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Contents

Thrice Monthly Volume 10 Number 21 July 26, 2022

OPINION REVIEW

- 7187 Effects of glucocorticoids on leukocytes: Genomic and non-genomic mechanisms
Jia WY, Zhang JJ

MINIREVIEWS

- 7195 Apheresis: A cell-based therapeutic tool for the inflammatory bowel disease
Yasmin F, Najeeb H, Naeem U, Moeed A, Koritala T, Surani S
- 7209 *Helicobacter pylori* infection and small intestinal bacterial overgrowth—more than what meets the eye
Dharan M, Wozny D
- 7215 Anatomy of the anterolateral ligament of the knee joint
Park JG, Han SB, Rhim HC, Jeon OH, Jang KM

ORIGINAL ARTICLE

Clinical and Translational Research

- 7224 Molecular mechanisms of Biyu decoction as treatment for psoriasis: A network pharmacology and molecular docking study
Wang Z, Zhang HM, Guo YR, Li LL
- 7242 Expression of hepatocyte nuclear factor 4 alpha, wingless-related integration site, and β -catenin in clinical gastric cancer
Hu Q, Li LL, Peng Z, Yi P

Case Control Study

- 7256 Improved Pittsburgh Sleep Quality Index scores on first postoperative night achieved by propofol anesthesia in patients undergoing ambulatory gynecologic surgery
Hu CH, Chou WY
- 7265 Efficacy of Guhong injection *versus* Butylphthalide injection for mild ischemic stroke: A multicenter controlled study
Zhang WW, Xin J, Zhang GY, Zhai QJ, Zhang HM, Wu CS

Retrospective Study

- 7275 Clinical values of Barcelona Clinic Liver Cancer subgroup and up-to-7 criteria in intermediate stage hepatocellular carcinoma with transcatheter arterial chemoembolization
Lee SW, Peng YC, Lien HC, Ko CW, Tung CF, Chang CS
- 7285 Intervention effect of encouraging mental and programmed nursing of patients in interventional operating room on their compliance and bad moods
Chi RB, Cai YY, Mao HP

- 7293** Preoperative neoadjuvant chemotherapy in patients with breast cancer evaluated using strain ultrasonic elastography
Pan HY, Zhang Q, Wu WJ, Li X
- 7302** Risk factors for delayed intracranial hemorrhage secondary to ventriculoperitoneal shunt: A retrospective study
Chen JC, Duan SX, Xue ZB, Yang SY, Li Y, Lai RL, Tan DH
- 7314** Sequential treatment of severe pneumonia with respiratory failure and its influence on respiratory mechanical parameters and hemodynamics
Niu BY, Wang G, Li B, Zhen GS, Weng YB
- 7324** Effects of alendronate sodium combined with InterTan on osteoporotic femoral intertrochanteric fractures and fracture recurrence
Wang KM, Wei SP, Yin XY, Meng QJ, Kong YM
- 7333** Correlation of magnetic resonance imaging quantitative parameters and apparent diffusion coefficient value with pathological breast cancer
Wang Z, Ren GY, Yin Q, Wang Q
- 7341** Risk factors for delirium after surgery for craniocerebral injury in the neurosurgical intensive care unit
Chen RY, Zhong CH, Chen W, Lin M, Feng CF, Chen CN

Observational Study

- 7348** Effect of osteoarthritic knee flexion deformity correction by total knee arthroplasty on sagittal spinopelvic alignment in Indian population
Puthiyapura LK, Jain M, Tripathy SK, Puliappadamb HM
- 7356** Imaging characteristics of orbital peripheral nerve sheath tumors: Analysis of 34 cases
Dai M, Wang T, Wang JM, Fang LP, Zhao Y, Thakur A, Wang D

Randomized Controlled Trial

- 7365** Comparison of involved-field intensity-modulated radiotherapy combined with S-1 *vs* radiotherapy alone for elderly patients with esophageal cancer
Liu LH, Yan MH, Di YP, Fu ZG, Zhang XD, Li HQ

