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– CASE PERPORT –

How I Treat Immune Thrombocytopenia: An Individualized, Patient-Centered Approach

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Abstract

Immune thrombocytopenia (ITP) is an acquired autoimmune disorder characterized by isolated thrombocytopenia resulting from immune-mediated platelet destruction and impaired platelet production. The clinical course of ITP is highly heterogeneous, ranging from asymptomatic disease to severe, relapsing thrombocytopenia with bleeding complications. Management of ITP remains challenging and requires an individualized, patient-centered approach that balances bleeding risk, treatment efficacy, long-term safety, and quality of life. We present a case series of three patients with chronic ITP from real-world clinical practice, illustrating different therapeutic pathways and decision-making strategies.

Methods: *The three patients included in this case series had persistent or chronic ITP with variable disease duration, bleeding risk, and treatment responses. Initial management strategies followed current guideline recommendations, including corticosteroid therapy and intravenous immunoglobulins when indicated. Subsequent lines of therapy were selected based on treatment response, patient comorbidities, lifestyle considerations, and tolerance, and included thrombopoietin receptor agonists (TPO-RAs) and, in selected cases, splenectomy.*

Results: *Across the three cases, corticosteroid therapy resulted in transient platelet responses, with relapse occurring after dose tapering or treatment withdrawal. Second-line therapeutic strategies, particularly TPO-RAs, led to clinically meaningful increases in platelet counts, enabling bleeding control and procedural safety. Treatment responses varied in terms of durability and required individualized dose adjustments and therapeutic switching. Shared decision-making played a central role in treatment selection, taking into account patient preferences, logistical considerations, and adverse effect profiles. Overall, satisfactory platelet responses were achieved, allowing for stabilization of disease and improvement in clinical outcomes.*

Conclusions: *This case series highlights the complexity and heterogeneity of ITP management in routine clinical practice. Our findings underscore the importance of personalized treatment strategies, timely escalation of therapy, and the judicious use of TPO-RAs in patients with inadequate or unsustained responses to first-line treatments. Real-world evidence from such case-based experiences complements clinical trial data and supports a flexible, patient-centered approach to optimizing long-term outcomes in ITP management.*

Keywords: *Immune thrombocytopenic purpura (ITP), bleeding disorder, thrombocytopenia*

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Introduction

Immune thrombocytopenic purpura (also known as idiopathic thrombocytopenic purpura) is an acquired bleeding disorder characterized by isolated thrombocytopenia in the absence of other etiologies. The diagnostic threshold for ITP is a platelet count less than 100x109[1].

At the core of the pathogenesis of ITP stands the development of an abnormal immune response targeted towards the body's own thrombocytes. The body produces autoantibodies, mainly IgG, that are directed against surface antigens, such as GPIIB/IIIa and GPIb/IX. These antibodies are recognized by the FcGamma receptors that exist on the surface of macrophages, which in turn leads to thrombocytes being phagocyted in the spleen and liver. As such, the lifespan of a regular thrombocyte gets shortened from 7-10 days to only a few hours. Both thrombocytes, as well as megakaryocytes can become targets for these antibodies. The binding of the antibodies to the megakaryocytes inhibits their development [2][3].

The main clinical manifestations of ITP are epistaxis, bleeding gums, petechiae, purpura and significant menstrual bleeding. These signs tend to appear more frequently when the number of thrombocytes drops below 20.000-30.000/mm3[4]. Besides the notion of purpura, which is a phenomenon that involves someone's skin, there is also the notion of "wet purpura", which refers to blood-filled blisters that appear over the oral mucosa, the existence which can suggest a more severe hemorrhagic episode [4].

Counterintuitively, ITP can be associated with a prothrombotic status. Sarpatwari et co. [5] have proved through a retrospective analysis an increase in the incidence of venous thromboses amongst the patients diagnosed with ITP in comparison with the normal population. There are several factors intrinsic to the disease that contribute to this status : an increase in the fraction of young and hyperactive thrombocytes, an increase in proinflammatory cytokines, the presence of megakaryocytes in the blood, an increase in PAI-1 in the blood, as well as the development of a resistance to the action of the C protein [5][6].

Fatigue is another symptom frequently reported by patients diagnosed with ITP that determine a significant decrease in their life quality [7]. The root causes are not fully understood, but it is believed that factors such as social support, ability to work, sleep quality and negative beliefs that cause fatigue in chronic illnesses play an important role [8]. Fatigue's impact on the patients quality of life has started being more paid attention to and, although treatment for ITP seems to reduce it, it is recommended that dedicated strategies be implemented regarding this symptom [7].

