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Acute pulmonary embolism from upper limb venous thrombosis following breast cancer surgery two case reports

Upper limb venous thrombosis

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Abstract

BACKGROUND

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Upper limb venous thrombosis (ULVT) is more rare than lower-extremity deep venous, and is related to Paget-Schroetter, central venous catheterization, and malignancy. There are few reports of pulmonary embolism (PE) from upper-extremity vein thrombosis due to surgery. Herein, we report two cases of PE that originated from upper limb venous thrombosis on the surgical side in patients undergoing modified radical mastectomy for breast cancer. These cases challenge the traditional theory that PE originate only from the lower extremities.

CASE SUMMARY

CASE SUMMARY

We describe two female patients, aged 68 and 65, who had undergone modified radical mastectomy for breast cancer. They did not have a central venous catheter and did not undergo preoperative neoadjuvant chemotherapy. They were transferred to the intensive care unit due to symptomatic PE on the first day after surgery. Colour Doppler ultrasound identified fresh thrombosis in their upper limb veins, which was the presumed source of the PE. They all received anticoagulation therapy, and one of them experienced bleeding that required discontinuation of the drug. Ultimately, they were discharged in stable condition.

CONCLUSION

CONCLUSION

ULVT as a source of PE after breast cancer surgery cannot be ignored.

Key Words: Pulmonary embolism; Upper limb venous thrombosis; Modified radical mastectomy for breast; Case report

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Core Tip: We report two cases of pulmonary thrombosis that originated from ULVT on the side undergoing modified radical mastectomy for breast cancer. Our findings should spur surgeons to pay more attention to upper limb venous thrombosis. These cases challenge the traditional theory that PE originate from the lower extremities. Although there is a lower incidence of clinical PE in patients with upper limb venous thrombosis, PE is a serious complication that can be potentially life-threatening. Upper limb venous thrombosis as a source of pulmonary thrombosis after breast cancer surgery cannot be ignored.

INTRODUCTION

INTRODUCTION

The incidence rates of female breast cancer are rising fast and have surpassed lung cancer as the leading cause of global cancer incidence in 2020 ^[1]. Modified radical mastectomy has become the standard surgical treatment of breast cancer. However, the frequency and potential morbidity of PE as a surgical complication in this patient population have not been clearly defined; specifically, the source of the thrombus is unknown. To the best of our knowledge, this is the first report of PE caused by ULVT after modified radical mastectomy for breast cancer.

CASE PRESENTATION

Chief complaints

Case 1

Chief complaints

Physical examination found a right breast mass for a week.

Case 2

Chief complaints

She found a mass on her right breast by herself.

History of present illness

case 1:

History of present illness

A 68-year-old woman presented to the Breast Diagnosis and Treatment Center of Shanxi Provincial Cancer Hospital due to a right breast mass that was found in a physical examination a week before. The Body Mass Index (BMI) of this patient is 24.6 kg/m² which is overweight. Classic clinical symptoms of venous thrombosis including pain and unilateral edema were not present. D-dimer concentration was normal. Therefore, the diagnosis of venous thrombosis is ruled out. She underwent modified radical mastectomy for invasive carcinoma of the right breast. She had not received neoadjuvant chemotherapy or a central venous catheter. However, more advanced age, overweight, hospitalization and surgery were shown to be associated with increased risk for venous thrombosis. The patient noticed swelling of the right upper limb, accompanied by mild dyspnoea on the first day after surgery, and her blood oxygen saturation dropped to 89% the following day (nasal cannula oxygen inhalation 3 L/min). She was transferred to the intensive care unit.

case 2:

History of present illness

A 65-year-old Chinese female was hospitalized in March 2021, mainly due to the discovery of a right breast mass. The tumour was located at 10 o'clock on the upper outside quadrant of the right breast. The area of the mass was 2*3 cm, with an irregular shape and unclear boundary. It was 2 cm from the nipple. Ultrasound-guided needle biopsy confirmed invasive carcinoma. There were no complaints from patient of arm swelling or pain and no signs of venous thrombosis on admission. The patient underwent modified radical mastectomy of the right breast as treatment. Axillary

dissection was performed with level I and II dissection, and the operation lasted 60 minutes. Although the operation time was short, but more advanced age, overweight (BMI 24 kg/m²) and hospitalization were independent risk factors for developing a subsequent venous thrombosis. After the operation, she developed hypoxemia and was transferred to the intensive care unit.

History of past illness

case 1:

History of past illness

She had no previous history of other diseases.

case 2:

History of past illness

She had a history of hypertension, and no other significant abnormalities were found.

