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UPPER EXTREMITY DEEP VENOUS THROMBOSIS IN ONCOLOGICAL PATIENTS – CASE REPORT

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Summary

Upper extremity deep venous thrombosis (UEDVT) makes approximately 4% to 20% of all venous thromboembolism (VTE). Cancer is the most relevant acquired thrombotic risk factor of VTE, because of its myriad of prothrombotic molecules released by neoplastic cells. In our case report we presented deep venous thrombosis (DVT) of the upper limb that is not associated with central venous catheter (CVC) or receiving chemotherapy or hormonal therapy.

A 55-year old female patient was admitted to our Department of Transfusion Medicine because of the swelling and pain in the left arm. One month earlier she underwent left segmentectomy and axillary dissection because of the breast cancer. Physical examination revealed left arm swelling and pressure pain. D-dimers were 770 μg/L (normal range 170-500 μg/L). Duplex ultrasound revealed thrombogenic mass in the left brachial vein, without total obstruction. She was treated with low molecular mass heparin (LMWH) and warfarin.

This uncommon presentation of hypercoagulable state in cancer patient points out one more time the importance of prophylactic use of anticoagulants in any hospitalized cancer patient receiving anticancer therapy. In University Hospital for Tumors we recommend anticoagulation prophylaxis for all cancer patients undergoing surgery. We use low doses of LMWH eight hours after surgery and once daily until discharge.

KEYWORDS: *deep venous thrombosis, LMWH, warfarin, d-dimers*

DUBOKA VENSKA TROMBOZA GORNJIH EKSTREMITETA KOD ONKOLOŠKIH BOLESNIKA – PRIKAZ SLUČAJA

Sažetak

Na duboku vensku trombozu gornjih ekstremiteta (DVTGE) otpada 4% - 20% svih slučajeva venskog tromboembolizma (VTE). Maligna bolest je značajniji stečeni rizični factor za razvoj VTE zbog protrombotskih tvari koje otpuštaju neoplastične stanice. U ovom radu prikazali smo slučaj bolesnice koja je razvila duboku vensku trombozu (DVT) ruke koja nije povezana sa središnjim venskim kateterom, aplikacijom kemoterapije ili hormonske terapije.

55 - godišnja bolesnica primljena je na Zavod za transfuzijsku medicinu zbog otekline i boli u lijevoj ruci . Mjesec prije bila je podvrgnuta kirurškom zahvatu zbog karcinoma dojke, učinjena je segmentektomija s disekcijom aksile. Fizikalnim pregledom nađe se otok lijeve ruke. Vrijednost D- dimera kod prijema bila je 770 g / L (normalni raspon 170-550 g / L). Obojanom ultrazvučnom obradom nađu se trombogene mase u lijevoj brahijalnoj veni, bez potpune opstrukcije. U terapiju je uveden niskomolekularni heparin (LMWH), a potom varfarin.

Ovakva rijeđa posljedica hiperkoagulabilnog stanja kod onkoloških bolesnika još je jedna potvrda važnosti procjene rizika i profilaktičke upotrebe antikoagulantne terapije.U Klinici za tumore preporuča se antikoagulantna terapija kod svih bolesnika podvrgnutih kirurškom liječenju. Koristi se LMWH osma sati nakon operacije, a potom jednom dnevno do otpusta.

KLJUČNE RIJEČI: *duboka venska tromboza, LMWH, varfarin, d-dimeri*

INTRODUCTION

VTE is a disease which may appear as lower extremities deep venous thrombosis (LEDVT) or more rarely of the upper extremities with possible life-threatening complications such as pulmonary embolism (PE) (1). UEDVT makes approximately 4% of all VTE events, and its incidence has increased in the last years when compared to data from past decades because of the increased use of CVC (2).

Cancer is the most relevant acquired thrombotic risk factor of VTE, because of its myriad of prothrombotic molecules released by neoplastic cells (3).

In addition to the production of procoagulant molecules, other thrombotic risk factors may also be involved in the pathogenesis of UEDVT in neoplastic patients. These include: surgery, concomitant medical illness, prolonged immobility, cancer therapies and the presence of CVC (1). The risk of postoperative VTE is approximately twice as high in cancer patients as in patients without cancer undergoing comparable surgery (4,5).

The high occurrence rate of VTE in neoplastic patients is mainly due to prothrombotic molecules released from malignant cells, such as tissue factors (TF) or cancer procoagulants (CP). Cancer cells may either express or release TF themselves, (3) or via stimulation of monocytes, macrophages or endothelial cells. This occurrence is mediated by a cytokine network, which is related to cancer growth (3). Interleukin 1 (IL-1) and Tumor Necrosis Factor (TNF) are the most well known cytokines involved in cancer-induced thrombophilia (3,1). The typical effect of procoagulant molecules in patients bearing neoplasia, is a subclinical hypercoagulable state that may be detected by screening for biochemical markers, such as D-dimers, prothrombin fragment 1+2 (6) and thrombin-antithrombin complexes (6). The subclinical hypercoagulable state may lead to relevant clinical thrombotic events (7,6).

Reviewing the existing data we found that DVT of the arm is an uncommon entity in patients with breast cancer unrelated to CVC.

