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Case Report

Uterine Myoma Associated with Deep Vein Thrombosis and Pulmonary Embolism — Report of Two Cases

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Abstract: Pulmonary embolism is a common cause of morbidity and mortality. It is usually a complication of deep vein thrombosis with thromboemboli originating from the deep veins of lower extremities. Uterine myoma is a rarely reported risk factor of deep vein thrombosis. In this article, we report two women who presented with menorrhagia and a large uterine myoma followed by the event of acute pulmonary embolism. Clinical examinations failed to identify any prothrombotic conditions except for compression of iliac veins by uterine myoma that caused deep vein thrombosis of leg via mechanism of venous stasis. We successfully treated these two patients with intravenous heparin, oral warfarin and hysterectomy. A large uterine myoma should not be ignored as one of the lethal predisposing factors for acute pulmonary embolism; the importance of hysterectomy should be emphasized in the treatment of these patients for further prevention.

Key Words: Pulmonary embolism; Deep vein thrombosis; Uterine myoma.

Introduction

Acute pulmonary embolism is a serious and potential fatal disorder that is commonly associated with deep vein thrombosis.[1,2] Leiomyomas are the most common tumors of the uterus and the female pelvis. They are estimated to be present in at least 20% of all women of reproductive age. There is no direct relationship between this benign disease and acute pulmonary embolism. To our knowledge, reports of large uterine myoma associated with acute pulmonary embolism are rare.[3-5,13] We present two additional cases with large uterine myoma leading to acute life-threatening pulmonary embolism. The mechanism and management of this special situation are also discussed.

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Case Report

Case 1

A 50-year-old woman presented with menorrhagia, progressive shortness of breath and right lower leg edema. She had been diagnosed as having a uterine myoma eight months previously and uterine arterial embolization was performed. On admission, the jugular vein was distended, the pulse rate regular at 128 beats per minute, blood pressure was 125/82 mmHg,

and respiratory rate 24 breaths per minute. Cardiac examination revealed a Gr. II/VI pansystolic murmur at left lower sternal border, an accentuated P2, and a S3 gallop. Breathing sound was normal. A large tumor was palpable in the patient's lower abdomen. Chest radiography disclosed pulmonary trunk engorgement with clear lung field. An electrocardiogram showed sinus tachycardia, Q wave in lead III, and inverted T waves in V1- V4 and lead III. Arterial blood gases at room air showed a PaO_2 of 44.6 mmHg and a $PaCO_2$ of 19.4 mmHg. Echocardiogram revealed a dilated and hypokinetic right ventricle and severe regurgitation of the tricuspid valve. Pulmonary artery pressure was estimated to be 67 mmHg. Lung perfusion imaging revealed multiple perfusion defects in both lungs (Fig. 1A and B). The venography of lower extremities showed a mass lesion over pelvis which caused obstruction of bilateral common iliac veins, and multiple filling defects over right popliteal vein and superficial femoral vein (Fig. 2, A and B). Pelvic sonography revealed a huge uterine myoma, measuring 145 × 93.5 × 104 mm^3 in size (Fig. 3A). Plasma levels of antithrombin III, protein C and protein S were within normal limits. Anticoagulation therapy was started. The symptoms gradually improved after intravenous heparin followed by oral warfarin. Echocardiogram, performed one month later, showed decreased right ventricular overload and minimal tricuspid regurgitation, and pulmonary artery pressure was calculated to be 35 mmHg. After successfully treatment with anticoagulant, the patient finally underwent hysterectomy smoothly 6 months later and the histopathologic finding showed leiomyoma.

Case 2

A 50-year-old woman was admitted to our Gynecologic ward because of abnormal vaginal bleeding. She had been diagnosed with a uterine myoma accompanied by menorrhagia one year previously. She also had history of hypertensive cardiovascular disease. One month prior to this entry, she developed shortness of breath. On admission, the jugular vein was distended, the pulse rate regular at

