Partial Splenic Angioembolization for Refractory Chronic Immune Thrombocytopenia: A Case Report

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ABSTRACT

Despite observed and theoretical effectiveness and safety in immune thrombocytopenia (ITP), partial splenic angioembolization has not yet been included in clinical practice recommendations. At present, this is the first and only recorded case of partial splenic angioembolization done for chronic ITP in our institution. This case report will add to the growing body of evidence of partial splenic angioembolization as a viable and attractive alternative in treating refractory ITP among patients who refuse or are otherwise unfit for surgery.

We present a 61-year-old female, known chronic ITP unresponsive to steroids, vincristine, rituximab, mycofenolate mofetil, avatrombopag and azathioprine. She refused splenectomy and was offered partial splenic angioembolization. She achieved a durable response at post-procedure days 67, 82, and 130 with platelet count at 50 x 10^9/L, 85 x 10^9/L, and 72 x 10^9/L, respectively, despite continued slow tapering of prednisone and discontinuation of TPO-RA and other immunosuppressive agents.

Immune thrombocytopenia (ITP) results from decreased platelet function and increased platelet destruction. About 10% of ITP becomes refractory to treatment within a year. Even among hematologists, the management of refractory chronic ITP remains to be challenging. Splenic artery angioembolization has traditionally been used as an optimization prior to splenectomy of massively enlarged spleens. Its effectiveness in treating ITP remains uncertain. However, current practice endorses it as a rescue therapy in patients deemed unfit for splenectomy.

Keywords: partial splenic angioembolization, splenic embolization, refractory ITP

INTRODUCTION

Immune thrombocytopenia (ITP) is an acquired thrombocytopenia caused by autoantibodies against platelet antigens. While its pathogenesis is incompletely understood, predominant mechanisms include reduced platelet lifespan from clearance or destruction from a primarily IgG-mediated autoimmunity, most often against platelet glycoproteins. Most cases present with asymptomatic thrombocytopenia. However, bleeding may ultimately occur in up to two-thirds of patients.[1] Initial therapy includes glucocorticoids or IV Ig. Subsequently, rituximab, thrombopoietin receptor agonists (TPO-RA) or splenectomy may be given if with no response to treatment.[2]

The management of refractory chronic ITP has always been a dilemma among hematologists. Therapeutic options limited by available resources in a low-income setting become even more constrained by patient's frailty status and preference of a conservative management approach. Splenectomy is commonly a viable option for refractory ITP and in some cases, splenic angioembolization prior to the procedure

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is done to decrease intraoperative blood loss. However, the use of the latter as an alternative therapeutic modality for chronic ITP, instead of a mere bridge to splenectomy, remains uncertain. Partial splenic angioembolization as an alternative treatment of refractory chronic ITP has never been used in our institution and overall data on its outcomes especially in those who are frail and are otherwise unfit for surgery is lacking.

CASE PRESENTATION

Here we present a 61-year-old female with ECOG functional status score of 3. She is a known case of chronic ITP diagnosed 45 years ago (1979) after presenting with vaginal bleeding. She was initially managed with an unrecalled dose of prednisone, gradually tapered, and subsequently discontinued four years ago (2020) after achieving durable adequate response. She was on treatment-free remission since then but was lost to follow-up due to the pandemic brought about by COVID-19. She was mostly asymptomatic during the interim save for easy bruisability associated with trauma. She reported having two hospital admissions, one of which was bleeding-related (melena), and regular out-patient consultations. During these consults, she had severe, refractory thrombocytopenia and was given prednisone at 1mkD, mycofenolate mofetil (MMF) at 1g/day, rituximab 500mg weekly for 4 doses, and dexamethasone 40mg pulse for 1 dose which did not result in any durable meaningful response. Patient was then admitted at our institution for decreased sensorium from septic encephalopathy and was referred to Hematology service for continuity of care of ITP. During this admission, she had recurrent minor bleeding from sacral decubitus ulcers, persistent hematuria after catheterization, and intermittent hemoptysis. No major bleeding episodes were documented during this admission.