Randomized Clinical Trial

- 7376** Dexmedetomidine in pediatric unilateral internal inguinal ring ligation
Liu G, Zhang L, Wang HS, Lin Y, Jin HQ, Wang XD, Qiao WN, Zhang YT, Sun JQ, Liu ZN

META-ANALYSIS

- 7386** Impact of cancer on mortality rates in patients with sepsis: A meta-analysis and meta-regression of current studies
Xiang MJ, Chen GL

CASE REPORT

- 7397 Updated clinical and glycomic features of mannosyl-oligosaccharide glucosidase deficiency: Two case reports
Abuduxikuer K, Wang L, Zou L, Cao CY, Yu L, Guo HM, Liang XM, Wang JS, Chen L
- 7409 Solitary necrotic nodules of the liver with "ring"-like calcification: A case report
Bao JP, Tian H, Wang HC, Wang CC, Li B
- 7415 Corticosteroid-induced bradycardia in multiple sclerosis and maturity-onset diabetes of the young due to hepatocyte nuclear factor 4-alpha mutation: A case report
Sohn SY, Kim SY, Joo IS
- 7422 Essential thrombocythemia with non-ST-segment elevation myocardial infarction as the first manifestation: A case report
Wang ZM, Chen WH, Wu YM, Wang LQ, Ye FL, Yin RL
- 7429 Extranasopharyngeal angiofibroma in children: A case report
Yan YY, Lai C, Wu L, Fu Y
- 7438 Deep Sylvian fissure meningiomas: A case report
Wang A, Zhang X, Sun KK, Li C, Song ZM, Sun T, Wang F
- 7445 Acute pulmonary embolism originating from upper limb venous thrombosis following breast cancer surgery: Two case reports
Duan Y, Wang GL, Guo X, Yang LL, Tian FG
- 7451 Managing spondylitis tuberculosis in a patient with underlying diabetes and hypothyroidism: A case report
Novita BD, Muliono AC, Wijaya S, Theodora I, Tjahjono Y, Supit VD, Willianto VM
- 7459 Ovarian mucinous tumor with mural nodules of anaplastic carcinoma: Three case reports
Wang XJ, Wang CY, Xi YF, Bu P, Wang P
- 7467 Transcatheter arterial infusion chemotherapy and embolization for primary lacrimal sac squamous cell carcinoma: A case report
Sun MH, Yi WD, Shen L, Zhou L, Lu JX
- 7474 Programmed cell death-1 inhibitor combination treatment for recurrent proficient mismatch repair/microsatellite-stable type endometrial cancer: A case report
Zhai CY, Yin LX, Han WD
- 7483 Novel compound heterozygous mutation of *SLC12A3* in Gitelman syndrome co-existent with hyperthyroidism: A case report and literature review
Qin YZ, Liu YM, Wang Y, You C, Li LN, Zhou XY, Lv WM, Hong SH, Xiao LX
- 7495 Successful treatment of hyperglycemia with liraglutide in a hospitalized 27-year-old patient with schizophrenia: A case report
Zhang L, Yu WJ, Zhu H, Li HF, Qiao J

