Case Reports in Oncology

Case Rep Oncol 2011;4:115–117
DOI: 10.1159/000324584

Published online:
February 25, 2011

ISSN 1662–6575
www.karger.com/cro

Extended Venous Thromboembolism Prophylaxis for High-Risk Patients Undergoing Surgery for Malignancy

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Key Words
Venous thromboembolism prophylaxis · Venous thromboembolism · Surgery · Deep vein thrombosis · Pulmonary embolism

Abstract
Background: In surgical patients with known malignancy, the odds ratio for an episode of a venous thromboembolism is approximately 6.5 compared to a group of patients without malignancy undergoing the same procedure [Heit et al.: Arch Intern Med 2000;160:809–815].
Case Report: We present a case of a 46-year-old Caucasian male with a history of adenocarcinoma of the rectum. The patient received neoadjuvant treatment prior to low anterior resection with diverting colostomy. He received short-term prophylaxis for venous thrombosis, but unfortunately developed a blood clot in a lower extremity several weeks after surgery.
Conclusion: There is a well-defined role in carefully selected patients for the use of extended prophylaxis to prevent venous thromboembolic complications following cancer surgery.

Introduction

Venous thromboembolic disease is the leading cause of death in patients with cancer [2]. Patients undergoing surgery, who have known malignancy, are documented to have a higher risk of developing perioperative venous thromboembolic disease. The ESSENTIAL trial demonstrated that 75% of patients undergoing major cancer surgery did not receive appropriate extended venous thromboembolism prophylaxis [3]. The RISTOS project

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demonstrated that a remarkable proportion of venous thromboembolic events occurred late (40% >21 days after surgery).

We report the case of a patient diagnosed with adenocarcinoma who underwent a low anterior abdominal resection with diverting colostomy. This paper discusses the appropriate selection of patients who would benefit from extended venous thromboembolism prophylaxis.

Case Presentation

Our patient is a 45-year-old Caucasian male with a past medical history significant for asthma. He did not have any prior history of venous thromboembolic disease. He initially presented to his physician with a chief complaint of several weeks of abdominal bloating and diarrhea associated with tenesmus. The patient denied having had fever, weight loss, fatigue, or hematochezia. His diagnostic evaluation included a colonoscopy, which revealed the presence of a 5-cm ulcerated rectal mass. The biopsy was significant for adenocarcinoma of the rectum. Staging studies showed no evidence of metastatic disease. The patient was referred to medical oncology. He was treated with neoadjuvant 5-FU with oxaliplatin, in addition to concurrent external beam radiation to the rectum (4,500 cGy to the pelvic and inguinal lymph nodes and the rectal mass, with an additional 540 cGy to the rectal mass) over a period of 5 weeks. Follow-up CT revealed no abdominal or pelvic lymphadenopathy. There was normal appearance of the rectum and distal sigmoid colon. There was no visualization of asymmetric wall thickening or soft-tissue mass. No perirectal lymphadenopathy was identified. The patient was referred to surgery, and the surgeon performed a low anterior resection with diverting ileostomy, mobilization of the splenic flexure, and proctoscopy. The duration of the surgery was approximately 3 h. The surgical staging of the rectal cancer was T3N1M0.

Post-surgical pharmacologic venous thromboembolism prophylaxis was initiated the day after surgery. Pharmacologic prophylaxis was continued for the duration of the hospitalization (8 days). The patient did not receive extended pharmacologic venous thromboembolism prophylaxis after discharge from the hospital.

Twenty-five days after surgery, the patient presented to his primary care physician with a chief complaint of left lower-extremity swelling. The clinician ordered a venous ultrasound, which revealed extensive deep vein thrombosis of the left saphenous and popliteal veins.

Discussion

Venous thromboembolic disease is a major contributor to morbidity and mortality in patients requiring cancer surgery. Identification of patients who would benefit from extended venous thromboembolism prophylaxis in the post-surgical setting is critical. The RISTOS project identified 5 risk factors for the development of venous thromboembolic disease for patients undergoing cancer surgery: (1) age >60 years; (2) previous venous thromboembolism; (3) advanced cancer; (4) anesthesia lasting >2 h, and (5) bed rest >2 days [4].

Several studies have demonstrated a statistically significant benefit of extended (28 days) pharmacologic venous thromboembolism prophylaxis. ENOXACAN II evaluated patients undergoing abdominal or pelvic surgery for malignancy. Enoxaparin (40 mg s.q. daily) was provided for 6–10 days after surgery. Patients were then randomized to receive enoxaparin 40 mg s.q. daily for an additional 21 days or were given placebo. At day 31 after surgery, venous ultrasound was performed. The placebo group exhibited a rate of thromboembolic disease of 12%, with a risk of hemorrhage of 3.6%. The group of patients receiving extended venous thromboembolism prophylaxis was found to have a rate of

thromboembolic disease of 4.8%, with an associated risk of hemorrhage of 5.1% (p = 0.02) [5].

CANBESURE was a randomized double-blinded study that evaluated patients undergoing abdominal or pelvic surgery for cancer. A dose of 3,500 IU s.q. of bemiparin was provided daily for 8 days after surgery. Patients were then randomized to receive placebo or bemiparin for an additional 20 days. Bilateral venography was performed after 20 days. The rate of deep vein thrombosis in the placebo group was 4.6%. The group of patients who received extended venous thromboembolism prophylaxis had a rate of 0.8% (p = 0.01). Bleeding risk was not statistically different between placebo and extended prophylaxis groups [6].

Rasmussen et al. [7] evaluated patients undergoing major abdominal surgery, including patients with and without malignant disease. Post-surgical venous thromboembolism prophylaxis with dalteparin was given for 7 versus 28 days postoperatively. All patients underwent venography on day 28 after surgery. Venous thromboembolic disease rate was 16.3% for patients receiving 7 days of prophylaxis versus 7.3% for patients receiving 28 days of extended prophylaxis (p = 0.012) [7].

In conclusion, these studies indicate the need for the development of a process to screen patients undergoing cancer surgery for an increased risk of post-surgical venous thromboembolic disease. In patients identified as being at high risk, extended venous thromboembolism prophylaxis should be instituted preferably with a low-molecular-weight heparin for a total duration of at least 28 days after surgery.

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