Investigations

During this hospitalization, she had persistent severe thrombocytopenia of <10 x 10^9/L (range: 1-8 x 10^9/L; normal range 150-450 x 10^9/L) and intermittent episodes of anemia from inflammation and blood loss. Consistently, peripheral blood smear showed normocytic, normochromic red cells with 0-2 small, granular platelets per oil immersion field and no platelet clumping. Review of records from previous hospitalizations (February to November 2023) revealed a bone marrow biopsy showing a hypercellular marrow for age (70-80%), erythrogranulopoiesis with maturation with no extraneous cells, and slightly increased megakaryocytes loose cluster consistent with a reactive marrow. Also noted were chronic hepatitis B infection on hepatitis profile, negative HIV screen, negative endoscopic H pylori urease test, and normal-sized spleen with no intraabdominal masses or enlarged lymph nodes on contrast-enhanced CT scan.

Differential Diagnosis

Patient was initially managed as complicated urinary tract infection and thrombocytopenia was attributed to infection. However, thrombocytopenia persisted despite the resolution of the abovementioned acute processes. This is consistent with a refractory chronic ITP. As a diagnosis of exclusion, the diagnosis of ITP can therefore be established through the constellation of the patient's clinical history and ancillary diagnostic investigations that would rule out other causes of thrombocytopenia.

Treatment

For the management of ITP, the patient was given dexamethasone pulses (40mg x 2 doses) with prednisone maintenance (1mkD, eventually slowly tapered), weekly vincristine (2mg IV x 3 doses), another cycle of rituximab (500mg weekly x 4 weeks), increased MMF dose (1.5g/day), Avatrombopag (20mg/day), and low-dose azathioprine (50mg/day) in a sequential, additive fashion. Supportive platelet transfusions were also given since the patient was having intermittent bleeding. Despite this, her platelet count remained below 10 x 10^9/L. Since patient was unresponsive to medical management, she was apprised for splenectomy but ultimately refused any major surgical procedures. Due to the patient's preference and her being a poor surgical candidate because of her overall frail status, partial splenic angioembolization was offered.

IV Ig at 1g/kg x 2 days was given as pre-procedural optimization of severe thrombocytopenia. After the 2nd day of IV Ig infusion, the patient's platelet count rose to 54 x 10^9/L and she underwent partial splenic angioembolization. Right transfemoral, celiac, and splenic angiograms were done using non-ionic contrast media (Ultravist-Iopamidol) and Fr 5 Cobra catheter. There was a good opacification of the splenic arterial system with parenchymal blush which showed a grossly normal-sized spleen (Figure 1A). The splenic vein was noted to be patent with no evidence of intraluminal filling defects.

Using a Cobra catheter and Progreat microcatheter, selective catheterization and embolization of the superselected arterial supply of the mid-portion and inferior polar regions of the spleen (Figures 1B and C) were done using polyvinyl alcohol particles (Contour, 250-355 microns). Post-embolization angiograms showed significant devascularization (around 60%) of the mid-inferior splenic regions with preserved arterial supply at the superior pole of the spleen (Figure 1D). There was no evidence of contrast extravasation and splenic vein remained to be patent. The patient tolerated the procedure well with hemostasis achieved by manual groin compression.

Outcome and Follow-up

At Day 1 post-procedure, her platelet count rose to 208 x 10^9/L. Post-discharge follow-up at day 14 post-procedure revealed recurrence of severe thrombocytopenia at 6 x 10^9/L,