- 7502** Refractory lymphoma treated with chimeric antigen receptor T cells combined with programmed cell death-1 inhibitor: A case report
Zhang CJ, Zhang JY, Li LJ, Xu NW
- 7509** Median arcuate ligament syndrome with retroperitoneal haemorrhage: A case report
Lu XC, Pei JG, Xie GH, Li YY, Han HM
- 7517** Novel frameshift mutation in the *AHDC1* gene in a Chinese global developmental delay patient: A case report
Lin SZ, Xie HY, Qu YL, Gao W, Wang WQ, Li JY, Feng XC, Jin CQ
- 7523** Selective nerve block for the treatment of neuralgia in Kummell's disease: A case report
Zhang X, Li ZX, Yin LJ, Chen H
- 7531** Traditional Chinese medicine manipulative reduction combined with percutaneous vertebroplasty for treating type III Kummell's disease: A case report
Hao SS, Zhang RJ, Dong SL, Li HK, Liu S, Li RF, Ren HH, Zhang LY
- 7539** Differential diagnosis and treatment of foot drop caused by an extraneural ganglion cyst above the knee: A case report
Won KH, Kang EY
- 7545** Effect of hydrogen intervention on refractory wounds after radiotherapy: A case report
Zhao PX, Luo RL, Dang Z, Wang YB, Zhang XJ, Liu ZY, Wen XH, Liu MY, Zhang MZ, Adzavon YM, Ma XM
- 7553** Chronic urticaria associated with lung adenocarcinoma — a paraneoplastic manifestation: A case report and literature review
Jiménez LF, Castellón EA, Marengo JD, Mejía JM, Rojas CA, Jiménez FT, Coronell L, Osorio-Llanes E, Mendoza-Torres E
- 7565** Spinal giant cell-rich osteosarcoma-diagnostic dilemma and treatment strategy: A case report
Tseng CS, Wong CE, Huang CC, Hsu HH, Lee JS, Lee PH
- 7571** Primary clear cell sarcoma of soft tissue in the posterior cervical spine invading the medulla oblongata: A case report
Liu CC, Huang WP, Gao JB
- 7577** *Pseudomonas aeruginosa*-related effusive-constrictive pericarditis diagnosed with echocardiography: A case report
Chen JL, Mei DE, Yu CG, Zhao ZY
- 7585** Maternal peripartum bacteremia caused by intrauterine infection with *Comamonas kerstersii*: A case report
Qu H, Zhao YH, Zhu WM, Liu L, Zhu M
- 7592** Considerations of single-lung ventilation in neonatal thoracoscopic surgery with cardiac arrest caused by bilateral pneumothorax: A case report
Zhang X, Song HC, Wang KL, Ren YY

- 7599** Rare primary rectal mucosa-associated lymphoid tissue lymphoma with curative resection by endoscopic submucosal dissection: A case report and review of literature

Tao Y, Nan Q, Lei Z, Miao YL, Niu JK

- 7609** Differences in examination results of small anastomotic fistula after radical gastrectomy with afterward treatments: A case report

Lu CY, Liu YL, Liu KJ, Xu S, Yao HL, Li L, Guo ZS

LETTER TO THE EDITOR

- 7617** Baseline differences may impact on relationship between dietary tryptophan and risk of obesity and type 2 diabetes

Ren XH, Ye YW, He LP

ABOUT COVER

Editorial Board Member of *World Journal of Clinical Cases*, Rajesh Kumar Rajnish, MBBS, MS, Assistant Professor, Department of Orthopaedics, All India Institute of Medical Sciences, Bilaspur, Bilaspur 174001, Himachal Pradesh, India. duktiraj@gmail.com

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Acute pulmonary embolism originating from upper limb venous thrombosis following breast cancer surgery: Two case reports

Yan Duan, Guo-Li Wang, Xin Guo, Li-Li Yang, Fu-Guo Tian

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Yan Duan, Guo-Li Wang, Xin Guo, Li-Li Yang, Department of Critical Care Medicine, Shanxi Provincial Cancer Hospital, Taiyuan 030013, Shanxi Province, China

Fu-Guo Tian, Breast Diagnosis and Treatment Center, Shanxi Provincial Cancer Hospital, Taiyuan 030013, Shanxi Province, China

Corresponding author: Fu-Guo Tian, Doctor, Chief Doctor, Breast Diagnosis and Treatment Center, Shanxi Provincial Cancer Hospital, No. 3 Zhigong New Street, Taiyuan 030013, Shanxi Province, China. 387769340@qq.com

Abstract

BACKGROUND

Upper limb venous thrombosis (ULVT) is rarer than lower-extremity deep venous thrombosis, and is related to Paget-Schroetter syndrome, 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 two patients undergoing modified radical mastectomy for breast cancer. These cases challenge the traditional theory that PE originate only from the lower extremities.

CASE SUMMARY

We describe two female patients, aged 68 and 65 years, respectively, 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

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 embolism (PE) that originated from upper limb venous thrombosis (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 originates from the lower extremities. Although there is a lower incidence of clinical PE in patients with upper limb venous thrombosis, since PE is a serious complication that can be potentially life-threatening, ULVT as a source of PE after breast cancer surgery cannot be ignored.

