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Therapeutic Plasma Exchange in Pediatric Severe Immune Thrombocytopenia: A Case Report and Literature Review

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Abstract

Treatment of severe Immune Thrombocytopenic purpura (ITP) accompanied by life-threatening bleeding events is challenging and a combination of treatment measures should be undertaken to rapidly increase the platelet count. Herein, we report a case of severe ITP in a seven-year-old boy who suffered from massive bleeding which was totally unresponsive to conventional therapeutic interventions. Since the patient was still symptomatic with severe thrombocytopenia after splenectomy, the patient underwent plasma exchange (PE) which was successful. To best of our knowledge this is the first case of severe ITP in children managed with plasma exchange due to unresponsiveness to standard treatments and splenectomy.

Keywords: Immune mediated thrombocytopenia, Plasma exchange, Children, refractory

Introduction

Primary immune thrombocytopenic purpura (ITP) is an acquired immune mediated disorder seemingly the most common autoimmune hematologic disorder [1-2]. Primary ITP, is characterized by isolated thrombocytopenia without a known initiating or underlying cause. The disease resolves within 6 months in 75% of children [1-3].

The mechanism of thrombocytopenia in ITP is due to increased platelet destruction by auto-antibodies or immune complexes bound to platelet surface antigens, primarily GPIIb/IIIa and/or GPIb/IX that cause accelerated platelet clearance in the reticuloendothelial system and by a relative impairment in platelet production [1-3]. While ITP is generally a benign disease, patients with severe thrombocytopenia are at high risk for serious bleeding such as intracranial and gastrointestinal bleeding which can rarely be fatal [4-5].

Noteworthy clinical manifestations of ITP include mild mucocutaneous bleeding and bruising while some patients may present with asymptomatic thrombocytopenia [6]. To make a diagnosis of ITP, one must first exclude other more common causes of thrombocytopenia

Including infections, drugs, and malignancy [4-8].

The goal of therapy in ITP is to increase the platelet count to prevent serious hemorrhage. Treatment decisions should be based on the potential for bleeding, patients' history of bleeding, current platelet count, and sign and symptoms [5,7]. First line treatment options to raise platelet counts include IVIG (intravenous immunoglobulin), corticosteroids and anti-D immunoglobulin [1-4]. In life threatening situations platelets should be infused together with IV high dose corticosteroids and IVIG [8]. Emergency splenectomy may be considered in selected nonresponsive patients [1-8].

Reports with recombinant Factor VIIa are limited but this hemostatic agent should be considered in critical situations and even in these cases it would not be expected to achieve a persistent response [9-13]. Plasmaphresis or PE

has been used for treatment of ITP with varying success. The general consensus is that PE as an isolated approach is not justified in the treatment of ITP [14]. The rationale for PE is based on the fact that circulating substances, such as toxins or autoantibodies, can accumulate in the plasma. It is hypothesized that removal of these factors can be therapeutic in certain situations; consequently plasma exchange is an option in salvage therapy of refractory ITP unresponsive to conventional therapies [14].

To best our knowledge the presented case is the first case of pediatric ITP in which PE was used successfully.

Case Presentation

A seven-year-old boy with non-significant medical history presented with hematuria, extensive petechiae, ecchymosis, and massive epistaxis. He was referred to our hospital as a severe refractory case of immune thrombocytopenic purpura who was unresponsive to steroid and IVIG in another hospital. Initial vital signs revealed tachycardia and low blood pressure due to hemorrhage. He was conscious and no organomegaly or lymphadenopathy was detected. Laboratory findings showed severe thrombocytopenia (platelet<10,000/mm^3) and numerous RBCs were seen in urine analysis. Other laboratory tests such as PT, aPTT, BUN, serum creatinine, serum transaminases, ESR and blood chemistry were within normal limits.

The Patient had received IVIG (1gr/Kg) and dexamethasone (6mg/m^2/day) followed by platelet transfusions (total of 5 units). Since the patient was unresponsive to dexamethasone, it was changed to methyl prednisolone (about 30 mg/kg/day for 3 days). Meanwhile, due to bleeding episodes, packed red blood cells were also transfused. After initial stabilization, the patient underwent bone marrow aspiration which revealed increased megakaryocytes without other specific findings. Despite receiving the abovementioned measures, the patient developed gastrointestinal bleeding and renal hematoma. As a result he was scheduled to receive rituximab as a refractory case. However, because of the deterioration of his general condition and intractable gastrointestinal bleeding we decided to perform an urgent splenectomy after administration of relevant vaccination.

