

The Role of the Surgeon in Primary Immune Thrombocytopenia: Case Report

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ABSTRACT

Idiopathic thrombocytopenic purpura (ITP) is important as it is one of the most common thrombocytopenias in adults. Despite their medical treatment, there is a percentage of refractory patients who persist with severe hemorrhages, requiring splenectomy; this is where the surgeon becomes involved in this condition. The objective of this work is to present our experience with this disease and laparoscopic splenectomy in the general surgery service of the General Hospital of Saltillo, Coahuila, Mexico. We present the case of a 40-year-old male with a diagnosis of ITP since he was 28 years old, who for the last 12 years presented recurrent symptoms of severe hemorrhagic events with partial and temporary improvement of the condition despite aggressive pharmacological treatment. We were requested to consult the general surgery service due to therapeutic failure of pharmacological treatment, and a protocol for laparoscopic splenectomy was initiated. The patient progressed adequately and was discharged after the procedure with follow-up by outpatient clinic with a biopsy negative for malignancy.

Keywords: Idiopathic thrombocytopenic purpura, Splenectomy, laparoscopy, Introducción

INTRODUCTION

Immune diseases are multifactorial and poorly understood thanks to their great diversity of both clinical and laboratory manifestations. Primary immune purpura (previously called

immune thrombocytopenic purpura),¹ characterized by being an isolated thrombocytopenia with a platelet count $<100 \times 10^9/\text{l}$ without apparent cause, is no exception to this statement.² The majority of patients may have an asymptomatic course, or present minimal manifestations of the disease, however, approximately 5-6% may trigger severe bleeding.

The initial treatment of ITP is pharmacological. However, when these resources fail, we resort to surgical treatment. Splenectomy corresponds to a second-line medical indication, indicated mainly in older patient's refractory to first-line medical therapy. This is where the role of the surgeon is fundamental, but when to perform it? Under what conditions? How many platelets is it safe to perform the procedure with?

Next, we present the pre-trans and post-surgical management of a 40-year-old male patient with ITP refractory to medical treatment.

CASE PRESENTATION

A 40-year-old male with no significant family history, has difficult-to-control systemic arterial hypertension diagnosed 6 months ago and currently being managed with telmisartan, bisoprolol and nifedipine. Patient presents as a smoker with a smoking index (TI) of 2.2 packs/year.

He has been diagnosed with ITP since he was 28 years old. During the last 12 years, the patient has presented recurrent symptoms of severe hemorrhagic events such as severe epistaxis, hematomas in soft tissues and hyposphagma associated with thrombocytopenia that has required transfusions. Managed with danazol, prednisone, mycophenolate acid, rituximab, platelet apheresis and erythrocyte concentrates, he has remained under follow-up in the hematology service, however, with partial and temporary improvement of the condition despite aggressive pharmacological treatment.

We were requested to consult the general surgery service due to therapeutic failure of pharmacological treatment, and a protocol for splenectomy was initiated.

At the time of evaluation, the patient was asymptomatic, with the last severe epistaxis a month ago.

Patient comes from the hematology clinic with complete vaccination for splenectomized patients. Anti-pneumococcal, anti-meningococcal and haemophilus influenzae type B vaccines are administered.

In addition to multiple studies in search of probable etiology of ITP (Table 1):

Table 1

Study	Result
Hemoglobin	15.4g/dL
Leukocytes	7.9 $10^3/\mu\text{L}$
Platelets	14,000 $10^3/\mu\text{L}$
TP	13.0 sec
TPT	71.9 sec

INR	1.07
Anti-cytoplasmic antibodies (C-ANCA)	0.40 UR/mL
Anti-cystoplasmic antibodies (P-ANCA)	0.68 UR/mL
Hepatitis B	Negative
Hepatitis C	Negative
Anti Helicobacter pylory antibodies IGG	60.3 UR/mL
HIV	Non reactive

Imaging studies are also performed, reporting the following in Doppler ultrasound:

- Hepatic steatosis grade II
- Splenomegaly 12.8cm
- Normal portal venous system, splenic vein and hepatic artery.

Without relevant findings, we proceeded to follow the surgical protocol for laparoscopic splenectomy. He entered the operating room with a total of 30,000 platelets. (Fig. 1 and 2). Patient progresses adequately and is discharged after the procedure with follow-up by outpatient clinic with biopsy negative for malignancy.



