

Increase in platelet count following short course therapy with recombinant alpha-2b-interferon in immune thrombocytopenic purpura in childhood

Behrenbeck U, Riedel F, Rieger CHL. Increase in platelet count following short course therapy with recombinant alpha-2b-interferon in immune thrombocytopenic purpura in childhood.

Two boys, aged three and seven years with immune thrombocytopenic purpura continued to show platelet counts below 20,000/mm³ inspite of treatment with high dose gammaglobulin and steroids. Alpha-2b-interferon injections were followed by normalisation of platelet counts in both patients. No side effects were seen. Alpha-interferon may be a safe and effective treatment for childhood-ITP.

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Immune thrombocytopenic purpura (ITP) occurs with an incidence of ten cases per one hundred-thousand children per year and represents one of the most common hematologic disorders in pediatrics. The disease is characterized by an immune-mediated destruction of antibody- and/or complement-coated platelets within the reticuloendothelial system (1). The condition is accompanied by an increased rate of platelet production within the bone marrow and an occasionally dramatic decrease in the life-span of circulating platelets. Between 10% to 30% of childhood ITP become chronic. Platelets counts of less than 150,000/mm³ for more than 14 days seem to strongly predict chronification (2). Most children with acute or chronic ITP have platelet counts between 30,000/mm³ and 120,000/mm³ and do not require more than conservative therapy, i.e. avoidance of sport or other vigorous physical activities, intake of aspirin etc. More active treatment has to be considered if platelet counts fall below 20,000/mm³, since intracranial haemorrhage constitutes a small but serious risk of chronic ITP necessitating long-term medical follow-up and sometimes neurosurgical intervention. Treatment regimes include intravenous gammaglobulin, steroids, ascorbic acid, cytostatic drugs and splenec-

tomy. Steroids, immunosuppressants and splenectomy carry a considerable risk of side effects. In addition, a number of patients will not respond to any of these treatments. Recently, the subcutaneous application of recombinant alpha-2b-interferon was introduced into the therapy of adult immune thrombocytopenic purpura (3). We report the successful use of alpha-2b-interferon in the treatment of two cases of unresponsive childhood ITP.

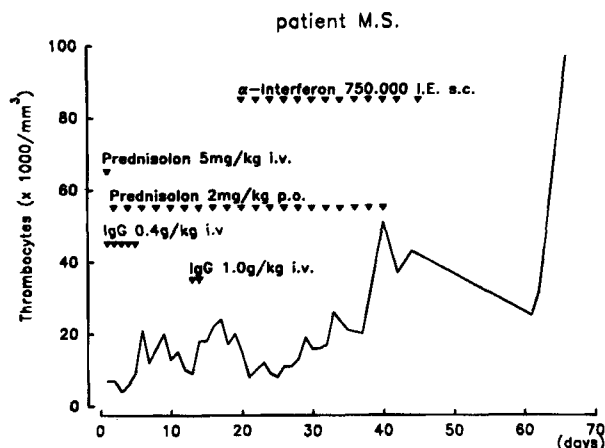


Fig. 1. Platelet concentrations in relation to treatment in patient MS.

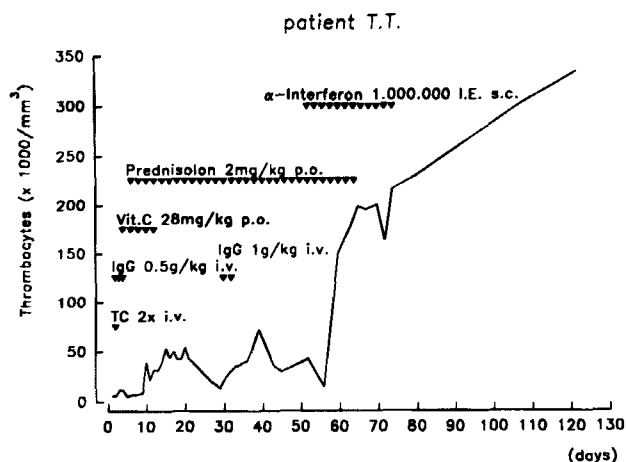


Fig. 2. Platelet concentrations in relation to treatment in patient TT.

