Fatal cerebral haemorrhage after COVID-19 vaccine

SHORT CASE REPORT

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BACKGROUND

New vaccines against COVID-19 are being rolled out globally. AstraZeneca’s vaccine ChAdOx1 nCoV-19 was not known to cause vaccine-induced thrombotic thrombocytopenia (VITT) at the time of this case.

CASE PRESENTATION

The patient was a previously healthy woman in her thirties with headaches that developed one week after vaccination with ChAdOx1 nCoV deteriorated rapidly, and she presented to the emergency department with slurred speech, uncoordinated movements and reduced consciousness. Computed tomography (CT) of the head showed a large right-sided haemorrhage with severe thrombocytopenia 37 x 10^9/l, (ref 145-390 x 10^9/l). In spite of efforts to reduce intracranial pressure, the patient died the following day.

Severe thrombocytopenia and antibodies to PF4 make a diagnosis of vaccine-induced immune thrombotic thrombocytopenia (VITT) likely.

A young woman had a headache for a few days, before developing a fatal cerebral haemorrhage with the ChAdOx1 nCoV-19 vaccine from AstraZeneca.

The patient was a female healthcare worker in her thirties, with no known heredity for cerebrovascular disease. Eleven months before the uncomplicated childbirth, but with 1500 ml of bleeding. At the end of her pregnancy, she had mild preeclampsia, which was treated with labetalol and improved quickly after childbirth, and labetalol was discontinued. At the one-month check-up, her blood pressure was normal without treatment. At the three-month check-up, the patient had been treated with duroferon 100 mg × 2 for iron deficiency, and she used desloratadine 5 mg for a few days.

As a healthcare worker with patient contact, the woman was offered a vaccine against COVID-19. She was vaccinated with the ChAdOx1 nCoV after vaccination, she developed a headache. The headache had a relatively abrupt onset and steady intensity. The patient attributed this to taking her usual medication.

Three days later, i.e. ten days after vaccination, her condition suddenly worsened. The patient’s partner had been out for a while, and when he returned, he found the patient with slurred speech and uncoordinated walking and movements. They then went to the emergency department, where examination revealed right-sided hemiparesis and her level of consciousness deteriorated. Computed tomography (CT) of the head showed a large right-sided haemorrhage with severe thrombocytopenia 37 x 10^9/l, (ref 145-390 x 10^9/l). In spite of efforts to reduce intracranial pressure, the patient died the following day.

A cerebrovascular event was suspected, and the patient was immediately admitted to the local hospital in the same building as the emergency intermediate care unit.
Upon admission, reduced consciousness was confirmed, with a GCS (Glasgow Coma Scale) score of 10–11. She had expressive aphasia, but was able to follow instructions. There was no neck stiffness. The pupils were of equal size and reactive to light bilaterally. She had central left-sided facial weakness and complete left-sided hemiparesis. She was able to spontaneously move her right extremities, follow instructions and lift her right arm and hand. She was also able to move her right upper extremity and squeeze her right hand.

The plantar reflexes were inverted bilaterally. The NIHSS stroke scale was calculated to be 22. Blood pressure now measured 132/80 mm Hg, and the body temperature 36.5°C. An ECG showed sinus bradycardia with a frequency of 48/min., degree atrioventricular (AV) block. The findings were interpreted as secondary to the cerebral pathology.

Intracerebral haemorrhage was strongly suspected, and the stroke alarm was triggered. A CT of the head was requisitioned and showed a left temporoparietal region in the supply region to the middle cerebral artery, incipient oedema with displacement of midline structures and ventricle. Both subarachnoid blood and some fresh blood were found in the brain parenchyma (Figure 1), but there was no visible blood in the venous structures.

Blood sample analyses upon admission showed several deviating test results (indicated in italics): b-hb 14.5 g/dl (11.7–15.3), b-leukocytes 12.5 × 10^9/L (2.0–7.5), b-lymphocytes 3.5 × 10^9/L (1.5–4.0), b-monocytes 0.7 × 10^9/L (0.2–0.8), b-platelets 37 × 10^9/L (145–390), b-MCV 94 fl (86–102), b-MCH 32 pg (27–34), p-fibrinogen 2.2 g/L (1.7–4.0), p-FDP-D-dimer > 7.0 mg/L (0–0.5), s-CRP 8 mg/L (0–5) and s-haptoglobin 2.4

**Figure 1** CT of patient’s head at a local hospital shows major parenchymal bleeding in the right hemisphere with breakthrough into the subdural space. There is a significant mass effect with midline displacement and incipient transtentorial herniation. Angiography (a) did not reveal any aneurysm or arteriovenous malformation. The findings of a major intracerebral haemorrhage and relatively pronounced thrombocytopenia, 1 g of tranexamic acid (Cyclocapron) was administered during the arterial contrast phase and is not suitable for ruling out cerebral venous thrombosis.

