# Thrombotic thrombocytopenic purpura: much done, but still a lot to do

Dear Editor,

On the occasion of the third International Day of Thrombotic Thrombocytopenic Purpura (TTP or Moschcowitz syndrome),[1] which was unanimously approved by the Italian Parliament, along with the scientific community involved with TTP and patient associations, we have developed a series of observations that I wish to share with you and the readers of *Bleeding, Thrombosis and Vascular Biology*.

The third International Day of TTP, which I myself promoted a few years ago, along with patient associations, was established at a time when there was a significant parliamentary debate on rare diseases. We were working for many years on the approval of law 175/2021, which for the first time established a framework law on rare diseases with points of extreme interest. However, as often happens in Italy, the law is still awaiting some implementing decrees to make it fully operational.

As it is well known, TTP was first described by the Austro-Hungarian physician Eli Moschcowitz at Beth Israel Hospital in New York in 1924, exactly 100 years ago. It is a rare hematological disease characterized by microangiopathic hemolytic anemia, thrombocytopenia due to consumption, and organ damage, and it falls under the group of thrombotic microangiopathies. It affects women at a ratio of 3:1, with all the consequences that may arise, including problems during a possible pregnancy. It is a disease mostly caused by a defect in a protease, ADAMTS13.

We must not forget that the age of onset of the disease is usually between 30 and 50 years. It often has an acute and fulminant onset, making it a true emergency from a clinical perspective. TTP behaves like a time-dependent disease, and getting a quick confirmation of the disease means intervening immediately with effective therapies and stopping or at least limiting the damage that subsequently occurs in a systemic manner. The prognosis, if the disease is not treated, is poor with a mortality rate above 90%, but if treated appropriately, mortality can be reduced to 15% with a recurrence risk of about 10% to 20%.

These are extremely interesting data, even from the perspective of health policy and therefore the organizational models of our healthcare system, for at least three evident reasons. The therapeutic approach must meet urgency-emergency criteria, requiring a particularly fast and reliable diagnosis. This means having the ADAMTS13 test available to ensure the diagnosis and especially risk management. However, it also means that this test should *not* be at the expense of patients, as it has been so far, but should be included in the Essential Levels of Assistance covered by the National Health Service. The activity of the ADAMTS13 molecule is, in fact, an important prognostic factor.

The emergency intervention that allows mortality to drop from 90% to a possible 15% requires that the patient is immediately and correctly taken care of as soon as he/she arrives at the emergency room and just as promptly submitted to the plasma exchange therapy, which will be repeated as long as necessary. Plasma exchange remains at present the most effective treatment. This means having all the necessary supplies readily available: from plasma to the safest technologies, as provided for by the Ministerial Decree of November 2, 2015: *Provisions on quality and safety requirements for blood and blood components.*

It took almost 70 years to bring together the triad of essential factors: competence of all professionals involved in the diagnosis and treatment process, collaboration among all members of the healthcare team, and organizational coordination that fully involves the managerial-administrative area as well. However, another factor needs to be added, which the scientific community sometimes tends to underestimate: the value of public communication that allows sharing the most updated level of scientific knowledge with all healthcare professionals.

As it often happens with rare diseases, and TTP falls even among very rare diseases, it is essential to talk about it, to raise immediate doubts or suspicion even among professionals not necessarily competent in the field but engaged in *hot* fronts where these patients might arrive, such as emergency rooms. For this reason, it was very useful and instructive that in the second episode of the popular Italian television series *Doc - Nelle tue mani*, the protagonist doctor first suspects and then seeks confirmation in the laboratory of a disease like TTP, which is difficult to diagnose if one is unfamiliar with it. Only after confirming the laboratory data, the doctor successfully treats a young patient with thrombotic purpura.

In light of these reflections, it is not surprising that from the third International Day of TTP, the following commitments emerged to be proposed to both the Government and the Parliament:

1. Free ADAMTS13 test for all patients who need it; one of the new laboratory diagnostic tests takes just over 30 minutes to provide a response on the enzyme activity level and thus confirm the diagnosis.
2. In recent years, there have been interesting scientific advances regarding TTP, but there has not been the same evolution in patient care and the services supporting them.
3. It is necessary to invest in scientific research and the development of new drugs, but also in social aspects that improve the quality of life of patients.
4. Special attention should be paid during pregnancy. In preparation to childbirth, coagulation factors levels increase and ADAMTS13 physiologically decreases slightly. For this reason, women with an ADAMTS13 deficiency may experience a hemolytic crisis in the third trimester of pregnancy.
5. Ensure the same treatment plan in all regions. Today, the diagnosis generally arrives late, but follow-up is also lacking and varies from region to region; these discriminations need to be eliminated.

## References

1. Cataland SR, Coppo P, Scully M, Lämmle B. Thrombotic thrombocytopenic purpura: 100 years of research on Moschcowitz's syndrome. Blood 2024 Jul 3. doi: 10.1182/blood.2023022277. Epub ahead of print.

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**Note of the Editor-in-Chief:*
*Dr. Paola Binetti, former member of Senate of the Italian Republic, has been the founder (in 2012) and President for more than 15 years of the parliament intergroup Rare Diseases.*