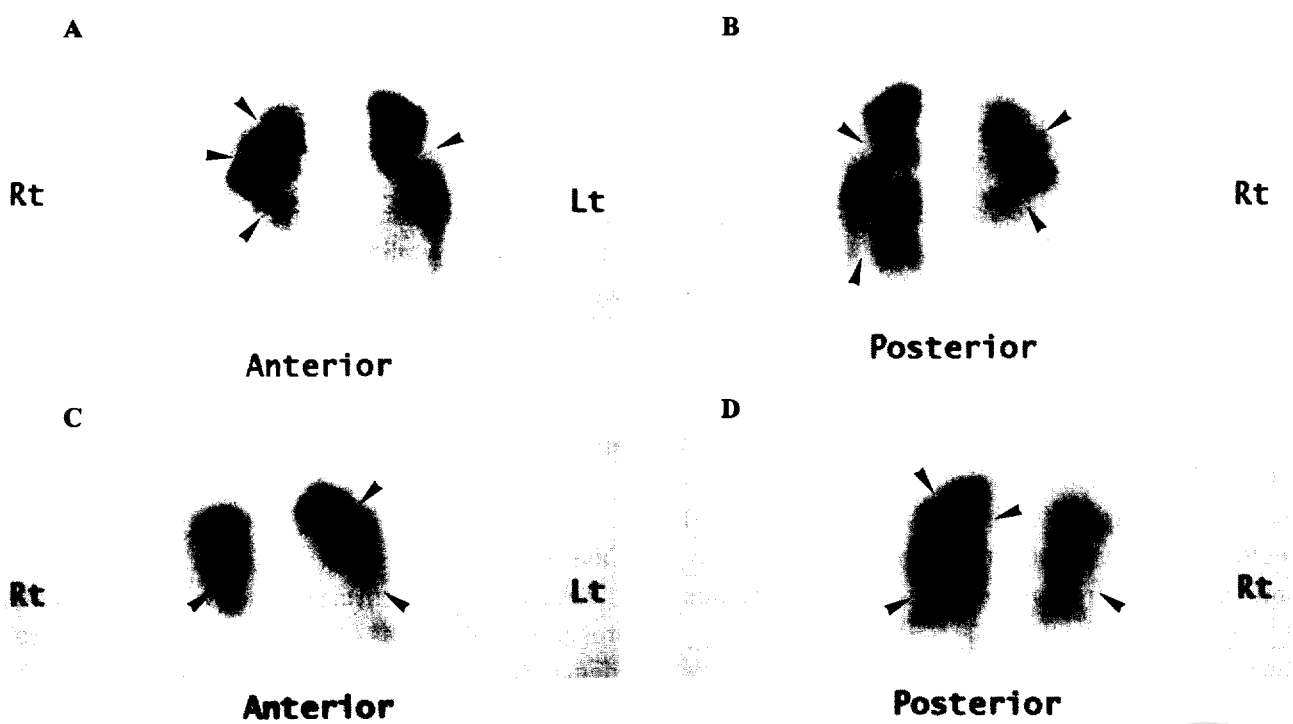

Fig. 1. Anterior and posterior views of perfusion lung scan in Case 1 (**A** and **B**) and Case 2 (**C** and **D**) showed multiple filling defects over both lungs. The arrowheads indicate the sites of perfusion defects in lungs.