The duty officer at the laboratory called while the patient was undergoing the CT examination and reported very low platelet levels in the admission samples. A CT of the head showed major parenchymal bleeding with breakthrough into the subdural space. Angiography (a) did not reveal any aneurysm or arteriovenous malformation. The findings of a major intracerebral haemorrhage and relatively pronounced thrombocytopenia, 1 g of tranexamic acid (Cyclocapron) was administered during the arterial contrast phase and is not suitable for ruling out cerebral venous thrombosis.

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admission samples showed normal levels.
Transfer to a university hospital was immediately decided. The duty haematologist at the university hospital was consulted by telephone about administering other blood products prior to transport. The patient was informed of the CT findings and the planned transfer to the university hospital. She was awake and seemed to understand the information that was imparted to her.

On the way from the CT room to the intermediate care unit, the patient became noticeably worse, her GCS score dropped to 5-6 and she received midazolam intravenously. While awaiting helicopter transport, she received general anaesthesia with fentanyl and propofol as well as a ventilation intubated and connected to a ventilator. Attempts were made to reduce the intracranial pressure through heavy sedation and hyperventilation. The ventilator settings were adjusted before transport in an effort to reduce \( pCO_2 \) to 4-4.5 kPa. Attempts with high arterial blood pressure (MAP), which was around 90-100 mm Hg before transport. The patient received a noradrenaline infusion was used. Despite attempts to lower the intracranial pressure, both pupils were dilated and tonic on departure from the local hospital.

Weather conditions were poor and the helicopter had to land before reaching the hospital. The patient was transported from there to the university hospital three hours after notification by the local hospital. Upon admission, the patient had bilateral papillary dilatation and intracranial haemorrhage.

Treatment with mannitol was initiated, and a CT of the head taken immediately after arrival showed progression of a major intracranial haemorrhage (Figure 2). Cerebral angiography (TCD) was consistent with cessation of blood circulation in the brain, and further interventions were continued.

![CT scan](image)

**Figure 2**: CT of the patient’s head at the university hospital showed increased haematoma. a) axially, b) sagittally and c) sagittally near the cerebellar tonsils through the foramen magnum. Low density in the cerebral cortex and reduced differentiation of global hypoxia.

Clinical tests showed no signs of cerebral activity, and plans were therefore made for organ donation. Malignancy had to be ruled out prior to the patient being referred for haematological examination due to thrombocytopenia. The patient’s medical record showed that her platelet levels had been normal from approximately one year before the latest one, 325 × 10^9/L (145–390). Blood smears and bone marrow aspirates were performed, with thrombocytopenia being considered most likely to be due to peripheral consumption, either through disseminated intravascular coagulation or thrombocytopenia. It was noted that the blood tests did not indicate a condition with disseminated intravascular coagulation.

The patient remained sedated until termination of the ventilator treatment. The incident was reported to the Norwegian Medicines Agency and the Norwegian Institute of Public Health, confirmed the cause of death as a major intracranial haemorrhage. No where the bleeding started. Neither were there any signs of visible thrombi in other large blood vessels, including the femoral arteries, an unexpected finding.

An autopsy, requested by the Norwegian Institute of Public Health, confirmed the cause of death as a major intracranial haemorrhage. No new investigations were carried out in which fresh small thrombi were found in the pulmonary artery. Antibodies to PF4 were also detected.

The incident described in this case study is still being investigated by the Norwegian Medicines Agency, and no final conclusion is therefore available.

**Discussion**

The case study describes a young woman who had a fatal cerebral event following vaccination with AstraZeneca’s ChAdOx1 nCoV-19 vaccine. Incidents of the same severity had been reported in Norway (2), and it was not a known adverse effect from the vaccine. However, COVID-19 vaccines using mRNA technology (3) were reported, and immunologically mediated thrombocytopenia was reported as a comp...

A few days after this incident, Oslo University Hospital, Rikshospitalet reported multiple cases of severe blood clots and bleeding in patients. These patients also had low platelet counts, and in these cases the link was found to be between the events and the vaccine (1). Since then, the con vessel thrombus formation and antibody investigations were carried out, and our patient was also found to have a tendency towards thrombus formation with small thrombi in the pulmonary artery. Antibodies to PF4 were also detected. Overall, there is therefore a strong indication that this was a case of VITT. Retrospective bleeding seen on the CT images represented a venous haemorrhagic infarction similar to that seen in several patients at Rikshospitalet (1) and have been predominant as a result of VITT. A venous infarction might explain the patient’s headache.
Experience with the condition is still limited, and this case study describes how a probable case of VITT can manifest itself clinically, radiologically, and symptomatically. The condition may be a headache, as in our patient, or visual disturbances, epileptic seizures, abdominal pain, chest pain, dyspnea, and other symptoms. Treatment is available, and the prognosis is significantly improved if the condition is identified before serious and irreversible complications occur.

Several countries are now reporting similar incidents after vaccination. The condition is rare, which is why it is important to shed light on these cases to ensure that vaccination with the AstraZeneca vaccine entails a higher risk of death, particularly for younger people, than the risk of dying of the disease the vaccine is intended to prevent.

The patient’s next of kin has consented to the publication of this article.

The article has been peer reviewed.

LITERATURE


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