Splenectomy: still a life-saving treatment in immune thrombocytopenia

Francesco Rodeghiero

Hematology Project Foundation, Vicenza, Italy, Founding member of ERCI (European Research Consortium on ITP, www.ercigroup.org)

E-mail: rodeghiero@hemato.ven.it

https://doi.org/10.3324/haematol.2025.287512

TITLE	Verschwinden der hämorrhagische Diathese bei einem Falle von “essentieller Thrombopenie” (Frank) nach Milzextirpation. Splenogene thrombolytische Purpura.
AUTHORS	Paul Kaznelson.
JOURNAL	Wiener Klinische Wochenschrift. 1916;29:1451-1454.

In November 1916, just a few months before his graduation in medicine, while he was completing his internship at the I. German Medical Clinic in Prague, Paul Kaznelson (Figure 1) published a scientific communication entitled “Verschwinden der hämorrhagische Diathese bei einem Falle von “essentieller Thrombopenie” (Frank) nach Milzextirpation. Splenogene thrombolytische Purpura” (Disappearance of hemorrhagic diathesis in a case of essential thrombocytopenia – according to Frank - after splenectomy. Spleenish thrombolytic purpura) in the prestigious medical gazette *Wiener Klinische Wochenschrift*.[1] Based on this publication, Kaznelson is universally credited to have described the first case of splenectomy in a patient with immune thrombocytopenia (ITP).

This disease, known as “purpura hémorrhagique protopathique” (according to Hayem, 1900) was more precisely defined by Frank in 1915. Frank changed its name to *essential thrombocytopenia* and provided clearer criteria to distinguish it from the hemophilias and the many other purpuras secondary to infections or scurvy. In addition to a relevant decrease of platelet count, patients with *essential thrombocytopenia* should have a normal coagulation time and no clot retraction, in the absence of evident red and white blood cell abnormalities, apart from some degree of anemia. To honor Frank’s inspiring insights, Kaznelson mentioned his name in the first part of the title of his 1916 paper but, at the same time, renamed the disease as *spleenish thrombolytic purpura*, to give relevance to his own proposal for a new pathogenic mechanism, similar to that causing hemolytic anemia.

The case regarded a 36-year-old woman admitted to his Clinic on June 29, 1916 because of impressive cutaneous purpura and severe epistaxis. A diagnosis of essential thrombocytopenia was made based on Frank’s criteria. Hemorrhagic manifestations had already been present since late childhood, being mainly skin purpura, gingivorrhagia, and epistaxis. After the age of 15 the patient experienced severe, recurrent menorrhagia, requiring repeated vaginal packing. At the age of 30 she bled severely after parturition. On admission, her platelet count was 200/μL (/mm^3 in the original paper) with a normal clotting time and absent clot retraction; the spleen was distinctly enlarged and palpable. The patient was in a miserable condition, requiring repeated unsuccessful nasal packing, and remained bedridden for 6 weeks before the epistaxis stopped. After a few days without relevant new bleeding she developed vomiting and severe headache. Fearing “meningeal hemorrhage” Kaznelson, with consent from the patient, transferred her to the German Surgical Clinic in Prague where splenectomy was performed

Figure 1. Paul Kaznelson at age 58 (1892-1959). Figure reproduced from Yoshida Y. *Ann Hematol. 2008;87:877-879.*

by Professor Schloffer. This surgeon trusted the young undergraduate's hypothesis that the spleen was "the tomb" of platelets in this unfortunate patient and accepted the risk of catastrophic surgery in an overtly bleeding patient. No fresh blood transfusion was given before surgery, despite a platelet count of 300/μL. The risk of surgical hemorrhage should not have discouraged them from proceeding with their plan. Indeed, the favorable experience of Hungarian surgeons who had carried out many appendectomies in similarly thrombocytopenic patients without hemorrhagic sequelae was sufficiently reassuring.

Already on the second day after surgery no new bleeding manifestations were observed and the platelet count was above 500,000/μL with normalization of blood clotting time and of clot retraction. Kaznelson explained this increase in the platelet count well above normal levels as a carried-on effect of the megakaryocyte hyperfunction aimed at compensating platelet destruction by the spleen (we currently know that megakaryocytes in ITP are hyperstimulated and sometimes increased in number but still variably insufficient to correct thrombocytopenia). After 14 days, the woman's skin purpuric manifestations had completely disappeared and 4 weeks later she was discharged. Cautiously, Kaznelson noted that it was not possible to predict the durability of the platelet count restoration since the abnormal platelet destruction by the spleen could be later assumed by other organs, such as the lymph nodes (this intuition is reminiscent of the mechanism of the mononuclear phagocyte system, which we now know is responsible for the elimination of platelets opsonized by autoantibodies).

