CANCER AND THROMBOSIS: RECENT ADVANCES

CURRENT ONCOLOGY—VOLUME 15, NUMBER 6

302

Richard J. Ablin, PhD, Research Professor of Immunobiology, University of Arizona College of Medicine and the Arizona Cancer Center, Tucson, Arizona, U.S.A., and Phil Gold, PhD, MD, Professor of Medicine, Physiology, and Oncology, McGill University, Montreal, Quebec, Canada, Section Editors.

KEY WORDS

Venous thromboembolism, risk factors, epidemiology, low molecular weight heparin

INTRODUCTION

The burden of venous thromboembolism (VTE) is a challenging problem in the medical management of cancer patients. The well-known association between cancer and VTE can now be rigorously studied with modern molecular techniques. Large population-based epidemiologic studies have shed light on the relative frequency of VTE and cancer types, and clinical trials of cancer therapy have defined additional risk factors that compound the thrombotic risk.

VTE AND CANCER PATIENTS

The treatment of cancer patients for VTE has been associated with a high risk of recurrent thrombosis and of bleeding complications. However, recent data point to improved patient outcome with the use of long-term low molecular weight heparin therapy. Cancer patients who also have VTE are at increased risk of mortality, but there are intriguing suggestions concerning the benefit of low molecular weight heparin for improved cancer survival. A recently published guideline facilitates the practice of evidence-based VTE prevention and treatment in cancer patients, and sets the stage for future directions in this important domain.

Attendant Problems

The inherent properties of blood vessels, endothelial cells, adhesion receptors, and soluble plasma coagulation proteins render these structures and molecules important in the propagation of coagulation and the regulation of cancer-cell growth. Perturbation of these components by cancer treatment interventions such as surgery, chemotherapy, and supportive care can further exacerbate prothrombotic properties.

Advanced cancer is more often associated with VTE, as are certain cancer types, including pancreatic, stomach, brain, lung, and hematologic malignancies. In cancer patients, VTE is not only a frequent cause of death, it also identifies a patient population with poor prognosis, and it is both clinically challenging and financially costly to treat. As cancer treatment modalities evolve, differences in the added thrombogenic risk for patients also emerge—for example, the addition of anti-angiogenic therapy is associated with one of the highest risks of thrombotic complications.

Optimizing Treatment

Given the strong association of cancer and VTE, how should thromboprophylaxis for cancer patients be optimized? Clearly, as recently reviewed in Current Oncology, patients undergoing cancer surgery and those hospitalized for investigations and treatment of cancer are good candidates for appropriate thromboprophylaxis. Because all currently used anticoagulants are inherently associated with a risk of bleeding and because they generate added cost, prophylaxis of cancer patients at lower thrombotic risk cannot be justified at this time. Probing the role of low molecular weight heparins in modifying cancer progression should be the subject of additional well-designed clinical trials. All cancer-associated VTE should be considered for long-term low molecular weight heparin therapy, given the more favourable clinical outcomes seen as compared with the outcomes seen with traditional oral anticoagulant therapy.

The recent guidelines from the American Society of Clinical Oncology underline the importance of optimizing anticoagulation management of cancer patients. The practice of appropriate thromboprophylaxis, up-to-date anticoagulation of cancer-associated VTE, and participation in good clinical trials evaluating...
cancer and coagulation should routinely be part of our comprehensive care of cancer patients.

REFERENCES

1. Trousseau A. Phlegmasia alba dolens. Clinique Medicale l’Hotel-Dieu de Paris. Vol. 3. London: New Sydenham Society; 1865: 695–727.

2. Buller HR, van Doormaal FF, van Sluis GL, Kamphuisen PW. Cancer and thrombosis: from molecular mechanisms to clinical presentations. J Thromb Haemost 2007;5(suppl 1):246–54.

3. Levitan N, Dowlati A, Remick SC, et al. Rates of initial and recurrent thromboembolic disease among patients with malignancy versus those without malignancy. Risk analysis using Medicare claims data. Medicine (Baltimore) 1999;78:285–91.

4. Khorana AA, Francis CW, Culakova E, Kuderer NM, Lyman GH. Frequency, risk factors, and trends for venous thromboembolism among hospitalized cancer patients. Cancer 2007;110:2339–46.

5. Haddad TC, Greeno EW. Chemotherapy-induced thrombosis. Thromb Res 2006;118:555–68.

6. Zangari M, Barlogie B, Anaissie E, et al. Deep vein thrombosis in patients with multiple myeloma treated with thalidomide and chemotherapy: effects of prophylactic and therapeutic anticoagulation. Br J Haematol 2004;126:715–21.

7. Prandoni P, Lensing AW, Piccioli A, et al. Recurrent venous thromboembolism and bleeding complications during anticoagulant treatment in patients with cancer and venous thrombosis. Blood 2002;100:3484–8.

8. Lee AY, Levine MN, Baker RI, et al. on behalf of the CLOT investigators. Low-molecular-weight heparin versus a coumarin for the prevention of recurrent venous thromboembolism in patients with cancer. N Engl J Med 2003;349:146–53.

9. Hull RD, Pineo GF, Brant RF, et al. on behalf of the LITE Trial investigators. Long-term low-molecular-weight heparin versus usual care in proximal-vein thrombosis patients with cancer. Am J Med 2006;119:1062–72.

10. Sørensen HT, Mellemkjaer L, Olsen JH, Baron JA. Prognosis of cancers associated with venous thromboembolism. N Engl J Med 2000;343:1846–50.

11. Kuderer NM, Khorana AA, Lyman GH, Francis CW. A meta-analysis and systematic review of the efficacy and safety of anticoagulants as cancer treatment: impact on survival and bleeding complications. Cancer 2007;110:1149–60.

12. Lyman GH, Khorana AA, Falanga A, et al. American Society of Clinical Oncology guideline: recommendations for venous thromboembolism prophylaxis and treatment in patients with cancer. J Clin Oncol 2007;25:5490–505.

13. Brose KMJ, Lee AYY. Cancer-associated thrombosis: prevention and treatment. Curr Oncol 2008;15(suppl 1):S58–67.

Correspondence to: Susan Solymoss, The Montreal General Hospital, Department of Medicine and Oncology, McGill University, 1650 Cedar, Montreal, Quebec H3G 1A4.

E-mail: solymoss@muhchem.mcgill.ca