Ischaemic stroke can follow COVID-19 vaccination but is much more common with COVID-19 infection itself

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Thrombotic complications occurring as part of COVID-19 related vaccine-induced immune thrombotic thrombocytopaenia (VITT) can include ischaemic stroke as well as cerebral venous thrombosis

The COVID-19 pandemic has had a major impact on stroke. While there was marked drop in hospitalised stroke cases worldwide particularly during the first wave,[1 2] epidemiological data have shown a real increase in stroke incidence with cases primarily occurring out of hospital and especially in care homes.[3] Therefore, COVID-19 infection itself is a risk factor for stroke, and a recent systematic review reported it occured in 1.4% of COVID-19 infections.[4] A characteristic pattern is found with increased large artery occlusion, and an increased proportion of cryptogenic strokes often affecting multiple arterial territories, while small artery stroke is less common.[4] Both stroke severity and mortality are increased compared with non-COVID-19 related stroke. A major factor underlying this increased risk is the generalised prothrombotic state seen in some patients with COVID-19, with activation of the coagulation pathway and elevated D-dimer and fibrinogen being common features. This 'sepsis-induced coagulopathy' is related to the infection-induced systemic inflammatory response.[4] Antiphospholipid antibodies have also been reported in some patients with COVID-19 and stroke. However, a reduction in platelet count does not appear a common feature.

Recently, reports of coagulopathy have appeared associated with COVID-19 vaccination and particularly the ChAdOx1 nCoV-19 vaccine. These have been characterised by thrombocytopaenia, similar to that seen in heparin-induced thrombocytopaenia but in the absence of heparin and with antibodies to platelet factor 4. In one series of 23 patients, 13 had cerebral venous thrombosis and 5 pulmonary emboli.[5] Median age was 46 with an age range of 21–77, and median time after vaccine was 12 days (range 6–24). Why the cerebral venous sinuses are preferentially affected remains uncertain.

The clinical spectrum is further extended by the paper from Al-Mayhani *et al*[6] describing three cases of ischaemic stroke associated with COVID-19 vaccination. In all cases, the ischaemic stroke was associated with large artery occlusion, both carotid and middle cerebral artery, while two also had venous thrombosis involving the portal and cerebral venous system. This report emphasises that the immune-mediated coagulopathy can also cause arterial thrombosis including ischaemic stroke, although venous thrombosis and especially CVST appear more frequent.

Treating cerebral venous thrombosis and ischaemic stroke associated with vaccine-induced immune thrombotic thrombocytopaenia (VITT) presents a challenge. Current guidelines, such as those from the Expert Haematology Panel on COVID-19 VITT,[7] recommend the use of a non-heparin anticoagulant agent such as direct oral anticoagulants (DOACs, fondaparinux, danaparoid or argatraban depending on the clinical picture, along with intravenous immunoglobulin infusions, and possibly plasma exchange. It has been suggested platelet infusions may exacerbate the condition.[7] Despite optimal therapy, a high mortality has been reported and complications are common, as illustrated in the first case reported by Al-Mayhami *et al*, in which fatal haemorrhagic transformation occurred into a large ischaemic infarct.[5]

During the current period of COVID-19 vaccination, a high index of suspicion is required to identify thrombotic episodes following vaccination. However, it is important to remember that these side effects are rare and much less common than both cerebral venous thrombosis and ischaemic stroke associated with COVID-19 infection itself, as illustrated by a recent large epidemiological study.[8]

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