pfizer-BioNTech vaccine 21 days apart, and breast milk samples were collected prior to vaccination and then once a week for six weeks following two weeks after the first dose. Demographic information was collected from mother and infant, and participants answered weekly questionnaires about their well-being and vaccine related adverse events. On average, participants were 34 (SD: 4) years of age and infants were 10.32 (SD: 7.3) months old. The level of anti–SARS-CoV-2-specific IgA and IgG antibodies in the breast milk increased, with IgA antibodies detectable two weeks after the first

dose (61.8% of samples tested positive for IgA at this time; 2.05 ratio; P < .001) and IgG antibody levels detectable at week four (20.5 U/mL; P = .004), with 91.7% of samples testing positive. At weeks five and six, 97% of breast milk samples had detectable IgG antibodies. No serious adverse events were experienced by mother or infant, 55.9% (n = 47) women reported an adverse event (e.g. local pain, fatigue, fever, etc.) after the first dose, and 61.9% (n = 52) reported them after the second dose. A total of four infants developed a fever during the study period after maternal vaccination, with symptoms of upper respiratory infection. All infections resolved on their own, except one who was admitted and treated with antibiotics. Antibodies found in the breast milk suggest the potential to protect infants against infection, however no functional assays were performed.

Key Takeaways:

- This study found significant secretion of SARS-CoV-2 specific IgA and IgG antibodies in breast milk for 6 weeks after vaccination, suggesting a potential to protect infants against infection; however no functional assays were performed.
    - IgA antibodies were detectable two weeks after the first dose (61.8% of samples tested positive for IgA at this time; 2.05 ratio; P < .001).
    - IgG antibody levels were detectable at week four (20.5 U/mL; P = .004).
- No serious adverse events were experienced by mother or infant.

Treatment of B-cell depleted COVID-19 patients with convalescent plasma and plasma-based products (Clin Immunol)

Bottom Line: Convalescent plasma may have a role in treating COVID-19 among patients with B-cell depletion.

Details: This study included eight adult patients with immunosuppression due to anti-CD20 biologic agents (i.e. Rituximab) who were hospitalized with COVID-19. Patients were given two units of convalescent plasma in addition to standard of care. Anti-spike IgG antibodies were measured in the donor plasma to be at a titer of 1:100 or greater. Patients received the convalescent plasma from 4-60 days from initial symptom onset. Of these patients, five had prolonged fever and PCR positivity and received the plasma late in the disease course (> 30 days). All eight patients had clinical improvement and none died. Of these patients, 50% had serologic testing after receiving plasma and all had notable increases in anti-spike IgG antibody levels (titers).

Key Takeaways: B-cell depletion with anti-CD20 biologic agents portends a poor prognosis and prolonged SARS-CoV-2 viral shedding. Convalescent plasma with high anti-spike IgG titers may have a role in accelerating viral clearance and clinical improvement in these patients.