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Recurrent Immune Thrombocytopenic Purpura in a Pediatric Patient: A Case of Viral-Triggered Autoimmunity and Therapeutic Challenges

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ABSTRACT

We report a case of refractory idiopathic thrombocytopenic purpura (ITP) in a patient with recurrent relapses despite conventional therapy, including corticosteroid tapering (deflazacort), adjuvant pimotimod (for recurrent infections and allergic rhinitis), and repeated intravenous immunoglobulin (IVIG) infusions. Platelet counts exhibited poor correlation with deflazacort dosing, and disease progression was complicated by allergic sensitization (Alternaria, bee venom), resulting in a torpid clinical course. Following limited response to standard therapies, an integrative approach was initiated using the natural supplement StemRegén (Aphanizomenon flos-aquae, AFA). After two months of oral administration, a progressive and sustained increase in platelet count was observed, with no significant adverse effects. This case suggests a potential immunomodulatory and platelet-stimulating effect of AFA, warranting further investigation into its role as an adjunctive therapy in refractory ITP. These findings highlight the need for exploring unconventional therapeutic strategies in patients with poor response to traditional treatments.

Keywords

Idiopathic Thrombocytopenic Purpura, Autoimmunity, Respiratory Infections.

Introduction

Idiopathic Thrombocytopenic Purpura (ITP): Pathophysiology and Therapeutic Challenges

Primary immune thrombocytopenia (ITP), formerly termed idiopathic thrombocytopenic purpura, is an acquired autoimmune disorder characterized by isolated thrombocytopenia (platelet count <100,000/μL) in the absence of secondary causes [1]. The pathophysiology involves autoantibody-mediated destruction of platelets, primarily targeting glycoprotein complexes (GPIIb/IIIa and GPIb/IX), alongside impaired megakaryopoiesis in the bone marrow [2-4]. These mechanisms lead to accelerated platelet clearance in the reticuloendothelial system and disrupted thrombopoiesis, resulting in clinically heterogeneous presentations ranging from asymptomatic thrombocytopenia to severe mucocutaneous bleeding [3-5].

ITP is classified as acute (typically self-limiting, more common in children) or chronic (persisting >12 months, prevalent in adults), with the latter often exhibiting a relapsing-remitting course [6]. First-line therapies include corticosteroids and intravenous immunoglobulin (IVIG), which modulate immune-mediated platelet destruction. For refractory cases, thrombopoietin receptor agonists (e.g., eltrombopag, romiplostim), B-cell depletion (rituximab), or splenectomy may be employed. However, 10–20% of patients remain treatment-resistant, highlighting the need for novel therapeutic strategies [7].

Emerging evidence suggests that integrative approaches—particularly bioactive compounds with immunomodulatory and regenerative properties—may complement conventional therapies. One such candidate is *Aphanizomenon flos-aquae* (AFA) [8], a cyanobacterial extract reported to stimulate endogenous stem cell mobilization and modulate inflammatory pathways. Preclinical studies indicate AFA's potential to influence cytokine networks (e.g., TGF-β, IL-10) and oxidative stress responses, though its

clinical applicability in ITP remains unexplored [8-11].

Here, we present a case of refractory ITP [12-14] where adjunctive AFA [15-19] administration was associated with sustained platelet recovery, suggesting a possible role in immunomodulation and hematopoietic support. To our knowledge, [20,21] this represents the first documented application of AFA in autoimmune thrombocytopenia, offering a foundation for further mechanistic and clinical investigations.

Case Description

A 3-year-old male with a history of immune thrombocytopenic purpura (ITP) for 17 months of age presented with severe thrombocytopenia (platelets: 12,000/μL) following a viral upper respiratory infection. Initial treatment with IV immunoglobulin (IVIG, 1 g/kg) and deflazacort (1 mg/kg/day) induced transient platelet recovery (72,000–156,000/μL), but fluctuations persisted (15,000–161,000/μL) over 18 months. Laboratory workup revealed positive ANA and IgM for Epstein-Barr virus, suggesting viral-triggered autoimmunity. Despite corticosteroid tapering and adjuvant pimotimod (for recurrent infections/allergic rhinitis), relapses occurred, necessitating repeated IVIG. Platelet counts correlated poorly with deflazacort dosing, and allergic sensitization (Alternaria, bee venom) complicated management. By 2018, sustained remission was achieved with monthly IVIG, though mycophenolate mofetil was considered for refractory cases. This case highlights the multifactorial etiology of pediatric ITP, emphasizing the role of viral triggers, immune dysregulation, and the challenges of balancing immunosuppression with infection/allergy risks.

Case Presentation

Patient Information

A 3-year-old male (DOB: November 13, 2015) with no prior hematologic or autoimmune history presented at 17 months of age (May 2017) with mucocutaneous bleeding (bruising, petechiae) following a viral upper respiratory infection.

Diagnostic Assessment

Initial laboratory evaluation revealed severe thrombocytopenia (platelet count: 12,000/μL). Secondary causes, including malignancy and congenital thrombocytopenia, were excluded. The diagnosis of ITP was established.

Therapeutic Interventions and Clinical Course

First-Line Therapy and Treatment Response

The patient was initially managed with standard first-line therapies for immune thrombocytopenia (ITP). Intravenous immunoglobulin (IVIG) at 1 g/kg (July 2017) elicited a transient platelet response (72,000 → 105,000/μL), consistent with the known but often short-lived efficacy of IVIG in modulating Fc receptor-mediated platelet clearance. Concurrently, oral deflazacort (1 mg/kg/day) was initiated, with subsequent dose adjustments (0.2–1 mg/kg/day) required due to fluctuating platelet counts (15,000–161,000/μL). This variability highlighted the challenges of maintaining remission in pediatric ITP, particularly in cases with concurrent immune dysregulation.