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INTRODUCTION

The incidence rate of female breast cancer is rising fast and has surpassed lung cancer as the leading cause of global cancer incidence in 2020[1]. Modified radical mastectomy (MRM) has become the standard surgical treatment for breast cancer. However, the frequency and potential morbidity of pulmonary embolism (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 upper limb venous thrombosis (ULVT) after MRM for breast cancer.

CASE PRESENTATION

Chief complaints

Case 1: 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 ago.

Case 2: A 65-year-old Chinese woman was hospitalized in March 2021, mainly due to the discovery of a right breast mass.

History of present illness

Case 1: The body mass index (BMI) of this patient was 24.6 kg/m², which suggested 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 was ruled out. She underwent MRM 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 an 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 at 3 L/min). She was transferred to the intensive care unit.

Case 2: The patient had a tumour located at 10 o'clock on the upper outside quadrant of the right breast. The area of the mass was 2 cm × 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 complaints from the patient of arm swelling or pain and no signs of venous thrombosis on admission. The patient underwent MRM of the right breast. Axillary dissection was performed with levels I and II dissection, and the operation lasted 60 min. Although the operation time was short, more advanced age, overweight (BMI 24 kg/m²), and hospitalization were independent risk factors of 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: The patient had no previous history of other diseases.

Case 2: The patient had a history of hypertension, and no other significant abnormalities were found.

Personal and family history

Cases 1 and 2: Both patients denied the history of similar diseases in close relatives.

Physical examination

Case 1: After admission, the patient's 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 was found on the patient's right upper limb, while there was no numbness. Her Wells score for PE was 9, which indicated a high probability of PE.

Case 2: On the first day after surgery, the patient had no discomfort. 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: Arterial blood gas analysis showed that the partial pressure of oxygen was 56 mmHg and the partial pressure of carbon dioxide was 28 mmHg. The patient's D-dimer concentration increased to 979 ng/mL (0-243 ng/mL), compared to only 145 ng/mL before surgery. Cardiac troponin and brain natriuretic peptide were normal. Electrocardiogram was also normal.

Case 2: The partial pressure of blood oxygen was only 46 mmHg without oxygen. In fact, the patient's 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 Wells score indicated a high probability of PE.

Imaging examinations

Case 1: The patient underwent computed tomography pulmonary angiography, and PE was confirmed. Multiple pulmonary embolisms were located in smaller subsegments of the pulmonary artery (Figure 1A-C). 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: 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, and the left pulmonary artery and some of its branches (Figure 2A and B). Four-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).

FINAL DIAGNOSIS

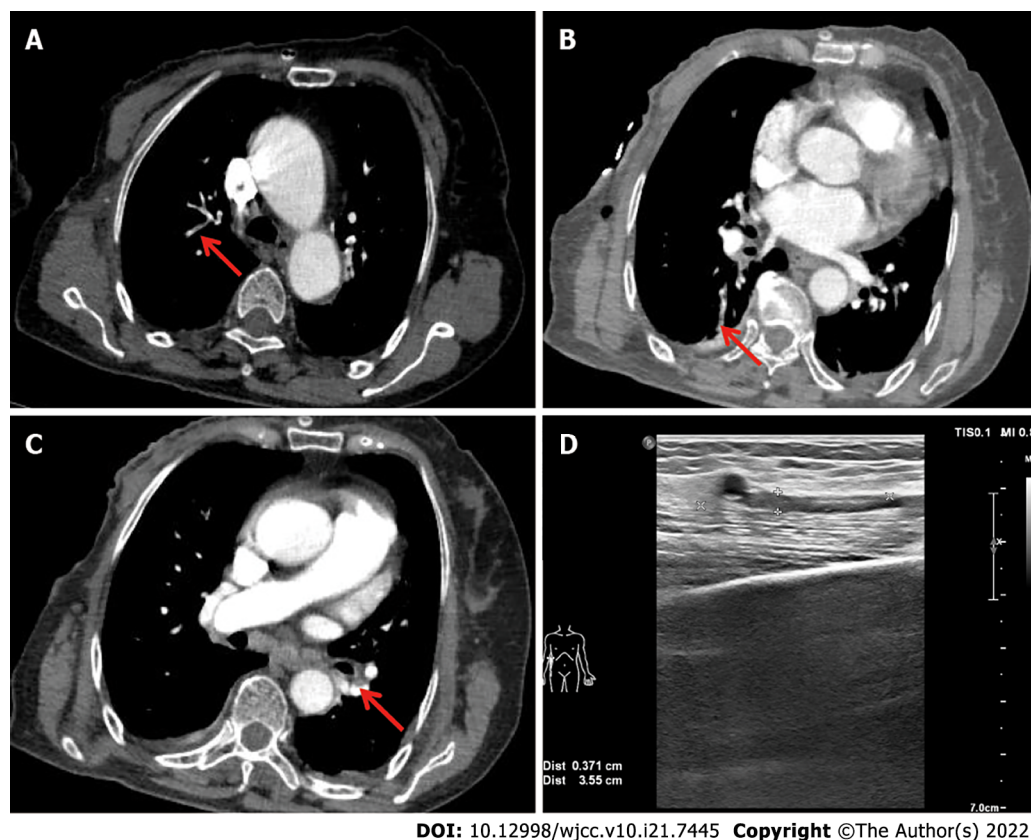
Cases 1 and 2: PE.

