Coagulation Abnormalities in Cancer Patients
clinical relevance

The management of cancer patients requires an awareness of the increased risk of thromboembolic events, including the classical migratory thrombophlebitis syndrome first described 130 years ago by Armand Trousseau.1 This clinical observation is strengthened by reports of various coagulation abnormalities present in cancer patients, including increased levels of plasma markers for coagulation activation such as fibrinopeptide A (FPA), and increased levels of tissue factor activity in tumor cells and in peripheral blood monocytes of cancer patients.

The study by Ogino et al in the current issue of Chest (page 1683) and related work by this group2 provide a striking demonstration of yet another marker of hypercoagulability in cancer patients—so-called “thrombosis-inducing activity (TIA).” Using an animal model, these investigators have shown that injection of plasma from some cancer patients into mice results in rapid death from pulmonary embolism. The death of these mice is prevented by heparin. The current study of a series of patients with advanced non-small-cell lung cancer shows a decrease in survival in patients with TIA, and almost half of the patients with TIA also had laboratory markers for disseminated intravascular coagulation (DIC) immediately preceding their death. It is of interest that the patients with TIA also had a higher risk of developing the adult respiratory distress syndrome.

The authors provide only limited information on their attempts to determine what component of plasma is responsible for TIA. Since only 53 percent of the cancer patients had TIA activity, further characterization will be necessary to try to define whether TIA activity results from some particular feature of malignant cells or whether it is an epiphenomenon seen in these terminally ill patients. Although TIA activity was associated with a worse prognosis, only one patient in their series died as a result of a thrombotic event (portal vein thrombosis). Unless a stronger connection can be made between the biology of TIA and clinical events, the ability to predict the occurrence of DIC in a patient who is dying of other causes has limited clinical utility.

For the clinician, the answers to several key questions are still unknown. First, what is the true frequency of thrombotic events in cancer patients at various stages of their illness and treatment? Although the risk of thrombosis has been estimated in older series to be between 1 and 11 percent of cancer patients,1,3 the risk varies with different cancers, concurrent medical conditions, and therapy. Second, are there laboratory markers that we should be using to identify patients at particular risk? Further studies which characterize the biologic features of malignancy that contribute to thrombosis are needed before any larger trial of clinical correlation can be attempted. The present paper by Hayashi et al may provide a new approach to this problem. Third, is the presence of a prothrombotic state in the patient important enough to tumor growth that antithrombotic therapy will have a favorable impact on survival? Elements of the clotting system have been shown to be important for the growth, invasion, and metastasis of experimental cancers.1 Furthermore, several large clinical trials have demonstrated some beneficial effect of anticoagulant or antiplatelet therapy on the natural history of cancer.4,5 This evidence provides compelling support for ongoing clinical trials of agents which interfere with coagulation; the measurement of TIA in such trials may prove of predictive value. The development of a reproducible immunoassay for TIA would make this a more realistic goal for application to larger clinical trials.

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References