Treatment Initiation

The decision to treat a patient with ITP depends on several factors, such as active bleeding, age, life quality and the necessity of undergoing surgery associated with a significant bleeding risk [9]. The most used parameter for deciding wether or not to start treatment is the platelet number. A platelet number below 20.000/mm3 (below 30.000/mm3 for patients aged 65 or more or that associate other risk factors for bleeding) is the cut-off for treament initiation [10]. In the case of patients that present with a platelet number above 30.000/mm3 and that don't associate other comorbidities that increase the bleeding risk, ASH guideline panel recommends regular monitoring instead of treatment initiation with glucocorticoids [11].

Glucocorticoid therapy, with or without IVIg, represents first line therapy in ITP [11]. ASH guideline panel suggests either dexamethasone (40 mg per day, 4 days) or prednisone (0,5-2 mg per kg per day) as first line treatment, advising against a long therapy with prednisone (over 6 weeks including treatment and tapering) due to the negative risk/benefit balance [11]. There are multiple options for the second line treament without there being a consensus regarding the best order of them [12]. In the case that a sharp increase in the numer of thrombocytes is needed, IVIg can be associated to the glucocorticoid therapy. If glucocorticoids are contraindicated, the first line treatment for ITP will be IVIg [11].

Clinical Cases

The next 3 cases illustrate the way we choose the adequate type of treatment for patients diagnosed with ITP that are either unresponsive to glucocorticoid therapy or are dependent on it.

Patient 1:

A 61-year-old male was referred to our clinic for evaluation of thrombocytopenia identified on routine blood tests performed prior to a scheduled colonoscopy. The colonoscopy was indicated due to known colonic polyposis and hemorrhoidal disease. The patient experienced self-limited hematochezia for several days following the procedure. At the time of initial consultation, the platelet count was 24,000/mm^3, and the

patient was asymptomatic, with no clinical signs of bleeding.

Following a comprehensive diagnostic workup, the patient was diagnosed with immune thrombocytopenia (ITP), and after shared decision-making, first-line treatment with corticosteroid therapy was initiated. A significant increase in platelet count was observed during treatment; however, following corticosteroid withdrawal, platelet levels declined and returned to pretreatment values.

Patient 2

A 54-year-old female with a history of immune thrombocytopenia (ITP), diagnosed one year earlier at another hematology center, presented to our clinic for a second opinion. She reported a three-year history of spontaneous ecchymoses occurring in the absence of identifiable trauma. At the time of presentation, she had no active bruising or bleeding manifestations.

Patient 3:

The third patient is a 36-year-old woman with a history of immune thrombocytopenia (ITP) diagnosed at the age of 11, which achieved remission following treatment at that time. At 22 years of age, she experienced a severe episode of thrombocytopenia during the third trimester of pregnancy. As she did not respond to corticosteroid therapy, intravenous immunoglobulins (IVIg) were administered with good effect, and delivery was performed by cesarean section. Postpartum, platelet counts remained persistently low, and after discussion of alternative therapeutic options, the patient ultimately underwent splenectomy.

Following splenectomy, the patient reported frequent infections, each associated with marked declines in platelet count. In this context, at the age of 30, treatment with romiplostim was initiated. After six months, due to the absence of a satisfactory response, a switch to eltrombopag (Revolade) was proposed and accepted. The clinical course under eltrombopag was variable, with intermittent platelet increases to approximately 250,000/mm³, but with persistent episodes of severe thrombocytopenia during most of the treatment period.

Treatment options

In 70-90% of the cases, patients don't reach a complete response after first line therapy and another subsequent treatment is needed. Splenectomy was the traditional second line treatment [13]. For patients diagnosed with ITP for more than 12 months, either splenectomy, rituximab or thrombopoietin agonists are currently viable options. Rituximab and splenectomy are suitable options for patients that wish to avoid long term treatment. Rituximab is preferred to splenectomy because of the eventual surgical complications and the higher risk of infection and thrombosis associated with splenectomy [11].

The American Society of Hematology (ASH) recommends postponing splenectomy in patients diagnosed with ITP (immune thrombocytopenic purpura) for up to 12 months, due to the possibility of spontaneous remission within the first year. For this category of patients, the use of either rituximab or thrombopoietin receptor agonists is recommended, with a preference for the latter due to the better durability of response observed in their case [11]

Romiplostim is administered weekly as a subcutaneous injection. The starting dose is 1 µg/kg/week and is increased by 1 µg/kg/week until a platelet count of over 50,000/mm³ is achieved [14]. It has been shown that patients treated with this thrombopoietin agonist experience acute platelet increases in 79% to 88% of cases at the start of treatment, and 38% to 52% of patients on continuous treatment show a sustained response [15]. If a rapid response is needed, treatment can be initiated at a dose of 3 µg/kg/week, and can subsequently be increased to 5, 7, and finally 10 µg/kg/week to obtain a response [14].