TREATMENT

Subsequently, this patient was treated with Enoxaparin (6150 IU subcutaneously twice-daily dose). However, she had to stop the Enoxaparin due to bleeding in the surgical area 2 d after treatment (Figure 2D). The patient developed a drop hemoglobin level from 122 g/L to 88 g/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 were transitioned to Rivaroxaban (15 mg PO twice daily) which is direct oral anticoagulants.

OUTCOME AND FOLLOW-UP

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.



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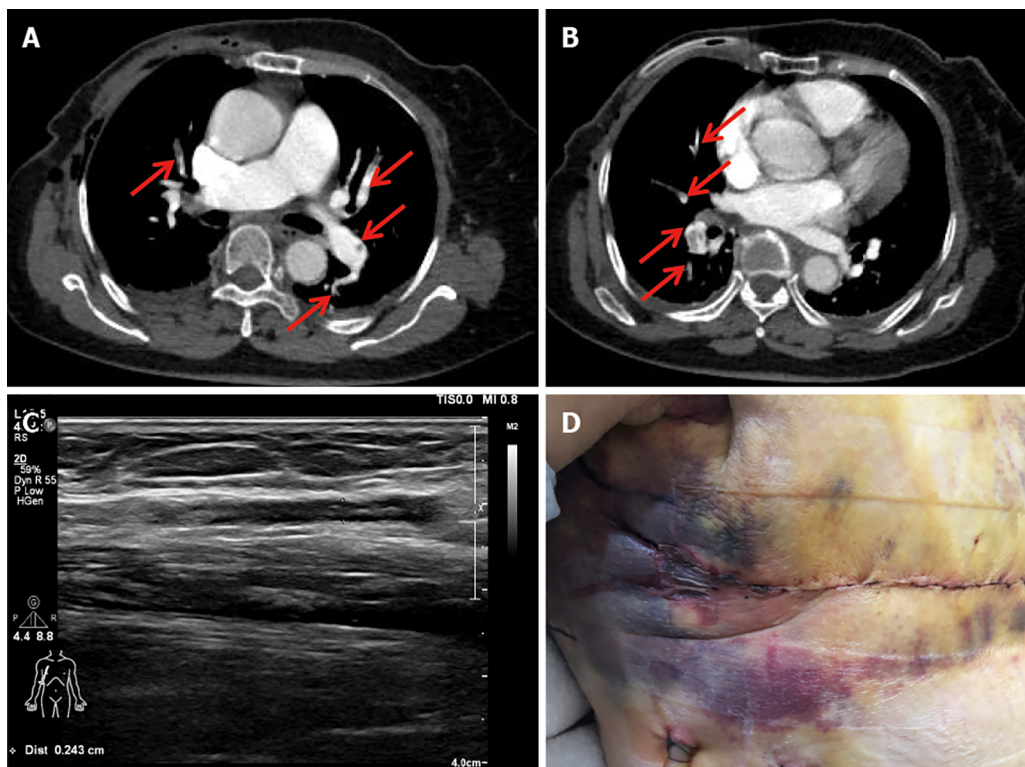
Figure 1 Computed tomography pulmonary angiograms and vascular Doppler ultrasound. A-C: Computed tomography pulmonary angiograms showing extensive bilateral filling defects in the segmental arteries of the right upper lobe (A), segmental arteries of the right lower lobe (B), and segmental arteries of the left lower lobe (C); D: Doppler ultrasound revealed a deep venous thrombosis in the brachial vein of the right upper limb.