Case 1

MS, a 3.3-year-old male patient developed petechial bleedings on his arms, legs, lips and gingiva during the course of a common cold. Laboratory examinations revealed a mild leucocytosis of $18,300/\text{mm}^3$ and a severe thrombocytopenia of $4,000/\text{mm}^3$. A bone marrow aspirate showed normal megakaryocytes. Anti-platelet antibodies could not be demonstrated. Administration of i.v. immunoglobulin followed by steroids failed to raise platelet counts. Alpha-2b-interferon in a dose of 750,000 I.E. s.c. (50,000 I.E./kg) was then administered every other day for a period of 24 days in combination with prednisolon (2 mg/kg body weight/day) (Fig. 1a). No adverse effects were noted. After an initial decrease platelet counts rose significantly (Fig. 1) and reached a concentration of $97,000/\text{mm}^3$ 66 days after initial presentation. In follow-up visits over 3 months platelet counts of more than $150,000/\text{mm}^3$ were found.

Case 2

TT, a 7.6 year-old male patient presented with bleedings on his arms, legs and oral mucosa without any history of trauma or infection. Laboratory examinations revealed a mild leucocytosis of $10,900/\text{mm}^3$ and a severe thrombocytopenia of $6,000/\text{mm}^3$. A bone marrow aspirate showed normal megakaryocytes. Anti-platelet-antibodies were not found. The administration of immunoglobulins followed by corticosteroids both failed to raise platelet counts. Alpha-2b-interferon in a dose of 1,000,000 I.E. s.c./day was then administered for a period of 24 days, during the first 14 days in combination with prednisolon (2 mg/kg body weight/day), (Fig. 2). No side effects were seen.

Immediately after the initial application of alpha-2b-interferon a pronounced rise in platelet count was seen, and platelet counts reached normal values. In a follow-up over 3 months platelet counts were found to be higher than $200,000/\text{mm}^3$.

Discussion

We report – to our knowledge for the first time – the use of alpha-2b-interferon in the treatment of childhood ITP. Recently, the subcutaneous application of recombinant alpha-2b-interferon has been introduced into the therapy of adult immune thrombocytopenic purpura (3). The rationale for this drug was that alpha-2a or alpha-2b-interferon might modify cellular and humoral immunologic interactions in a beneficial way as previously seen in decreased autoantibody production (4). Paradoxically, alpha-2b-interferon was originally used to lower platelet counts in the treatment of thrombocythemia and myeloproliferative disorders (5). However, in HIV-associated thrombocytopenia alpha-2a-interferon improved platelet counts (6, 7). The mode of action of alpha-2a-interferon in ITP has yet to be defined. Besides their antiviral effect interferons have been demonstrated to stimulate antigen-presentation by macrophages, expression of Fc-Receptors leading to improved binding of immune complexes, lymphokine-production and differentiation of cytotoxic T-cells. Any of these qualities could theoretically serve to modulate the immuneresponse to platelets.

Although a spontaneous increase in platelet concentrations cannot be ruled out in our patients the rapid platelet rise after interferon therapy makes this explanation unlikely, at least in case 2. The response to interferon in the second patient was delayed by 14 days. This pattern has also been reported, however, for several patients in a previous study. In both patients treatment was tolerated without any problems. In particular, no febrile reactions, impairment of renal or hepatic function or allergic reactions were noted. From our experience it is not possible to draw conclusions concerning a possible response to interferon in chronic ITP.

Data from a study in adults, however, suggest a positive effect in this type of patient, too (3).

We suggest that interferon is an additional relatively inexpensive immunosuppressive drug for treatment of childhood ITP. Since platelet counts around $10,000/\text{mm}^3$ may be associated with intracranial hemorrhage and since a history of symptoms for more than 14 days at presentation seem to be strongly predictive of chronification (2), interferon may be considered when immunoglobulins and steroids have failed.

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