Immunologic and Viral Profiling

Immunologic workup revealed a positive antinuclear antibody (ANA) in July 2017, which spontaneously resolved by July 2018, suggesting transient autoimmunity potentially linked to viral triggers. Serology confirmed acute Epstein-Barr virus (EBV) infection (IgM-positive), aligning with evidence implicating EBV in the pathogenesis of pediatric ITP through molecular mimicry or bystander activation. Additionally, IgE-mediated sensitization to *Alternaria* and bee venom (November 2018) underscored the patient's atopic predisposition, which may have contributed to immune complexity and therapeutic resistance.

Adjuvant Therapies and Clinical Challenges

Given the patient's recurrent upper respiratory infections and allergic rhinitis, the immunomodulatory agent pimotimod was introduced in September 2017 as an adjuvant to mitigate infection-related relapses. Monthly IVIG rescue therapy was maintained during severe thrombocytopenic episodes (e.g., October 2018: platelets 25,000 → 260,000/μL post-infusion). However, the need for repeated interventions emphasized the refractory nature of the case.

Corticosteroid-Associated Morbidity

Long-term deflazacort use was complicated by suspected osteoporosis (later ruled out by endocrinology) and a pathologic tibia/fibula fracture (December 2018) following minor trauma. This complication, attributed to corticosteroid-induced bone fragility, necessitated urgent reevaluation of the therapeutic strategy. The fracture event critically underscored the limitations of prolonged corticosteroid use in pediatric ITP and the imperative for steroid-sparing alternatives.

Platelet Counts Improved Progressively

Date	Platelet Count (/μL)	Intervention	Adverse Events
May 2017	12,000	IVIG 1g/kg ×1 + Deflazacort 1mg/kg	None
Jul 2017	72,000 → 105,000	(Post-IVIG)	Positive ANA
Jul 2017	30.000	Corticoids	Tibia/fibula fracture
Dec 2018	29,000	**AFA initiated**	None
Jan 2019	65,000	AFA continued	None
Feb 2019	98,000	AFA continued	None

Integrative Intervention

Given refractory thrombocytopenia and corticosteroid intolerance, immunomodulatory therapy with Aphanizomenon flos-aquae (StemRegén, 2 capsules/day) was initiated. Platelet counts improved progressively from baseline (pre-treatment): 29,000/μL after 4 weeks of treatment improve to 65,000/μL and at 8 weeks count was 98,000/μL.

Clinical resolution of bleeding was observed, and no adverse effects were reported. Mycophenolate mofetil was considered but

deferred due to the favorable response.

Discussion

Refractory immune thrombocytopenia (ITP) in pediatric patients presents a significant therapeutic challenge, particularly when standard first- and second-line therapies fail to achieve sustained remission or are associated with unacceptable adverse effects. The chronicity of ITP in children, while less common than in adults, is associated with increased morbidity due to both the disease itself and the cumulative toxicity of immunosuppressive treatments. In this case, the patient experienced persistent thrombocytopenia despite multiple courses of intravenous immunoglobulin (IVIG) and corticosteroids, with the latter resulting in a pathologic fracture and increased susceptibility to infections—well-recognized complications of long-term steroid use in the pediatric population.

The management of refractory ITP often necessitates escalation to additional immunosuppressive agents such as mycophenolate mofetil, rituximab, or thrombopoietin receptor agonists (TPO-RAs). However, these agents carry their own risks, including infection, cytopenias, and, in the case of TPO-RAs, potential thrombotic complications. In this context, there is growing interest in adjunctive or alternative therapies that may modulate immune function with a more favorable safety profile.

Aphanizomenon flos-aquae (AFA), a cyanobacterium-derived nutraceutical, has been reported to possess immunomodulatory properties, including the enhancement of natural killer cell activity and modulation of inflammatory cytokine production. In this case, the introduction of AFA (StemRegén) was temporally associated with a progressive and sustained increase in platelet counts and resolution of bleeding symptoms, without observed adverse effects. While causality cannot be definitively established in a single case, the improvement in hematologic parameters following the addition of AFA, after failure of conventional therapies, suggests a potential therapeutic benefit.

The mechanism by which AFA may exert its effects in ITP is not fully elucidated but may involve downregulation of aberrant immune responses implicated in platelet destruction and support of hematopoietic progenitor cell function. Importantly, the use of such nutraceuticals should be approached with caution, as robust clinical trial data are lacking, and the regulatory oversight of these products is less stringent than for conventional pharmaceuticals.

This case underscores the need for individualized, multidisciplinary management strategies in refractory pediatric ITP, balancing efficacy with the minimization of treatment-related toxicity. It also highlights the importance of ongoing research into novel and integrative therapies, including immunomodulatory nutraceuticals, which may offer additional options for patients with limited responses to standard care. Further prospective studies and randomized controlled trials are warranted to better define the role, safety, and efficacy of such agents in the pediatric ITP population. In summary, while standard immunosuppressive and thrombopoietic therapies remain the cornerstone of refractory ITP management, adjunctive use of immunomodulatory nutraceuticals such as AFA may represent a promising avenue for select patients, particularly those with contraindications or intolerance to conventional agents. Clinicians should remain vigilant regarding the evidence base and safety profile of these interventions, and consider their use within the context of comprehensive, patient-centered care.

Conclusion

In this pediatric patient with refractory ITP and corticosteroid intolerance, adjunctive immunomodulatory therapy with Aphanizomenon flos-aquae was associated with sustained hematologic response and clinical remission. This case supports further investigation of integrative approaches in the management of chronic ITP.

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