Eltrombopag is administered orally in tablet form. It is important to take the pills on an empty stomach, 2 hours before ingesting dairy foods and 4 hours after [14]. Randomized studies have shown a response to eltrombopag in 59%–75% of cases, and 62% of patients on continuous treatment showed a durable response [15]. The starting dose is 50 mg/day. If no response is observed within two weeks, the daily dose may be increased to a maximum of 75 mg/day [14].

Avatrombopag is administered orally in tablet form. The starting dose is 20 mg/day, and is later adjusted to maintain a platelet count between 50,000 and 150,000/mm³ [16]. An initial increase in platelet count was observed within 3–5 days after the first dose, with a maximal response appearing between 13–16 days after initiation. On average, the maximum platelet count observed after 10 days in patients treated with 20 mg/day of avatrombopag was 372,000/mm³ [17]. Due to the potential for the platelet count to exceed 400,000/mm³ in the first weeks after starting treatment, patients should be

monitored for signs and symptoms of thrombosis [16]. Among patients with ITP treated with avatrombopag, 76% showed a response, with 53% showing a sustained response [17].

Therapy	*Dosage*	*Durable Response Rate*	*Route of Administration*	*Adverse effect*
Romiplostim	*1-10µg/kg once weekly*	*38-52%*	*Subcutaneous injection*	*Venous and arterial thrombembolism, bone marrow reticulin deposition, development of neutralizing antibodies,*
Eltrombopag	*25-75 mg once daily*	*62%*	*Oral (restricted)*	*Venous and arterial thrombembolism, bone marrow reticulin deposition, cataract, transaminitis*
Avatrombopag	*20-40 mg once daily*	*53%*	*Oral*	*Headache, arthralgia, venous and arterial thrombembolism,*

Table 1 Clinical Characteristics of Thrombopoietin receptor agonists: Dose, Administration, Response Duration, and Safety Profile

When choosing the type of thrombopoietin receptor agonist, important factors include the availability of the medication, the cost of therapy, and the patient's personal values and preferences, as each agent in this therapeutic class has its own advantages and disadvantages. While eltrombopag and avatrombopag are administered orally, romiplostim must be given as a subcutaneous injection, which often requires a weekly visit to a healthcare facility. Eltrombopag administration imposes dietary restrictions, as the intake of foods rich in calcium and other cations reduces the absorption of the medication. In contrast, avatrombopag does not impose dietary restrictions; in fact, its absorption is improved when taken with food [18]. However, eltrombopag demonstrates a higher durable response rate (62%) compared to avatrombopag (53%).

All these aspects must be considered and explained to the patient when selecting the appropriate thrombopoietin receptor agonist.

How did we approach our patients?

Patient 1

The 61-year-old patient presented with a platelet count of 24,000/mm³ and no clinical signs of bleeding. Although current ASH guidelines recommend deferring treatment initiation in asymptomatic patients with platelet counts above critical thresholds, the consulting gastroenterologist emphasized the need to proceed with colonoscopy due to underlying colonic polyposis and hemorrhoidal disease and requested a higher platelet count prior to the procedure. Several treatment options were discussed with the patient and, given that the colonoscopy was not an immediate medical emergency, corticosteroid therapy with dexamethasone 8 mg daily was initiated, with planned dose adjustments based on treatment response.

After seven days, the platelet count increased to 96,000/mm³, and dexamethasone tapering was initiated by reducing the dose by 2 mg. A transient decline to 63,000/mm³ was observed at day 14; however, after an additional two weeks, the platelet count rose again to 87,000/mm³, prompting further dose reduction to 4 mg daily. Given the fluctuating platelet counts, the gastroenterologist considered the hemostatic profile insufficiently stable for the procedure and elected to postpone the colonoscopy until a more sustained platelet response could be achieved.

After 14 days of dexamethasone at 4 mg daily, the platelet count was 65,000/mm³, and the corticosteroid regimen was deemed ineffective. As the patient had been diagnosed with ITP less than one year earlier, splenectomy was not considered appropriate at that time. Furthermore, the patient developed corticosteroid-related adverse effects, including insomnia, abdominal discomfort, and altered bowel habits. In this context, initiation of therapy with a thrombopoietin receptor agonist (TPO-RA) was considered the most suitable option. To avoid dietary restrictions and to allow closer monitoring through regular laboratory assessments, the patient opted for romiplostim.

At the time of the first romiplostim administration, the platelet count was 65,000/mm³. Following initiation at a dose of 1 µg/kg, platelet levels increased to approximately 100,000/mm³ and have remained stable at this level with continued treatment at the same dose. The patient subsequently underwent colonoscopy without complications.

Patient 2

This case concerns a 54-year-old female patient who presented to our clinic after receiving treatment for one year at another hematology center. At presentation, the platelet count was 19,000/mm³, and the patient had been on continuous corticosteroid therapy throughout the preceding year. As no medical documentation from the previous treating institution was available, a clear treatment history could not be established; therefore, corticosteroid therapy was continued in order to evaluate treatment responsiveness. The patient was prescribed methylprednisolone (Medrol) 8 mg/day and was monitored on a monthly basis.

