Hypothesis: Thrombotic thrombocytopenic purpura (TTP) is a rare and serious hematological disease. First-line therapy is plasma exchange, often used in combination with corticosteroids, vincristine, aspirin, and dipyridamole. The role of splenectomy for patients resistant to or dependent on plasma therapy and for the prevention of TTP relapses is not yet determined. Laparoscopic splenectomy (LS) is effective and safe for the treatment of the chronic relapsing form of TTP.

Intervention: We performed LS in 8 patients with refractory or relapsing TTP. The operative as well as the early and late postoperative course and complications were recorded.

Results: The mean duration of LS was 70 minutes (range, 35-180 minutes). There were no serious bleeding complications during or after surgery. Convalescence was rapid, and the mean hospital stay was 2.5 days (range, 1-9 days). Patients were followed up for a mean of 32 months (range, 19-54 months). Seven patients are in remission with no relapse of TTP. One patient with familial TTP had multiple relapses before and after surgery.

Conclusions: Laparoscopic splenectomy for refractory or relapsing TTP is safe and associated with low morbidity and fast recovery. It is effective in the long-term prevention of TTP relapses in most patients, and it should probably be considered early in the course of chronic, relapsing TTP.

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HROMBOTIC thrombocytopenic purpura (TTP) is a rare disorder characterized by thrombocytopenia, hemolytic anemia, and less commonly, neurologic impairment, renal dysfunction, and fever. The disease was uniformly fatal in the past, but the use of plasma exchange therapy has resulted in survival rates of more than 80%. Since survival rates have improved, it has become apparent that 20% to 40% of patients with TTP will either not respond or will have a relapse after initial response. In some patients, a pattern of frequent relapses requiring plasma exchange therapy may develop. Relapses can occur as early as a few weeks after recovery or following a disease-free interval of many years. There is no consensus as to the best form of treatment for these cases. Treatment with splenectomy has been successful in patients with no response to plasmapheresis. However, the usefulness of splenectomy in preventing relapse of TTP is uncertain and debatable. Following the establishment of a standard technique for laparoscopic splenectomy (LS), which is used for all elective splenectomies in our institute, we describe the use of LS in 8 patients who had either no response or had a relapse after initial response.

See Invited Critique at end of article

RESULTS

Of 143 LSs performed between November 1995 and October 1998, 8 patients underwent LS for TTP. Six had relapsing TTP and were in hematological remission when undergoing surgery. Two patients underwent surgery while in an acute episode that had not responded to plasma exchange. The mean age of patients was 33 years (range, 18-55 years). There were 5 female and 3 male patients. The mean time from diagnosis was 68 months (range, 1-192 months). Six patients underwent LS for relapsing TTP, and 2 underwent surgery during the first episode owing to a lack of response to any other therapy. The mean number of relapse episodes after which...
PATIENTS AND METHODS

For the diagnosis of TTP, patients had to have thrombocytopenia (platelet count <150 x 10^3/µL), microangiopathic hemolytic anemia, and no condition other than TTP (such as disseminated intravascular coagulation or sepsis) that could explain these symptoms. During periods of disease activity, patients received plasma exchange therapy on a frequent (usually daily) basis until remission was achieved. Remission was defined as a platelet count exceeding 150 x 10^3/µL for 3 consecutive days. Relapse was defined as a decrease in the platelet count (to <150 x 10^3/µL) and return of schistocytic hemolytic anemia in patients who had had a normal platelet count (>150 x 10^3/µL) for more than 30 days and were receiving no medications other than acetylsalicylic acid. All patients received oral antplatelet therapy (acetylsalicylic acid or dipyridamole) daily from the day of initial presentation, except on days when their platelet counts were less than 50 x 10^3/µL. Patients were given a polyvalent pneumococcal vaccine (Pasteur Merieux, Lyon, France) at least 2 weeks before surgery.

During the study period, all patients with hematological disorders who required a splenectomy underwent LS with no exclusions. The only exclusion criterion was a massively enlarged spleen, extending beyond the left iliac crest.