Figure 1 and 2. Spleen measuring 13 x 11 x 4.5 cm Weight 300g, Minimally invasive incisions with Pfannenstiel incision

DISCUSSION

ITP is a disease characterized by an isolated decrease in the number of platelets below 100,000/mm³, without finding a triggering cause to explain it.^{1,2}

Classification criteria based on duration were revised, so chronic ITP was defined as disease lasting more than 12 months.³

ITP has an incidence of 2-4 per 100,000 adults each year and a prevalence of 9-20 per 1000,000 adults, being more common in women, reaching gender equality at the age of 60 years.⁴

Regarding its pathophysiology, platelet destruction by antibodies is the canonical mechanism of platelet destruction in ITP. Although approximately 20 to 40% of ITP patients have no

detectable anti-GP autoantibodies, suggesting alternative mechanisms of platelet destruction. Different possible mechanisms by which thrombocytopenia occurs have been described, some of them are the following:¹

- Antiplatelet glycoprotein antibodies (mainly, II b/III a)
- Cytotoxicity by CD8+ T cells.
- Mechanisms that act on megakaryocytes and inhibit platelet synthesis.
- Inadequate levels of thrombopoietin contribute to this decreased synthesis.

Most patients are asymptomatic or have only mild mucocutaneous hemorrhage; however, serious bleeding occurs in 5 to 6% of patients.²

Updated American Society of Hematology (ASH) guidelines recommend initiation of disease-specific treatments if platelet counts are $<30 \times 10^9/L$, through medical treatment.⁶

Regarding the initial treatment of choice, corticosteroids such as dexamethasone and prednisone are used. Approximately 40% of patients will respond to this measure. Other treatments such as intravenous anti-RhD, rituximab show partial improvement. As alternatives for those who do not respond to corticosteroids, other drugs such as Romiplostim and eltrombopag can be used, recently developed drugs that mimic the action of thrombopoietin.^{6,7,8}

Emergency treatment will be assessed according to the hemorrhagic events and the hemodynamic stability of the patient, requiring combined pharmacological treatment and transfusion of erythrocyte and platelet concentrates.

And as a second-line therapy in the absence of response to medical treatment, the surgeon's intervention with a splenectomy is the most effective therapy in patient's refractory to treatment, with multiple bleeding events.⁷

According to the ASH, surgical treatment can be performed laparoscopically or openly. I consider laparoscopy to be the method of choice in spleens <20 cm due to the already known advantages of minimally invasive surgery, such as rapid recovery, less pain, less days of hospital stay. It is recommended to wait 12 months after the diagnosis of ITP due to the high rate of disease regression during the first year, as well as the administration of vaccines against encapsulated organisms (*Streptococcus pneumoniae*, *Neisseria meningitidis* and *Haemophilus influenzae*) at least 2 weeks before splenectomy.⁶ Regarding the platelet count, it is safe to perform the procedure with a platelet count equal to or $> 30,000$, and if a count $< 30,000$ is present, platelet apheresis transfusions may be performed during the procedure, at the time of clamping the splenic vessels. It is important to emphasize that having a count lower than suggested should not be an impediment or contraindication to performing the procedure, since in these patients we will not be able to maintain normal platelets.¹⁵

CONCLUSION

The role of the surgeon in ITP is of utmost importance in patient's refractory to treatment, associated with persistent symptoms.

We should not postpone surgical treatment waiting to find an ideal platelet level, since this can hardly be achieved. The procedure can be performed with a platelet count >30,000 and platelet apheresis can be used for the trans-surgical procedure.