Splenectomy was conducted without any improvement in platelet count while gastrointestinal and renal bleeding were ensuing after 48 hours. Ultimately, the patient underwent PE. Rapid and excellent responses were achieved after the first session of PEand the platelet count rose dramatically to 57,000/mm^3.

The patient continued daily PE sessions for 3 more days and then every other day for one more week (a total of 5 sessions), which was completed by weekly administration of rituximab. He was discharged with penicillin prophylaxis and is currently in a good condition with platelets in normal range after 18 months.

Discussion

An immune etiology is the most common cause of thrombocytopenia in children. It can be a primary process as in ITP or secondary to other conditions [1-13]. It is usually characterized by adequate or increased numbers of megakaryocytes in bone marrow and the absence of non-immune etiologies. In ITP pathogenic autoantibodies bind to platelets resulting in platelet clearance [3-12]. The treatment of ITP logically consists of suppressing antibody production, removing the main site of platelet destruction and stimulating platelet production by bone marrow [5-13].

Management of ITP can be challenging if it is refractory to standard treatments and is not alleviated with platelet transfusions. The platelet count can spiral down and hemorrhagic emergencies can arise [15-17]. We reported a case of refractory ITP in which PE was lifesaving. The rapid increment in platelet counts improved dramatically the patient's clinical condition. It has been hypothesized that PE exerts its effects by removing platelet destroying antibodies [18]. We consider PE as part of the treatment strategy consisting of blocking the production of new antibodies responsible for the pathogenesis of the underlying disease [14,18].

We reviewed the published literature on the use of PE for ITP. Finn and colleagues reported two cases of refractory ITP that were unresponsive to standard therapeutic interventions and frequent platelet transfusions. A combination treatment of PE and platelet transfusion successfully raised the platelet count to a level that permitted life-saving surgical interventions. PE in these two cases likely

reduced platelet antibodies significantly, and decreased platelet destruction. The researchers proposed that a trial of combination of PE and platelet transfusion can be attempted in emergent thrombocytopenic situations with an underlying immune mechanism [19].

A report of 10 patients with both acute and chronic immune thrombocytopenia who were treated with high volume PE showed an initial response in 80% of the patients. Response was defined as a platelet count greater than 100,000/mm^3 at the end of the series of PE [20]. The effect of PE was assessed through an analysis of its use for ITP in Canada from 1980 to 1997, in 23 patients with acute ITP. Thirteen of these 23 patients were treated with PE plus prednisone and 10 were treated with prednisone alone. At 6 months follow-up, 11 of 19 patients were considered complete responders and six were considered partial responders. The difference in response rates between patients treated with PE and prednisone was not statistically significant. Antibody concentration was reduced following PE in 10 of the 12 patients, and a response to PE was seen in all 10 cases. In the mentioned study, antibody levels did not change in the patients who received steroid treatment in contrast to those receiving PE [21]. We found that PE increased the length of time before splenectomy but did not alter the need for splenectomy. Short term benefits of PE were accomplished with no increase in morbidity or mortality which confirms that PE is a safe procedure in patients with refractory ITP [21]. In another study, eight patients refractory to IVIG and prednisone were treated with a protocol of combined PE and IVIG. Four of the eight patients responded to the combined therapy with a mean peak platelet count of 132,000/mm^3.

PE combined with IVIG may be a useful treatment for some patients with refractory ITP who have uncontrollable bleeding or require major surgery. The development of resistance to IVIG may be mediated by an increase in the level of antiplatelet antibodies. PE may then allow IVIG infusion to be effective again in elevating the platelet count by lowering antiplatelet antibody levels [22].

Our recommendation is to try PE approach even before splenectomy in young children with acute ITP in emergent life-threatening situations where the platelet count needs to be increased very quickly in a patient refractory to standard treatments and platelet transfusion in order to save time for other interventions.

Conclusion

We suggest that PE approach is worth trying in thrombocytopenic emergencies in which an immune etiology is suspected.

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