To the editor:

Role of splenectomy in inherited thrombocytopenias

I read with interest Drachman’s recent review entitled Inherited thrombocytopenia: when low platelet count does not mean ITP. One of the aims of this paper is to assist clinicians in distinguishing between genetic and acquired thrombocytopenia (especially immune thrombocytopenic purpura [ITP]) in order to avoid unnecessary and potentially harmful treatment. It is therefore surprising that at the end of this paper the author suggests that “splenectomy should be reserved for those individuals with severe inherited thrombocytopenia and no option for stem cell transplantation.” There is no doubt that transplantation is the treatment of choice in young children whenever the bleeding tendency is life threatening and an HLA-matched donor is available, since this procedure normalized platelet count in more than 200 patients with Wiskott-Aldrich syndrome (WAS), congenital amegakaryocytic thrombocytopenia, Bernard-Soulier syndrome (BSS), or amegakaryocytic thrombocytopenia with radioulnar synostosis. In contrast, in the field of inherited thrombocytopenias there is a definite indication for splenectomy only for WAS, in that, in a series of 39 patients, surgery normalized platelet count and morphology in almost all cases, and the median survival of splenectomized subjects was 25 years, compared with less than 5 years in un sple nec tom ized ones. To the best of my knowledge, only anecdotal improvements of bleeding tendency have been observed in other inherited thrombocytopenias. Moreover, Naje an and Lecompte reported that surgery did not modify platelet count in 10 of 10 patients who underwent splenectomy because of a wrong diagnosis of ITP, and several other reports indicated that splenectomy did not reduce bleeding diathesis in BSS, gray platelet syndrome (GPS), thrombocytopenia 2 (a new entity due to mutation of the THC2 gene), and MYH9-related disease (MYH9-RD, a new category that includes syndromic and nonsyndromic thrombocytopenias deriving from MYH9 mutations), although it increased platelet count in a small percentage of patients. My colleagues and I have observed subjects with inherited thrombocytopenias who were splenectomized because the genetic origin of their disorder was not recognized: 3 were affected by MYH9-RD, 3 by homozygous BSS (one unpublished [C.L.B., February 11, 2004]), and 1 by heterozygous BSS (C.L.B., unpublished observation, October 14, 2002). Platelet count increased steadily in only one patient with homozygous BSS, but the bleeding tendency did not improve. The different efficacy of splenectomy in WAS and other genetic thrombocytopenias is not surprising, since increased peripheral destruction of platelets is the cause of thrombocytopenia in the former, while a defect of megakaryocytic differentiation, maturation, or platelet production is the main mechanism of thrombocytopenia in most of the latter disorders. Moreover, the functional platelet defect of BSS, MYH9-RD, and GPS persists after splenectomy and hampers clinical improvement also in the rare cases in whom thrombocytopenia is reduced. In conclusion, I suggest that, excluding WAS, splenectomy is not indicated in inherited thrombocytopenias because it does not reduce bleeding tendency in nearly all cases and it predisposes patients to severe infections.

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Response:

Splenectomy unlikely to benefit most patients with inherited thrombocytopenia

I agree with Dr Balduni’s comments regarding the lack of evidence to support splenectomy in congenital thrombocytopenia syndromes except for Wiskott-Aldrich syndrome (WAS). One of the primary goals of the manuscript is to assist clinicians in recognizing inherited syndromes in order to avoid splenectomy, prolonged use of steroids, and other potentially harmful therapies. Congenital thrombocytopenias other than WAS involve failure of megakaryocyte development. In these cases, splenectomy will neither prolong platelet survival nor increase production. Rather, eliminating a reservoir for normal platelets (approximately one third of platelets are sequestered in the spleen of a healthy individual) may result in minor and sometimes short-lived improvements in platelet counts. For the majority of these syndromes, platelet function is adequate for basal hemostasis, and splenectomy is never indicated. In severe...
marrow failure syndromes (eg, congenital amegakaryocytic thrombocytopenia), splenectomy will not result in clinically significant improvement. However, it is possible that for certain individuals a small change in circulating platelet number may improve hemostasis. For example, affected males with GATA1 mutations in one family reported diminished frequency and severity of bleeding episodes in adulthood after splenectomy despite persistent thrombocytopenia. It is not clear whether this change was due to splenectomy. I believe that splenectomy should be reserved for those rare individuals for whom hematopoietic stem cell transplantation is unavailable and the potential impact of a small absolute increase in circulating platelets is clinically significant.

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References


To the editor:

Association of HCV-related mixed cryoglobulinemia with specific mutational pattern of the HCV E2 protein and CD81 expression on peripheral B lymphocytes

Interaction of the hepatitis C virus (HCV) envelope (E) 2 protein with the cellular receptor CD81 leads to B lymphoproliferation in vitro, a major characteristic of mixed cryoglobulinemia (MC). Within E2, 2 CD81 binding sites have been described in vitro comprising the hypervariable region 1 (HVR1) and HVR2. In patients with chronic hepatitis C, CD81 expression on peripheral B lymphocytes is increased. We hypothesize, that specific amino acid (aa) sequences within E2 and CD81 expression on B lymphocytes may act as determinants for the development of MC in vivo.

There were 58 consecutive patients with chronic hepatitis C tested for MC. Cryoprecipitates were detectable in 14 (24.0%) of
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