Personal and family history

case 1:

2

Personal and family history

She denied a history of similar diseases in close relatives.

case 2:

2

Personal and family history

She denied a history of similar diseases in close relatives.

Physical examination

Case 1:

After admission, her temperature was 36.0 °C respiratory rate was 25 breaths per minute, and she had tachycardia (heart rate 105 beats/min). Her initial haemodynamics were stable and her blood pressure was 117/91 mmHg. Mild swelling were found on

the patient's right upper limb, while no numbness was found. Her Wells pulmonary embolism score was 9, which indicated a high probability of PE.

Case 2:

On the first day after surgery, the patient had no discomfort and left her bed. However, she developed hypoxaemia, and routine postoperative testing showed that her blood oxygen saturation had decreased on the second day after surgery.

Laboratory examinations

case 1:

Laboratory examinations

Arterial blood gas shows that the partial pressure of oxygen was 56mmHg and the partial pressure of carbon dioxide was 28mmHg. Her D-dimer concentration increased 979 ng/mL (0–243 ng/mL), compared to only 145 ng/mL before surgery. Cardiac troponin and BNP were normal. Electrocardiogram was also normal.

case 2:

Laboratory examinations

The partial pressure of blood oxygen was only 46 mmHg without oxygen. In fact, her breathing rate was nearly 30 times per minute. Her haemodynamics were stable and ECG was normal. Her brain natriuretic peptide increased to 320 pg/mL (0–100 pg/mL). Moreover, D-dimer increased significantly from 178 ng/mL before surgery to 3286 ng/mL (0–243 ng/mL). Her pulmonary embolism clinical probability score (Wells score) indicated a high probability of [PE](#).

Imaging examinations

case 1:

Imaging examinations

Then, this patient underwent computed tomography pulmonary angiography (CTPA), and [PE](#) was confirmed. Multiple pulmonary embolisms were located in smaller subsegments of the pulmonary artery (Figure 1). Four-limb Doppler ultrasonography

was performed, which is very important for speculating on the source of the venous thrombosis event. A fresh thrombus was found in the brachial vein of the right upper limb, which was in the operative extremity (Figure 1D).

case 2:

Imaging examinations

A spiral CT scan showed bilateral massive PE located in both lower pulmonary arteries and branches, the superior branch of the right upper pulmonary artery, the left pulmonary artery and some of its branches (Figure 2). A 4-limb surveillance Doppler ultrasound showed upper limb venous thrombosis in the operative extremity involving the vena basilica, the presumed source of the venous thromboembolism (VTE) event (Figure 2C).

MULTIDISCIPLINARY EXPERT CONSULTATION

case 1: no

case 2: no

FINAL DIAGNOSIS

case 1: PE

case 2: PE

TREATMENT

case 1:

The simplified Pulmonary Embolism Severity Index (sPESI) was 2 points, which is considered a high-risk score. Upon diagnosis of PE, 5,000 IU Enoxaparin subcutaneously every 12 h was administered for the initial management. Five days later, anticoagulation agent was changed to rivaroxaban (15mg PO twice daily). These anticoagulants were shown to be more effective in the treatment with acute PE.

case 2:

Subsequently, this patient was treated with Enoxaparin (6,150 IU subcutaneously twice-daily dose. However, she had to stop the Enoxaparin due to bleeding in the surgical area 2 days after treatment (Figure 2D) . The patient developed a drop hemoglobin level from 122g/L to 88g/L. Bleeding in the surgical field did not require invasive intervention and blood transfusion, nor did it affect the overall clinical outcome. After the bleeding had stopped, anticoagulant drugs was transitioned to Rivaroxaban (15mg PO twice daily)which is direct oral anticoagulants (DOACs).

OUTCOME AND FOLLOW-UP

case 1:

The rivaroxaban dosing was lowered from 15mg twice daily to 20mg every day after 21 days which made routine laboratory tests when upon discharge unnecessary. Color flow Doppler ultrasound performed was negative for thrombus in the brachial vein at 4 wk after Modified radical mastectomy. During this period, she received adjuvant chemotherapy consisting of four cycles of cyclophosphamide plus epirubicin, followed by four cycles of docetaxel. Treatment duration was for a minimum of 6 mo.

case 2:

Six days after restarting anticoagulation, the patient was discharged in stable condition. Rivaroxaban was given at a dose of 15 mg twice-daily for the initial three weeks followed by a 20 mg once-daily dosing thereafter. At 6 mo, the patient returns for outpatient follow-up. She has remained on anticoagulant treatment and denies bleeding episodes. The thrombosis of the vena basilica was ruled out using colour venous ultrasonography. Laboratory investigations demonstrated the concentration of D-dimer was normal. During anticoagulant therapy, this patient received six cycles of doxorubicin plus cyclophosphamide chemotherapy.