In our case report we presented DVT of the upper limb that is not associated with CVC or receiving chemotherapy or hormonal therapy. The tumor in the breast did not compress the veins in arm and there were no enlarged lymph nodes in the axilla. The cause of the DVT is breast cancer and surgery which provides hypercoagulability in patient blood

CASE REPORT

A 55-year old female patient was admitted to our Department of Transfusion Medicine and Hemostasis because of the swelling and pain in the left arm.

One month earlier she underwent left segmentectomy and axillary dissection because of the breast cancer. Pathologists revealed that the size of the tumor was 1.4 cm and that there was no lymph node metastasis. She didn't receive any anticoagulation prophylaxis after surgery.

At the time of admission, she wasn't receiving any chemo or hormonal therapy. We found out that in the past she did not have any thromboembolic events. Physical examination revealed left arm swelling and pressure pain. Complete blood count (CBC), prothrombin time (PT), partial thromboplastin time (PTT), and blood chemistries were all within normal limits. D-dimers were 770μg/L (normal range 170-500μg/L). Duplex ultrasound revealed thrombogenic mass in the left brachial vein, without total obstruction. LMWH was started immediately, dalteparin 7.500 IU s.c. (under skin application) daily according to body mass. After 6 days when we noticed decline in D-dimers level (550 μg/L) and markedly improved swelling, therapy dosage was reduced to 5.000 IU s.c. At the same time warfarin was initiated. On tenth day dalteparin was off and we continued only with warfarin. She was recommended to use anticoagulation therapy during her chemotherapy treatment.

DISCUSSION

This uncommon presentation of hypercoagulable state in cancer patient points out the importance of prophylactic use of anticoagulants in any hospitalized cancer patient receiving anticancer therapy (surgery, chemo, hormonal of radiotherapy).

Effective VTE prevention measures have been widely reported to be under-utilised and inconsistently applied (8,9). For example, a recent UK survey reported that 71% of hospitalized patients

judged to be at moderate or high risk of DVT did not receive any form of prophylaxis (9). VTE leads to short and long term morbidity and mortality and is costly to treat. In addition to diagnostic tests, patients with VTE require treatment with anticoagulants and a longer hospital stay. They often require further diagnostic tests and prolonged treatment to manage the complications of VTE after discharge (9).

Both the European Society for Medical Oncology (ESMO) (11) and the Association of the Scientific Medical Societies (AWMF) in Germany (12) recommend prophylaxis for hospitalized patients with cancer. While ESMO equally recommends LMWH, UFH and fondaparinux, the German guideline prefers LMWH over the other options based on extrapolations from three placebo controlled randomized trials with LMWH, in which between 5 and 15% of patients had cancer at baseline (12,13).

The National Comprehensive Cancer Network (NCCN) recently published clinical practice guidelines on venous thromboembolic events in cancer patients (14). The defined at risk population for these guidelines is the adult cancer inpatient with a diagnosis of (or clinical suspicion for) cancer. The guidelines recommend prophylactic anticoagulation (category 1 recommendation) with or without a sequential compression device as initial prophylaxis, unless the patient has a relative contraindication to anticoagulation, in which case mechanical prophylaxis (sequential compression device or graduated compression stockings) is recommended. (A category 1 recommendation indicates "uniform NCCN consensus, based on high-level evidence.")

The American Society of Clinical Oncology (ASCO) recently released guidelines on VTE prevention and treatment in patients with cancer (15), their key recommendations for prevention are summarized in table 1.

Notable differences from the recommendations of the Seventh ACCP Conference are the ASCO guidelines' inclusion of fondaparinux among recommended prophylactic options for this population and more explicit recommendations on the prophylactic use of LMWH. Also, for treatment of cancer patients with established VTE, ASCO specifies that LMWH is the preferred anticoagulant for both initial and continuing treatment.

Table 1.

AMERICAN SOCIETY OF CLINICAL ONCOLOGU RECOMMENDATIONS FOR VTE PREVENTON IN PATIENTS WITH CANCER. (VTE = VENOUS THROMBOEMBOLISM, UFH = UNFRACTIONATED HEPARIN, LMWH = LOW-MOLECULAR-WEIGHT HEPARIN).

Hospitalized patients with cancer should be considered candidates for VTE prophylaxis with UFH, LMWH, or fondaparinux in the absence of bleeding or other contraindications to anticoagulation.
All patients undergoing major surgery for malignant disease should be considered for thromboprophylaxis with low-dose UFH, LMWH, or fondaparinux starting as early as possible for at least 7–10 days, unless contraindicated. Mechanical methods may be added to anticoagulation in very high-risk patients but should not be used alone unless anticoagulation is contraindicated. LMWH for up to 4 weeks may be considered after major abdominal/pelvic surgery with residual malignant disease, obesity, and a previous history of VTE.
Ambulatory patients with cancer receiving systemic chemotherapy do not require routine pharmacologic prophylaxis unless they are receiving thalidomide or lenalidomide, owing to these agents' thrombotic risk.

In University Hospital for Tumors we recommend anticoagulation prophylaxis for all cancer patients undergoing surgery. We use low doses of LMWH eight hours after surgery and daily until discharge.

CONCLUSION

Patients undergoing surgery for cancer have an increased risk of VTE and fatal PE, even when thromboprophylaxis is used. Nevertheless, prophylaxis with either LMWH or UFH does reduce VTE event rates in these patients. In specific surgical cancer populations, especially those undergoing abdominal surgery, out-of-hospital LMWH prophylaxis is reasonable.

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