## Scientists tie platelet factor 4 to AstraZeneca COVID vaccine-related clots

UK researchers have uncovered the novel mechanism behind rare abnormal blood clotting seen in some AstraZeneca/Oxford vaccine recipients, according to a study today in the *New England Journal of Medicine*.

The study involved clinical and lab evaluation of 23 previously healthy patients who experienced blood clots and thrombocytopenia (low platelet counts) 6 to 24 days after receiving the first dose of the AstraZeneca vaccine. Most clots were cerebral venous thrombosis, while some were arterial thrombosis and venous thromboembolisms such as pulmonary embolisms.

Twenty-one patients had antibodies for clot-promoting platelet factor 4 (PF4) on enzyme-linked immunosorbent assay (ELISA) before heparin administration. They appeared to be of the immunoglobulin G (IgG) subtype. Functional heparin-induced thrombocytopenia (HIT) testing confirmed the positive PF4 ELISA result in five of seven patients tested.

“These findings confirmed the presence of platelet activation similar to that seen in patients with HIT, as measured by the addition of donor platelets to patient serum in the absence of heparin,” the researchers wrote. “This effect was not increased with the addition of heparin in physiologic doses but was fully suppressed with the addition of an excess of heparin.”

Seven of 23 patients (30%) died. Autopsy results were available for one patient, who had evidence of clotting in many small blood vessels, particularly in the lungs, intestine, cerebral veins, and venous sinuses, and extensive hemorrhage in the brain.

All patients had normal or low concentrations of fibrinogen, which is involved in blood clotting, and high levels of D-dimer, a sign of blood clots. Median patient age was 46 years, and 61% were women.

The authors said that while COVID-19 vaccination remains critical to pandemic control, “a pathogenic PF4-dependent syndrome, unrelated to the use of heparin therapy, can occur after the administration of the ChAdOx1 nCoV-19 [AstraZeneca] vaccine. Rapid identification of this rare syndrome is important because of the therapeutic implications.”

The researchers recommended against the use of platelet transfusions in these patients because of the risk of worsening the blood clotting and suggested the use of a nonheparin anticoagulant agent and intravenous immunoglobulin for treatment of the first blood clot occurrence.

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