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INTEREST OF PLASMA EXCHANGES IN THROMBOTIC MICROANGIOPATHIES REVIEW OF THE LITERATURE IN THE LIGHT OF AN OBSERVATION OF ACQUIRED THROMBOTIC THROMBOCYTOPENIC PURPURA WITH POSSIBLE ASSOCIATION WITH THE ASTRAZENECA/ OXFORD ANTI COVID-19 VACCINE

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ABSTRACT

We report the case of a patient admitted to the emergency department in whom the diagnosis of thrombotic thrombocytopenic purpura was made after a series of laboratory and clinical analyzes.

The clinical signs appeared 3 weeks after his second AstraZeneca / Oxford anti-COVID-19 vaccination and worsened after a month. The patient benefited from plasma exchange sessions, targeted therapy based on 4courses of Rituximab, Sodium Valproate 500 mg, and Prednisone 20 mg. Both biological and clinical evolution is favorable from the first week of treatment.

Successful treatment of TTP regardless of its etiological origin is based on plasmapheresis, corticosteroids and Rituximab, and the only treatment that can be offered urgently is plasma exchange.

The onset of PTT along with other clinical signs immediately after AstraZeneca / Oxford vaccination suggests the potential, but unproven, role of AstraZenica vaccination in PTT pathogenicity.

Keywords: Microangiopathy - Thrombotic thrombocytopenic purpura - AstraZeneca/Oxford anti - COVID-19 vaccine - Plasma exchange - Schizocytosis.

INTRODUCTION

Thrombotic microangiopathy is a disorder characterized by microangiopathic hemolytic anemia, thrombocytopenia, and microthrombosis, leading to ischemic tissue damage, schizophrenia, fluctuating and reversible neurological disorders, and in some cases Fever and renal failure may also occur. Among these pathologies, we distinguish thrombotic thrombocytopenic purpura (TTP), a particularly severe form characterized by spontaneous thrombosis in the blood microcirculation, rich in platelets and Willebrand factor (FW) [1]. It is a

pathology affecting platelet aggregation that results in defective proteolytic cleavage of von Willebrand factor (vWF) due to an inherited or acquired deficiency of the ADAMTS13 enzyme [2].

The aim of our work was to discuss current advances in TTP therapy in light of the observed causal likelihood associated with the AstraZeneca/Oxford vaccine.

PATIENT AND OBSERVATION

We report the observation of a 40-year-old patient, with a history of chronic smoking, the Packet-Year is of the order of 10, having received the two doses of the AstraZeneca/Oxford vaccine 3 weeks before the onset of his symptoms. , admitted to the emergency department for management of headaches evolving for 15 days complicated by a haemorrhagic syndrome with an altered state of consciousness.

Cutaneo-mucous examination shows a 2 cm necrosis lesion on the inner side of the left heel. The blood ionogram and the inflammatory assessment show the absence of phosphocalcic disorder and inflammatory syndrome, respectively. His blood culture and ECBU are sterile, and his immunological assessment is unremarkable. During his stay in intensive care, the patient presented with status epilepticus and then respiratory distress requiring a 5-day intubation.

The cerebral MRI shows a left temporal intra parenchymal hematoma and the thoraco-abdomino-pelvic CT shows the presence of a lesion infra centimetric, hypodense of the hepatic segment II, without suspicious bone lesion.

Laboratory diagnosis of thrombotic thrombocytopenic purpura was made after exclusion of other TTP-like conditions such as disseminated intravascular coagulation (DIC), malignant hypertension, or hemolytic-uremic syndrome (HUS), based on the following criteria: Normochromic normocytic regenerative haemolytic anemia with an Hb level of 5.4 g/dl, thrombocytopenia at 11,000/µL, and presence of schistocytes at 16% on the blood smear.
The patient was investigated for possible causes of secondary TTP such as autoimmune diseases and HIV infection and the results of the investigation were all negative.

The patient received 14 plasma exchange sessions, one session per day, and targeted therapy based on 4 courses of Rituximab (700 mg/week), SODIUM VALPROATE 500 mg every 8hours, to compensate for his status epilepticus, associated with 3 doses per day of Prednisone 20 mg.