DISCUSSION

ULVT is an infrequent condition that is characterized as primary or secondary upper-extremity venous thrombosis. The prevalence of patients with ULVT is 3%-11% [2-5]. Paget-Schroetter syndrome and thoracic outlet syndrome are the main causes of primary ULVT. While central venous catheter placement is the commonest risk factor for secondary ULVT, accounting for 45%-62% of upper-extremity venous thromboses [3,6,7], malignancy is also a risk factor. A total of 29.2%-38% of patients with upper-extremity venous thromboses are diagnosed with malignant tumours [3,6]. 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 [8]. However, the specific risk of ULVT related to MRM for breast cancer is therefore unclear.

MRM has become the standard operative treatment for breast cancer. Identifying and reducing thrombotic complications after surgery are 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 ULVT had clinically overt PE [3]. However, despite the lower incidence of clinical PE in patients with ULVT than those with lower-limb DVT, the 3-mo outcome was similar among groups in terms of the incidence of major or fatal bleeding, recurrent DVT, recurrent PE, or fatal PE, and those with ULVT had a higher mortality rate. Furthermore, malignant tumours are an important risk factor for poor prognosis in patients with ULVT. Cancer patients with ULVT have increased incidences of major bleeding, recurrent VTE, and death. These findings show that the occurrence of ULVT with cancer cannot be ignored.

We report two cases of PE originating from ULVT after MRM 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 [9]. Second, during axillary lymph node dissection, direct manipulation, twisting, and stretching of the axillary vein increase the chance of intimal damage to the vessel. Third, MRM 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



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Figure 2 Computed tomography pulmonary angiograms, vascular Doppler ultrasound, and surgical wound. A: Computed tomography angiography demonstrated massive thrombosis in the segmental arteries of the right upper lobe, segmental arteries of the left upper lobe, and segmental arteries of the left lower lobe (red arrow heads); B: CT angiography revealed filling defects in the segmental arteries of the middle lobe and segmental arteries of the right lower lobe (red arrow heads); C: Doppler ultrasound revealed a venous thrombosis in the right vena basilica; D: Subcutaneous ecchymosis caused by anticoagulant therapy.

been related to haematologic alterations and the systemic release of thrombogenic factors[10]. 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 dyspnea, and hypoxaemia. Screening surveillance Doppler ultrasound and D-dimer test found that there was no thrombosis before surgery. These two cases of PE after MRM developed on the first day after mastectomy. As a result, surveillance colour flow Doppler ultrasound of the upper extremities and D-dimer testing 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 currently exist to help assess and manage upper extremity deep venous thrombosis after MRM for breast cancer. 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 ULVT. This is the presumed source of symptomatic or fatal PE in patients undergoing MRM, which should stimulate further research in this area.

FOOTNOTES

Author contributions: Wang GL, Guo X, and Yang LL were the patient's doctors, reviewed the literature, and contributed to manuscript drafting; Duan Y reviewed the literature and contributed to manuscript drafting; Tian FG

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Country/Territory of origin: China

ORCID number: Yan Duan 0000-0003-2088-5734; Guo-Li Wang 0000-0002-4797-2021; Xin Guo 0000-0003-0594-4978; Li-Li Yang 0000-0002-3364-1416; Fu-Guo Tian 0000-0003-0953-970X.

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