DISCUSSION

ULVT is an infrequent condition that is characterized as primary or secondary upper-extremity venous thrombosis. The prevalence of patients with upper extremity venous

thrombosis is 3–11% [2,3,4,5]. Paget-Schroetter syndrome and thoracic outlet syndrome are the main causes of primary upper extremity venous thrombosis. While central venous catheter placement is the strongest risk factor for secondary upper-extremity venous thrombosis, accounting for 45–62% of upper-extremity venous thromboses [6,7,8], malignancy is also a risk factor. A total of 29.2–38% of patients with upper-extremity venous thromboses are diagnosed with malignant tumours [6,7]. Additionally, a small study reported that upper extremity Deep Vein Thrombosis (DVT) was identified in 6% of patients who had undergone shoulder arthroplasty. These venous thromboses were found in the operative extremity [9]. However, the specific risk of upper limb venous thrombosis related to modified radical mastectomy for breast cancer is therefore unclear.

Modified radical mastectomy has become the standard operative treatment for breast cancer. Identifying and reducing thrombotic complications after surgery is very important. In particular, PE is a serious complication that can be potentially life-threatening. The prognosis related to upper-extremity deep venous thrombosis includes a risk of recurrent thromboembolic events, and limiting the risk of post-thrombotic syndrome and mortality is key to improving breast cancer outcomes. The findings from the RIETE Registry reveal that 9.0% of patients with upper limb venous thrombosis had clinically overt PE [6]. However, despite the lower incidence of clinical PE in patients with upper limb venous thrombosis than those with lower-limb DVT, the 3-month outcome was similar ⁴ among groups in terms of the incidence of major or fatal bleeding, recurrent DVT, recurrent PE, or fatal PE, and those with upper-extremity venous thrombosis had a higher mortality rate. Furthermore, malignant tumours are an important risk factor for poor prognosis in patients with upper extremity venous thrombosis. Cancer patients with upper-extremity venous thrombosis have increased incidences of major bleeding, recurrent VTE and death. These findings show that the occurrence of upper limb venous thrombosis with cancer cannot be ignored.

We report two cases of PE from upper limb venous thrombosis after modified radical mastectomy for breast cancer. Intimal injury, venous stasis, and

hypercoagulability, which are Virchow's triad, have been postulated to explain the pathogenesis of VTE after MRM. First, malignant tumours appear to cause a prothrombotic or hypercoagulable state by changing the balance between the coagulation and fibrinolysis systems [10]. Second, during axillary lymph node dissection, direct manipulation, twisting and stretching of the axillary vein increases the chance of intimal damage to the vessel. Third, modified radical mastectomy requires the patient to be in an abduction posture on the affected side of the upper extremity for an extended period of time, which may result in significant pooling of blood in the upper limb extremities. Surgical procedures have also been related to haematologic alterations and the systemic release of thrombogenic factors [11]. Fourth, postoperative compression bandaging and immobilization of the upper limb on the surgical side cause venous stasis because of the lack of muscular pumping.

The clinical symptoms of these two patients were tumescence, mild dyspnoea and hypoxaemia. A screening surveillance Doppler ultrasound and D-dimer test found that there was no thrombosis before surgery. These two cases of PE after modified radical mastectomy developed on the first day after mastectomy. As a result, a surveillance colour flow Doppler ultrasound of the upper extremities and D-dimer should be performed in these patients on the second day. The second patient had subcutaneous haemorrhage after being treated with low-molecular-weight heparin, which was considered to be related to the larger wound area of her breast cancer surgery. Therefore, prophylactic anticoagulation and the dosage of anticoagulant drugs must be carefully considered due to bleeding, wound complications and reoperation in these patients. More importantly, prevention rather than treatment is considered necessary in these patients undergoing breast cancer surgery. No objective clinical guidelines to help assess and manage upper extremity deep venous thrombosis after modified radical mastectomy for breast cancer currently exist. Functional exercise of the upper limbs on the operative extremity, pneumatic compression devices, or intraoperative heparin administration may be effective during perioperative DVT prophylaxis.

CONCLUSION

These two cases of pulmonary thrombosis caused by upper extremity thrombosis may change the strategy of perioperative thrombosis management for breast cancer and should spur surgeons to pay more attention to upper limb venous thrombosis. This is the presumed source of symptomatic or fatal PE in patients undergoing MRM, which should stimulate further research in this area.

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