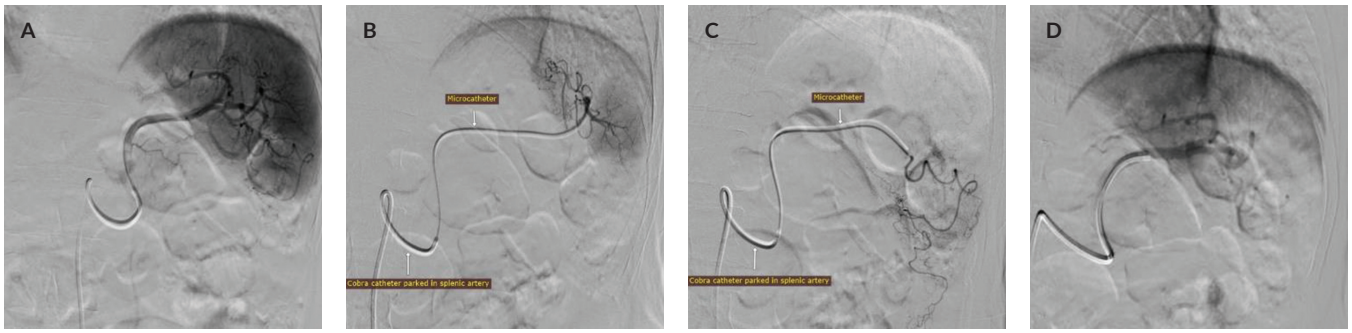

Figure 1. **(A)** Splenic angiogram pre-embolization. **(B)** Superselected middle branch of the splenic artery. **(C)** Superselected inferior polar branch of the splenic artery. **(D)** Splenic angiogram post-embolization showing about 60% devascularization of the middle to inferior regions of the spleen.

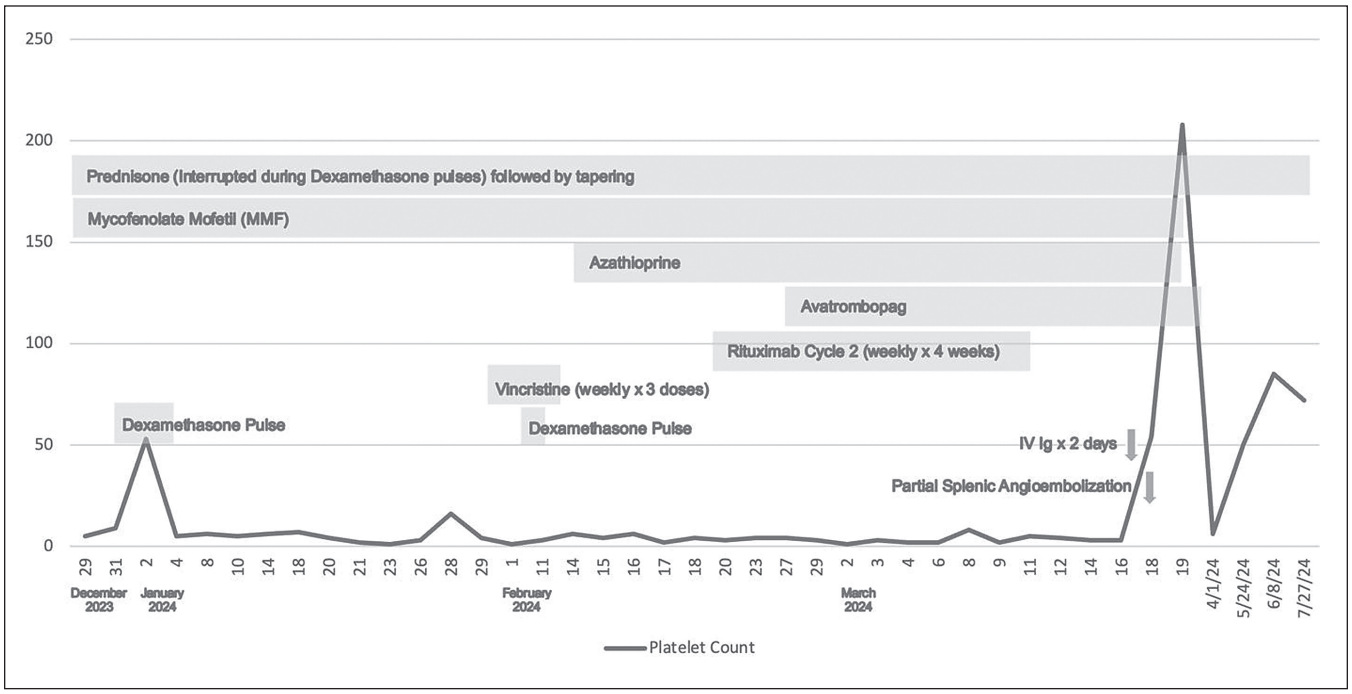

Figure 2. Pictographic summary of platelet count trend during multi-agent therapy and discontinuation after partial splenic angioembolization.

consistent with the waning effects of the previously given IV Ig. Subsequent follow-up at post-procedure days 67, 82, and 130 revealed increased platelet count with durable response at 50 x 10^9/L, 85 x 10^9/L, and 72 x 10^9/L, respectively, despite continued slow tapering of prednisone and discontinuation of TPO-RA and other immunosuppressive agents (Figure 2).