Following induction of general anesthesia, a nasogastric tube was positioned. The patient was placed in the right lateral position with the table slightly extended to enlarge the space between the costal margin and the iliac crest. The abdomen was insufflated with carbon dioxide, and three 5- to 10-mm laparoscopic ports were introduced to allow a 30° laparoscope and surgical instruments into the abdominal cavity. A thorough search for accessory spleens was performed. Typically, the ligaments surrounding the spleen, the gastrosplenic ligament, and the adjacent omentum were searched. The splenic flexure of the colon was dissected down using an ultrasonic dissection device (Harmonic Scalpel; Ethicon Endosurgery, Cincinnati, Ohio). After the anterior aspect of the hilum was exposed, the short gastric vessels were divided using the same instruments. The left gutter was dissected, and the spleen was separated from the kidney and the diaphragm, except for the posterior attachments of the upper pole. At this point, the spleen's only remaining attachment is the vascular supply, and the gap between the splenic hilum and the tail of the pancreas is enlarged. The spleen was lifted, and an endoscopic stapling device was used to divide the hilum. The last attachments to the diaphragm were incised. The spleen was placed in a plastic bag, the opening of which was delivered out through the most lateral port. The opening of the bag was held, and the spleen crushed using a regular ring clamp with the additional use of a powerful suction device. After the spleen was withdrawn, the operative field was irrigated, and another inspection for bleeding and a missed accessory spleen was performed. At the end of the procedure, the nasogastric tube was removed. Several hours following surgery, patients were allowed to drink and eat as tolerated and were discharged when mobile and pain control was adequate.

Thrombotic thrombocytopenic purpura is a syndrome with diverse causes, not all of which have been elucidated. The histological findings point to a pathological interaction between the vascular endothelium and the platelets. It is not known whether a primary endothelial cell injury with loss of its nonthrombogenic properties leads to enhanced platelet aggregation or whether platelet activation causes endothelial damage.9 Certain proteins that are synthesized and released from injured or stimulated endothelial cells are detected in the plasma of patients with TTP. These proteins suggest that the main factor in the pathogenesis of TTP may be endothelial cell injury. Unusually large forms of von Willebrand factor (vWF) occur in the plasma of patients with chronic relapsing forms of TTP. The unusually large vWF multimers consist of an increased number of mature vWF units, and they are more efficient in binding under high fluid shear forces to the platelet GPIb and GPIIb-IIIa receptors, as well as playing a role in triggering platelet aggregation in TTP.10,11 A recent study demonstrated congenital deficiency of a plasma protease specifically cleaving vWF in siblings with familial TTP.12 Subsequent studies13,14 have shown that, if not all, patients with nonfamilial TTP have an acquired deficiency of vWF-cleaving protease owing to a circulating autoantibody. These results suggest that vWF-induced agglutination of circulating platelets may be caused by constitutional as well as acquired deficiencies of vWF-cleaving protease.

The role of splenectomy in the treatment of TTP has been a subject of controversy since it was first used.15 The contribution of the spleen in the pathogenesis of TTP is unknown. Some authors suggest that marked intrasplenic phagocytosis may play a role in the pathogen-
esis of TTP. Others have shown enhanced endothelial cell apoptosis in splenic tissues of patients with TTP. It is also conceivable that the therapeutic effect of splenectomy is owing to the removal of the B cells responsible for the production of autoantibodies and/or inhibitors of vWF-cleaving protease.

Since plasma exchange became the initial therapy, splenectomy was suggested in patients refractory to plasma exchange or when disease activity recurred after an initial response. We have not seen relapses in our patients with relapsing TTP except in 1 patient with familial TTP. Long-lasting remission after splenectomy in patients with relapsing TTP or chronic TTP have been described by others in small series and case reports.

These suggest that splenectomy at least postpones relapses. Splenectomy has had variable success in treating TTP but with considerable morbidity and mortality, 17% to 39%, especially in patients unresponsive to plasmapheresis who have acute illness. The application of laparoscopic techniques for splenectomy was first reported in 1992. Since then, several retrospective studies have demonstrated that LS is feasible and safe, and LS is associated with lower morbidity rates and faster recovery time compared with conventional open splenectomy.

Laparoscopic splenectomy carries additional advantages, including reduced operative trauma, less postoperative pain, cosmetic advantage, early hospital discharge, and the ability to resume normal activity within a few days. This was accomplished in our series as there were minimal intraoperative or postoperative complications, the mean hospital stay was short, and all patients returned to normal daily activities within few days. We conclude that, although the pathomechanism underlying the beneficial effect of splenectomy are considered obscure, LS is a safe and effective procedure for patients with refractory or relapsing TTP.

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REFERENCES