In a subsequent paper published in 1919,[2] Kaznelson discussed in more detail his personal interpretation of essential thrombocytopenia as due to platelet destruction by the spleen as opposed to insufficient production by megakaryocytes. He provided an update of the first case and described two additional patients with ITP who underwent splenectomy and a third one who was not splenectomized. To support his pathogenic hypothesis of the relevant role of the spleen, he noted that this organ was variably enlarged and palpable in three of the four cases of essential thrombocytopenia he had observed. Again, he emphasized the different laboratory pattern of essential thrombocytopenia compared to hemophilia, particularly with regard to bleeding time which is normal in this latter hereditary disease. With regard to the women described in 1916, he wrote that more than 1 year after splenectomy she was still free from any bleeding manifestations, despite a platelet count fluctuating widely around 100,000/μL but always above the critical threshold of 20-30,000/μL (in agreement with our current belief that this threshold is usually sufficient to avoid significant bleeding). Acutely, Kaznelson noted that splenectomy does not cure the disease but just reduces its severity (again in keeping with our current knowledge). The second patient was a woman aging 25 who had suffered from bleeding from the age of 5 years. Soon after splenectomy her platelet count increased to normal levels but just a few months later dropped down to around 10,000/μL; nevertheless no major hemorrhages recurred. The third splenectomy was done in a girl aged 10 years, who had suffered for the preceding 3 years with cutaneous purpura and recurrent epistaxis. In this case, 3 days after splenectomy the girl's platelet count rose from around 600-700/μL to 267,000/μL, but 4 days later it dropped down to low levels between 5,000-28,000/μL. Nevertheless, during the several months of follow-up, purpuric manifestations and epistaxis were of much less severe. Based on the observation of these three cases, Kaznelson pointed out again, as in his first paper, that the spleen was not the only organ in which thrombocytolysis could occur, extending this phenomenon to the reticulo-endothelial system which had already been described by Aschoff and Landau. This astute hypothesis is in keeping with the inferior efficacy of splenectomy in patients showing prevalent liver uptake in studies of Indium-labeled autologous platelet sequestration. Kaznelson noted that the spleen enlargement was most evident in the first 1916 case, of minor entity in the second and not present in the third, further supporting his belief that the spleen was not the only organ responsible for platelet lysis. Kaznelson concluded that splenectomy is advisable in essential thrombocytopenia, the disease that would later be termed ITP, independently of the presence of splenomegaly. He continued to defend his opinion against the diffidence of some respected colleagues up to 1942 when he wrote a rebuttal that can probably be considered his last publication.

Notwithstanding some naïve interpretations, we should pay tribute to Kaznelson's hazardous courage that made splenectomy a life-saving treatment for several thousands of patients. Indeed, splenectomy was the only effective treatment for severe ITP up to the introduction of corticosteroids in the early 1950s, after Kaznelson's death. Today, with the availability of many effective treatments and innovative drugs under investigation, splenectomy is generally offered as a last chance for refractory patients, and less than 5% of patients accept this option. However, it is confirmed to have the highest potential for an entire life free of or with a much more tolerable thrombocytopenia in over 70% of patients, thus avoiding prolonged or life-long medicalization.[3,4] This is even more true now given appropriate patient selection, prevention of thrombosis and infections and the availability of simple non-invasive surgery.[5] Indeed, 2019 guidelines for ITP were unable to determine which approach among rituximab, thrombopoietin receptor agonists and splenectomy was superior, leaving the choice to patients' preferences. Let's hope that medical treatments able to definitely cure this disease will be found in the near future.

Disclosures

No conflicts of interest to disclose.

References

1. Kaznelson P. Verschwinden der hämorrhagische Diathese bei einem Falle von “essentieller Thrombopenie” (Frank) nach Milzextirpation. Splenogene thrombolytische Purpura. Wien Klin Wochenschr. 1916;29:1451-1454.
2. Kaznelson P. Thrombolytische Purpura. Zeitschrift für Klinische Medizin. 1919;87:133-164.
3. Kojouri K, Vesely SK, Terrell DR, George JN. Splenectomy for adult patients with idiopathic thrombocytopenic purpura: a systematic review to assess long-term platelet count responses, prediction of response, and surgical complications. Blood. 2004;104(9):2623-2634.
4. Vianelli N, Palandri F, Polverelli N, et al. Splenectomy as a curative treatment for immune thrombocytopenia: a retrospective analysis of 233 patients with a minimum follow up of 10 years. Haematologica. 2013;98(6):875-880.
5. Rodeghiero F. A critical appraisal of the evidence for the role of splenectomy in adults and children with ITP. Br J Haematol. 2018;181(2):183-195.