DISCUSSION

Immune thrombocytopenia (ITP) results from decreased platelet function and increased platelet destruction. With an estimated incidence of 2-5 per 100,000 in the general population, it is the most common acquired cause of thrombocytopenia after chemotherapy-induced thrombocytopenia. It is a diagnosis of exclusion and response to treatment remains to be the only confirmation of the diagnosis.[3,4] Among adults less than 40 years old, it has an overall mortality of 2%, which increases to a 5-year mortality rate of 47.8% among patients older than 60 years.[5]

The management of ITP remains to be challenging. Glucocorticoids and IV Ig comprise the first-line choice of therapy. Among individuals whom first-line therapy does not produce a stable, safe platelet count, that is, >20-30 x 10^9/L, multi-agent combinations with second-line agents (rituximab, TPO-RA, MMF) or splenectomy is recommended.[2]

About 10% of ITP becomes refractory to treatment within a year. Many definitions of refractory ITP were

proposed over the years. Before the advent of medical alternatives, lack of response or relapse after splenectomy was generally regarded as refractory.[6] More specifically, the American Society of Hematology (ASH) guidelines defined refractory ITP as refractory based on an inability to achieve platelet count of 30,000/uL and doubling of baseline platelet counts. On the other hand, Miltiadous et al. reserved the term "refractory" for patients with no meaningful response to ≥2 therapies, lack of a single medication to which they respond to, and very low platelet counts accompanied by bleeding.[3]

Surgical management is reserved for those who failed medical management or those with acute life-threatening bleeding. Splenectomy removes the primary site of platelet destruction and an important site of antiplatelet antibody production.[7] When splenectomized, 80% of adults will respond to splenectomy. Elderly patients, however, have higher failure rates.[5] According to the ASH, splenectomy should only be reserved for those who failed medical management to avoid associated lifelong risks such as fatal sepsis and vulnerability to bacterial infections.[8]

Splenic artery angioembolization has traditionally been used as bridge or optimization prior to splenectomy of massively enlarged spleens.[5] Its effectiveness in treating ITP remains uncertain.

Partial splenic angioembolization uses alcohol particles to embolize superselected splenic vessels to effectively devascularize a major splenic region. It aims to decrease splenic sequestration of platelets while preserving enough functional splenic tissue, obviating the need for vaccinations, and decreasing the risk of overwhelming infection associated with asplenia.[8] For this reason, it is used in conditions that are complicated by hypersplenism such as in liver cirrhosis, hereditary spherocytosis, thalassemia, autoimmune hemolytic anemia, and ITP.[9] Data on its use and utility in chronic ITP is lacking. In a Japanese report of 21 patients, seven and eight patients achieved a complete response (platelet count >10 x 10^9/L) and partial response (platelet count >5 x 10^9/L) during follow-up of up to 61 months, respectively. However, no published reports reviewing response of Filipino patients were documented on literature review.[10]

Despite observed and theoretical effectiveness and safety in ITP, partial splenic angioembolization has not yet been included in clinical practice recommendations. Current practice endorses it as a rescue therapy in patients deemed unfit for splenectomy (i.e., those with severe thrombocytopenia with persistent bleeding)[7] but its use remains to be explored.

Owing to patient's overall reluctance regarding splenectomy, partial splenic angioembolization as an alternative intervention was pursued in this case. While the observed outcome seems promising, it is difficult to make assumptions and generalizations due to the rarity and paucity of data on the use of partial splenic angioembolization in refractory chronic ITP. Despite having a documented improvement in the patient's platelet count, follow-up was limited to 130 days post-procedure and durability of response cannot be ascertained. A long-term follow-up on the patient's clinical status and platelet count is needed to fully assess durability of treatment outcomes.

CONCLUSION

Partial splenic angioembolization is an attractive alternative in the treatment of refractory chronic ITP. At present, this is the first and only recorded case of partial splenic angioembolization done for chronic ITP in our institution. This case report will add to the growing body of evidence of partial splenic angioembolization as a viable treatment option for refractory chronic ITP among frail patients who refuse or are otherwise unfit for surgery.

Informed Consent

An informed consent was obtained from the patient and her family for the creation of this manuscript and publication of information in a journal.

Statement of Authorship

Both authors certified fulfillment of ICMJE authorship criteria.

Author Disclosure

Both authors declared no conflicts of interest.

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