After two months, the platelet count increased to 42,000/mm³ but subsequently declined to 14,000/mm³ during corticosteroid tapering, leading to the conclusion that the current corticosteroid regimen was ineffective. The patient declined splenectomy due to concerns regarding surgical risks and the lifelong increased susceptibility to infections. Treatment with romiplostim was also considered unsuitable, as the patient resides at a considerable distance from the clinic, making weekly visits for subcutaneous administration and laboratory monitoring impractical. Consequently, treatment with eltrombopag was initiated.

Eltrombopag was started at a dose of 25 mg daily, resulting in an increase in platelet count from 14,000/mm³ to 80,000/mm³ within two weeks. During follow-up, platelet counts demonstrated a fluctuating course, necessitating dose adjustments, including temporary treatment interruption when platelet levels reached 400,000/mm³. The patient reports satisfaction with the treatment and has experienced no major complications or treatment-related adverse events.

Patient 3

The third patient has a complex medical history. Having been diagnosed with ITP at the age of 11 and having been cured at the time, presents at 22 years old in the third trimester of pregnancy with severe thrombocytopenia. At first, corticoid therapy is initiated but the patient is refractory. IVIg was administered with an increase in the platelet count and the patient undergoes C-section. After giving birth, the platelet count drops again, and it is mutually decided with the patient to perform a splenectomy after vaccination with the aim of achieving a long-term response. After the surgery, the patient is given Medrol 64mg/per day with ulterior tapering and followed up once a month.

The patient does not maintain a normal platelet count over a prolonged period and, over the course of eight years, is closely monitored and intermittently treated with oral corticosteroids when platelet levels decline significantly, most often following infectious episodes, which occur frequently. 8 years after splenectomy, in accordance with the patient's preference, the decision is made to initate another treatment due to the relapse. Thrombopoietin receptor agonists (TPO-RAs) are considered and, given the patient's anxiety related to recent abrupt declines in platelet count associated with clinically significant bleeding, initiation of romiplostim is recommended, as it allows for closer monitoring and dose adjustment. There is an immediate increase in the platelets number, but ultimately it stabilizes around 35.000/mm3 with a maximal dose of 10µg/kgc after 8 months since the beginning of the treatment. The response is not sustained, and the patient develops severe thrombocytopenia, necessitating a change in treatment.

Due to an unfavorable response and evidence from the literature supporting the efficacy of switching between thrombopoietin receptor agonists (TPO-RAs), treatment with eltrombopag is initiated. An initial rapid platelet response is observed, with counts rising from 35,000/mm³ to 266,000/mm³ within one week. However, the patient subsequently loses response, with platelet counts declining to below 10,000/mm³, prompting reconsideration of therapy. Despite six years of

continuous treatment, during which platelet levels remain persistently low at approximately 20,000/mm³ for several months, eltrombopag ultimately fails to achieve a sustained favorable response, and the treatment is deemed ineffective, leading to a decision to change therapeutic strategy.

After exhaustion of nearly all available therapeutic options, treatment with avatrombopag is initiated in the hope of achieving a durable response. At treatment initiation, the platelet count is 17,000/mm³. The patient starts avatrombopag (Doptelet) at a dose of 20 mg daily, resulting in a rapid increase in platelet count to 158,000/mm³ after one week, prompting dose reduction to three times weekly. One week later, the platelet count rises to 750,000/mm³, leading to immediate discontinuation of therapy. Following a two-week drug-free interval, the platelet count decreases to 97,000/mm³, and treatment is reinitiated at a reduced dose of 20 mg twice weekly. Since dose adjustment, the patient has maintained stable platelet counts of approximately 100,000/mm³, without further acute declines or treatment-related adverse events.

Conclusion

In conclusion, the management of immune thrombocytopenia (ITP) requires an individualized approach that considers both the clinical characteristics of the disease and the personal context of the patient. Given the heterogeneity in presentation and treatment response, therapeutic decisions should be guided not only by platelet counts and bleeding risk but also by the patient's comorbidities, treatment history, and lifestyle. Incorporating the patient's values and preferences into the decision-making process is essential to ensure adherence, optimize outcomes, and improve quality of life. Personalized care remains the cornerstone of effective ITP management.

Abbreviations

ITP - Immune thrombocytopenia
TPO-RA - thrombopoietin receptor agonist
IgG – immunoglobulin G
PAI-1 – plasminogen activator inhibitor -1
ASH – American Society of Hematology
IVIg – intravenous immunoglobulin

Ethics Statement and Conflict of Interest Disclosures
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AI technologies were used solely to refine English language and spelling.

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