Hemophilia A, Idiopathic Thrombocytopenia and HTLV-III-Infection Impressive Remission after Splenectomy: A Case Report

H. Mönch a
H. Köstering a
P. Schuff-Werner a
C. Mueller-Eckhardt b
G.A. Nagel a

a Department Hematology/Oncology, Center for Internal Medicine, University of Goettingen
b Institute for Clinical Immunology and Transfusion Medicine, University of Giessen

Requests for reprints to: Dr. med. Helga Mönch, Abt. Hämatologie/Onkologie, Zentrum Innere Medizin, Universität Göttingen, Robert-Koch-Straße 40, D-3400 Göttingen

The simultaneous occurrence of hemophilia A and idiopathic thrombocytopenia with impressive remission after splenectomy is reported sporadically in the literature [1, 2]. In this report we describe a patient, who acquired HTLV-III infection without signs of AIDS after treatment with factor VIII. Hepatitis B infection and other viral infections had been documented, too. In 1984 immune-thrombocytopenia was diagnosed so that HTLV-III and/or other virus infections may have caused thrombocytopenia.

Case Report

A 27-year old patient suffered, from birth, from a factor VIII deficiency, requiring substitution three times weekly. In addition, a brother and a nephew in his family suffered from hemophilia A. The patient is known to have chronic hepatitis B (anti HBc positive, anti HBs positive, and IgM HBc negative) since 1966. Hemorrhagic complications occurred in 1972 with a subdural hematoma, and in 1977 synovectomy in the region of the right ankle joint after a joint bleeding occurred.

In September 1984 petechiae appeared for the first time, concurrent with thrombocytopenia of 18,000/µl. The bone marrow showed an increase in megakaryocytes. The simultaneous proof of an IgG load of the autologous thrombocytes allowed a diagnosis of autoimmune thrombocytopenia. No free serum platelet auto- or allo-antibodies were found in our patient. After immuno-suppressive treatment with Decortin (starting with 100 mg/day) an increase in thrombocytes 178,000/µl was obtained. In March 1985 a renewed thrombocytopenia showed no remission after treatment with high-dose Decortin and additional Imurek. In July 1985 the patient was hospitalized with herpes zoster on the right leg and a painful lymphadenopathy in the right inguinal region. We found a positive proof of herpes zoster (titer 1:512), herpes simplex (titer 1:32), and cytomegalia (titer 1:32). The thrombocytes were reduced to 7,000 µl. Repeated treatment with Decortin and Imurek showed no therapeutic success, and even the application of high-dose gamma globuline (Sandoglobulin 30 g/day for 5 days) revealed no increase in thrombocytes. In September 1985 a splenectomy was performed without complications, with,...
concurrent substitution of factor VIII and thrombocytes. Postoperatively, the thrombocytes increased to 900,000/µl. Upon dismissal in December 1985, the normal thrombocytes values were determined. Presently, the patient is still in remission (fig. 1).

<table>
<thead>
<tr>
<th>400-</th>
<th>300-</th>
<th>200-</th>
<th>100-</th>
</tr>
</thead>
<tbody>
<tr>
<td>Imurek 100 mg</td>
<td>Q Q Q Q</td>
<td></td>
<td></td>
</tr>
<tr>
<td>900000/µl</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8 200-</td>
<td>100-</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


Fig. 1. Platelet counts during the therapy with immuno-suppressiva and after splenectomy in a patient with hemophilia A and idiopathic thrombocytopenia.

Methods
Platelet associated IgG was determined by a radioimmune IgG test [8]; free serum platelet antibodies were detected by the platelet immunofluorescence test [6]. Platelet survival was determined by indium labeling as described by Kiefel [9]. Antibodies to HTLV III were tested by an enzyme-linked immunosorbent assay (ELISA) and confirmed by immuno-blotting [10]. Flow-cytometric evaluation of T-lymphocytes and their subsets were done with a FACS-III-analyzer system using the monoclonal antibodies Leu 2 (T-suppressor/cytotoxic cells), Leu 3 (T-helper/inducer-cells) and Leu 4 (pan-T-cells) from Becton-Dickinson Laboratory Systems (Heidelberg) [11].

Results and Comments
The simultaneous occurrence of hemophilia and chronic autoimmune thrombocytopenia, which, after unsuccessful treatment with prednisone, was brought to remission by splenectomy, is reported sporadically in the literature. Besides our case, Ratnoff et al. [1] reported on 5 patients, 4 of which showed maintained remission under prednisone therapy and one after splenectomy. A further report by Hach et al. [2] describes a patient, aged 29 years, with chronic immuno-thrombocytopenia and cellular immune deficiency, who, after 20 months treatment with prednisone, reached remission after splenectomy.

The pathogenesis of chronic immuno-thrombocytopenia is not yet clear. In our patient, the chronic form of an idiopathic thrombocytopenia could be substantiated by the proof of platelet-bound IgG, lack of significant splenomegaly, and shortening of survival time of thrombocytes. In the treatment of immuno-thrombocytopenia, glucocorticoids and glucocorticoids are first-line therapy. In therapy-refractory cases either the application of immuno-suppressiva or infusions with immuno-globulin are chosen as promising results have recently shown [5,7]. In our patient glucocorticoids and immunosuppressiva only led to a transitory increase in thrombocytes; a treatment with immunoglobulin over 5 days also showed no therapeutic effect. Only when a splenectomy was
performed after 12 months of unsuccessful immunosuppressive treatment, did this result in an impressive increase in thrombocytes. The patient is now still in remission.

An IgG-load of autologous thrombocytes, with concurrent thrombocytopenia, was described for different diseases (e.g. liver affections and viral infection) by Mueller-Eckhardt et al. [3]. Our patient exhibited positive antibody titers against herpes zoster, herpes simplex and cytomegalia. He had also been suffering from a chronic B-hepatitis since 1966. Thus, the possibility exists that the chronic hepatitis B as well as previously endured virus infections may have caused the development of the idiopathic thrombocytopenia. On the other hand, our patient showed a chronic HTLV-III-infection, confirmed by ELISA and immunoblot technique, without signs of immune deficiency (table I), a constellation frequently found in patients with hemophilia [4]. It has been discussed by Strieker et al. [12] that this retrovirus may play a role in the development of autoimmune ITP. It is known from the literature [13] that virus infections may also result in immuno-thrombocytopenia. In our case, therefore, it remains unclear, which kind of virus may have induced the thrombocytopenia.

References