The clinical and biological evolution of the patient is favorable with the last assessment: PLT: 248,000/µL, CRP: 1.1mg/L; White blood cells: 16,700/µL ; Polynuclear Neutrophils : 13,000/µL; HB: 9.2g/dl. **(Table 1):**

Table 1 : Blood test of the patient on admission and on discharge from the hospital Department

Date/Investigation	Hemoglobinqg /dL (HB)	Reticulocytes %	Blood platelets $\times 10^9$/L (PLT)
At admission	5,4	16%	11
15 days after the startof treatment	8	6%	200
After the end of hospitalization	9,2	< 1%	248

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DISCUSSION

Thrombotic thrombocytopenic purpura (TTP) is a rare multisystem disorder. The incidence of TTP is approximately six to eight cases/million inhabitants per year [3].

TTP can be of primary origin or associated with other causes. Among the most common causes are bacterial, viral (HIV, Cytomegalovirus) and fungal infections, pregnancy, pancreatitis, certain cancers, organ transplantation, antiphospholipid syndrome, associated systemic diseases such as systemic lupus erythematosus , and drugs including mitomycin C, cyclosporine, quinine, clopidogrel and ticlopidine [4].

The first-line treatment for acute-phase TTP is plasma exchange with fresh frozen plasma (FFP) **[5]**. Plasma exchange is a treatment that combines the withdrawal of a large volume of plasma and the transfusion of a plasma substitute product in sufficient quantity to maintain the patient in a state of normovolaemia, neutralize the autoreactive antibodies and thus reconstitute the level of ADAMTS13 [6].

A study reported by Y. BENHAMOU et Al. in December 2020, revealed that a treatment of TTP which consists of a "triplet" combining plasma exchanges (PE), immunosuppression by corticosteroids and Rituximab, and Caplacizumab prevents the evolutions unfavorable effects of the disease and very significantly reduces the burden of care [7]. These data are in agreement with those found in our observation. The patient underwent 14 plasma exchange sessions, marked by a variation in the rate of schistocytes for 30 days until their rate stabilized
< 1%.

Another study provided among M. Patient et al. in 2017 revealed that corticosteroids, plasma exchanges and if necessary Rituximab or cyclophosphamide allowed a complete remission of 2/3 of patients with TTP, with an overall survival rate of 90% [8].

From an etiological point of view, some authors have reported the causal link between certain vaccines and TTP, such as the anti-influenza vaccine [9, 10], the pneumococcal vaccine [11] and the vaccine antirabies [12].

It was recently reported in a study carried out by M. Al-Ahmad et al. in 2021, the case of a patient in whom there was the appearance of a TTP after having received his 2nd dose of the AstraZeneca/Oxford vaccine, and who was successfully treated with 8 sessions of plasma exchange, corticosteroids and Rituximab[13].

Based on the results obtained, we report a possible causal link between vaccination with AstraZeneca against COVID-19 and PTT since the patient has no history of hematological, thrombocytopenic or immunological disorders. No medication apart from vaccination was administered and screening for secondary causes of TTP was completely negative.

Until March 2021, a dozen countries such as Italy, Lithuania, Denmark, and others suspended the use of the AstraZeneca/Oxford vaccine, as a precautionary measure after reports of blood clots and a death. However, the European Medicines Agency (EMA) and UK regulator said there was no indication that the vaccination was linked to thromboembolic events. The EMA said case reports of thromboembolic events had been received from one batch, which was delivered to 17 EU countries and included one million doses [14].

CONCLUSION

The cause of TTP is unclear. This may be related to vaccines. This study demonstrates a potential but unproven role of AstraZeneca's anti-COVID-19 vaccination in PTT pathogenicity. Regardless of the etiology, successful treatment of TTP is plasmapheresis, corticosteroids, and rituximab. The only treatment available in an emergency is plasma exchange.

POTENTIAL CONFLICT OF INTEREST

None declared.

AUTHORS CONTRIBUTION

All authors have contributed to the conduct of this work. All authors also declare that they have read and approved the final version of the manuscript.

ETHICAL CONSIDERATION

All the data has been collected anonymously following patient confidentiality.

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