



## Effect of COVID-19 Vaccination on TTP Relapses

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### DESCRIPTION

Acquired Thrombotic Thrombocytopenic Purpura (aTTP) is a rare disease with an incidence of 3-10 cases per million adults per year. It is characterized by small-vessel platelet-rich thrombi that cause thrombocytopenia, microangiopathic hemolytic anemia and sometimes organ damage [1]. It constitutes a medical emergency and with appropriate treatment the survival rate is more than 90 percent.

The disease is defined by a severe reduction in the activity of protease ADAMTS 13 (<10%), mainly caused by the presence of inhibitory antibodies. ADAMTS13 is a plasma metalloprotease, an enzyme which acts as a Von Willebrand Factor (VWF) cleaving protease. It cleaves the ultralarge, molecules of VWF that are synthesized by endothelial cells and secreted into the plasma. This cleavage to smaller sized multimers prevents ultralarge multimers from aggregating, especially in areas (vessels) of high shear stress. When protease activity is reduced, ultralarge VWF multimers accumulate on the endothelial surface, where platelets attach and aggregate leading to microthrombi.

The majority of the cases in adults are an acquired form. Several factors can trigger the syndrome, such as medication, autoimmune disorders, cancer, infections, even pregnancy. aTTP has occasionally been described after vaccination, especially against viral agents, such as influenza vaccine [2].

Since the onset of COVID-19 pandemic, an association between COVID-19 vaccines and thrombotic microangiopathies was speculated. Low platelet count after vaccination against SARS-CoV-2 has gained attraction after vaccine-induced immune thrombotic thrombocytopenia. VITT has been described as a rare but severe complication of adenoviral-based vaccines [3].

Thrombotic Thrombocytopenic Purpura (TTP) is an important differential diagnosis, but there are only few reports of TTP following SARS-CoV-2 vaccination. (Approximately 10-15 de novo cases both with mRNA and adenovirus-based vaccines) [4]. Recurrence of TTP has been reported just once after Moderna vaccine [5]. The mechanism linking TTP with these vaccines is poorly understood. Similar to natural infections, vaccines may induce anti-ADAMTS13 antibodies.

### STUDY

In our center 100 patients with TTP were treated the last 15 years. We strongly recommended to them vaccination against Sars-Cov-2, taking in account the high rates of thrombotic events and the risk of microangiopathies caused by the virus itself.

We temporarily excluded one patient, whose aTTP syndrome was possibly related to vaccination. As the coronavirus pandemic was expanding, we decided to include this patient in the vaccination program against Sars-CoV-2, too.

The last month, in an effort to record the patients who were vaccinated against Sars-CoV-2, we reached out to 48 patients. From them, 35 were vaccinated with Pfizer (mRNA), 3 with Moderna (mRNA), 1 with AstraZeneca and 1 with Jonson & Johnson (adenovirus-based).

The remain 8 patients are not yet vaccinated till this report is being written. None of them appeared with relapse of TTP syndrome at least 3 months after the third dose with either vaccine. The last year, since the onset of vaccinations, we had 3 patients with TTP (1 newly diagnosed and 2 relapses), not related to vaccination, as their last dose was at least 4 months before the onset of symptoms.

### CONCLUSION

Therefore, based on the experience of our center, there is no clear connection between COVID-19 vaccines and at least recurrence of the disease.

However, we have more data for mRNA vaccines, due to the fact that the majority of our patients were vaccinated with Pfizer.

We conclude that patients with history of TTP should be encouraged to get vaccinated against Sars-cov-2, as the risk of relapse is very low.

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