Interest conflict

We declare ourselves without conflict of interest

References

1. Donato H, Bacciedoni V, Rapetti MC, Elena G, et al. Trombocitopenia inmune. Guía de diagnóstico y tratamiento. *Arch Argent Pediatr* 2019; 117 Supl 6: S243-S254.
2. Liu, Xg., Hou, Y. & Hou, M. How we treat primary immune thrombocytopenia in adults. *J Hematol Oncol* 16, 4 (2023).
3. Controversias en el tratamiento de la trombocitopenia inmune pediátrica - *Anales de Pediatría* Vol. 89. Núm. 3. páginas 189.e1-189.e8 (Septiembre 2018) Berruero, Rubén, Dapena, José Luis, Sebastián, Elena
4. Meillón-García LA, García-Chávez J, Gómez-Almaguer D, et al. Trombocitopenia inmune primaria (TIP) del adulto en México: características nacionales y su relación con la literatura internacional. *Gac Med Mex.* 2014 ;150(4) :279-288.
5. Piel-Julian ML, Mahevas M, Germain J, Languille L, Comont T, LapeyreMestre M, et al. Risk factors for bleeding, including platelet count threshold, in newly diagnosed immune thrombocytopenia adults. *J Thromb Haemost.* 2018;16(9):1830-42
6. Neunert C, Terrell DR, Arnold DM, Buchanan G, Cines DB, Cooper N, Cuker A, Despotovic JM, George JN, Grace RF, Kühne T, Kuter DJ, Lim W, McCrae KR, Pruitt B, Shimanek H, Vesely SK. American Society of Hematology 2019 guidelines for immune thrombocytopenia. *Blood Adv.* 2019 Dec 10;3(23):3829-3866. doi: 10.1182/bloodadvances.2019000966. Erratum in: *Blood Adv.* 2020 Jan 28;4(2):252. PMID: 31794604; PMCID: PMC6963252.
7. ESplnec Godeau B. Is splenectomy a good strategy for refractory immune thrombocytopenia in adults? *Br J Haematol.* 2023 Oct;203(1):86-95. doi: 10.1111/bjh.19077. PMID: 37735555.
8. González-Porras JR, Parrondo García FJ, Anguita E. Cost-per-responder analysis for eltrombopag and rituximab in the treatment of primary immune thrombocytopenia in Spain. *Farm Hosp.* 2020 Oct 15;44(6):279-287. English. doi: 10.7399/fh.11525. PMID: 33156746.
9. Callejas Rubio JL, Ríos Fernandez R, García Martín P. Guidelines of the Spanish ITP Group for the diagnosis, treatment and follow-up of patients with immune thrombocytopenia. *Med Clin (Barc).* 2022 Jun 10;158(11): e1. English, Spanish. doi: 10.1016/j.medcli.2021.09.019. Epub 2021 Dec 9. PMID: 34895892.
10. National Hematology Committee, Sociedad Argentina de Pediatría; Donato H, Bacciedoni V, Rapetti MC, Elena G, Lavergne M, Rossi N, Cedola A, Parias Nucci R. Trombocitopenia inmune. Guía de diagnóstico y tratamiento [Guideline for diagnosis and treatment of immune thrombocytopenia]. *Arch Argent Pediatr.* 2019 Dec 1;117(6): S243-S254. Spanish. doi: 10.5546/aap.2019.S243. PMID: 31758894.
11. Fernández-Plaza S, Gonzalez de Pablo J, Gálvez E, Zubicaray J, Sevilla J, Sebastián E. Manejo de la trombocitopenia inmune primaria. Comparación de dos cohortes históricas. *An Pediatr (Barc).* 2021; 95:86--92.
12. Simsek A. Distribution of peripheral blood cells after splenectomy in immune thrombocytopenia patients. *Cir Cir.* 2022;90(2):157-164. English. doi: 10.24875/CIRU.21000246. PMID: 35349562.

13. Monteagudo E, Astigarraga I, Cervera Á, Dasí MA, Sastre A, Berruero R, Dapena JL; en representación del Grupo de Trabajo de la PTI de la Sociedad Española de Hematología y Oncología Pediátricas (SEHOP). Protocolo de estudio y tratamiento de la trombocitopenia inmune primaria: PTI-2018 [Protocol for the study and treatment of primary immune thrombocytopenia: PTI-2018]. *An Pediatr (Engl Ed)*. 2019 Aug;91(2): 127.e1-127.e10. Spanish.
14. Cindy Neunert, Deirdra R. Terrell, Donald M. Arnold, George Buchanan, Douglas B. Cines, Nichola Cooper, Adam Cuker, Jenny M. Despotovic, James N. George, Rachael F. Grace, Thomas Kühne, David J. Kuter, Wendy Lim, Keith R. McCrae, Barbara Pruitt, Hayley Shimanek, Sara K. Vesely; American Society of Hematology 2019 guidelines for immune thrombocytopenia. *Blood Adv* 2019; 3 (23): 3829–3866.
15. Castro G, Guillermo, Montalvo V, Domingo, Moyano N, Cristian, & Osorio P, Rocio. (2017). Esplenectomía laparoscópica en pacientes con púrpura trombocitopénica idiopática: Primera experiencia en el Hospital Regional de Arica. *Revista chilena de cirugía*, 69(3), 230-233.
<https://dx.doi.org/10.1016/j.rchic.2016.10.007>