Lung Transplants in Patients With Prior Bone Marrow Transplants

To the Editor:

We read with interest the case report by Calhoun et al., which appeared in the September 1992 issue of Chest, concerning a successful single lung transplantation (SLT) in a patient with respiratory failure following allogenic bone marrow transplant (BMT).

We too have performed a lung transplant for a patient who had acute lymphoblastic leukemia and developed respiratory failure following BMT from an histocompatibility leukocyte antigen-matched sibling. The patient, a 27-year-old man, developed graft-vs-host disease (GVHD) associated with increasing dyspnea and progressive obstructive defect on spirometry. He subsequently underwent successful left SLT, histologic examination of the explanted lung showing extensive obliterative bronchiolitis (OB). His early postoperative course was complicated by recurrent episodes of both perivascular and bronchial rejection diagnosed on transbronchial lung biopsy. There was initially a favorable response to augmented immunosuppression with pulsed intravenous methylprednisolone and oral prednisolone. Despite further augmentation with both OKT3, however, the antihuman T cell monoclonal antibody and thalidomide (1 g/d) there was a progressive fall in pulmonary function leading to his death 271 days posttransplant. Transbronchial biopsies from the transplanted lung revealed OB as early as 47 days post lung transplant and confirmed on open lung biopsy on day 191.

The development of OB post lung transplantation is thought in part to be a manifestation of chronic rejection and interestingly is also a sequel of GVHD complicating BMT. In both, OB is assumed to have an immunologic basis. While the underlying cause of the pulmonary fibrosis in the case of Calhoun et al. was unknown, the authors made no comment as to whether OB was evident. It is tempting to speculate that the pre-existing OB post BMT may have played a role in the early development of OB post SLT via an immunologic mechanism.

Despite this initial experience, we feel that a single lung transplant should still be considered in patients who develop respiratory failure following BMT but that this case must act as a cautionary tale of "lightning strikes twice."

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REFERENCES

Oral Anticoagulant Therapy Recommendations

To the Editor:

It is regrettable that my warning against intense warfarin regimens, such as are recommended in Britain and in North America, was not taken into consideration in the update by Hirsh et al., which appeared in the October 1992 supplement of Chest. My warning concerns the recommendations made by the Federation of Dutch Thrombositis Centers, which together provide oral anticoagulation laboratory control for about 250,000 patients receiving active treatment. It is on good grounds that the Federation recommends 3.0 international normalized ratio (INR) as the target for primary and secondary prevention of venous thrombosis and thromboembolism, 3.5 INR in case of recurrence under the former regimen and for patients at risk for a cardiogenic embolism from any source (including tissue heart valve replacement) and those with atherothrombotic disease, and 4.0 INR for patients with mechanical heart valve prosthesis; the risk of hemorrhage at such levels remains acceptable.

In sharp contrast to these recommendations, Hirsh et al propose to aim at levels between 2.5 and 3.5 INR in patients with artificial heart valves. In their argumentation, ironically, they refer to a recently completed randomized trial performed by the McMaster group, which shows that the degree of protection by oral anticoagulants when aiming at 3.0 to 4.5 INR was increased by the addition of aspirin in a dose of 100 mg/d without a significant increase in major bleeding or cerebral hemorrhage. In my view, Hirsh et al herewith support Dutch policy to aim at 3.5 to 4.8 INR without the addition of aspirin.

Similar considerations hold for their argument for an optimal therapeutic range of 2.0 to 3.0 INR in patients with tissue heart valves; from the data presented by the McMaster group, one is justified in concluding that 2.0 to 2.25 INR and 2.5 to 4.0 INR are equally ineffective in the protection of patients against systemic embolization.

Another major mistake made by Hirsh et al is the statement that in the two large-scale studies of the secondary prevention of myocardial infarction performed in The Netherlands and in Norway, both with intensive anticoagulation, there was no increase in bleeding complications. The bleeding complications observed in the Dutch study were even considered worthy of separate publication.

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