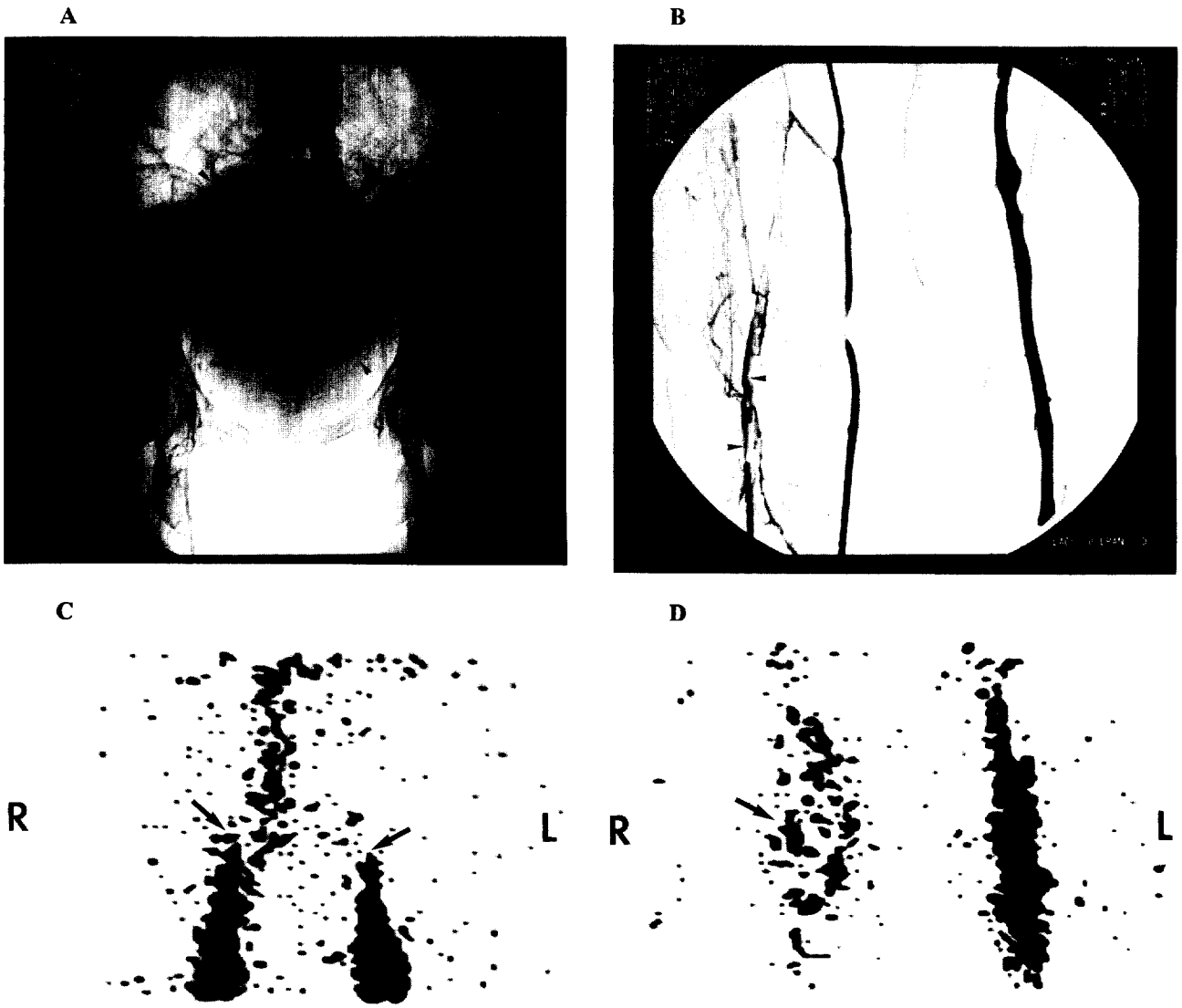

Fig. 2. Venography in Case 1 showed a mass lesion (arrowheads) over pelvis which made bilateral common iliac vein obstruction (curved arrows) **(A)** and multiple perfusion defects (arrowheads) over right popliteal vein (**B**). Tc-99m MAA venography in case 2 disclosed cutoff (arrows) with collateral sign of radio-uptake in the bilateral bifurcations of internal and external iliac veins (**C**) and collateral sign of radiouptake (arrow) over the right calf (**D**).

105 beats per minute, blood pressure 169/104 mmHg, and respiratory rate 20 breaths per minute. Cardiac examination revealed an accentuated P2, and a Gr. III/VI systolic murmur was audible over left sternal border. Breathing sound was normal. A large tumor was palpable in the patient's lower abdomen. Chest radiography displayed pulmonary trunk engorgement with clear lung field. An electrocardiogram showed sinus tachycardia, Q wave in lead III, and inverted T waves in leads V1-V5, III and AVF. Arterial blood gases with nasal O_2 at 3 L/min showed a PaO_2 of 74.6 mmHg and a $PaCO_2$ of 21 mmHg. Echocardiogram revealed a dilated and hypokinetic right ventricle and severe regurgitation of the tricuspid valve. Pulmonary artery pressure was estimated to be 82 mmHg. Lung perfusion imaging disclosed multiple perfusion defects in both lungs (Fig. 1, C and D). Tc-99m MAA venography of lower extremities showed cutoff lesions with collateral sign of radio-uptake in the bifurcations of internal and exter-

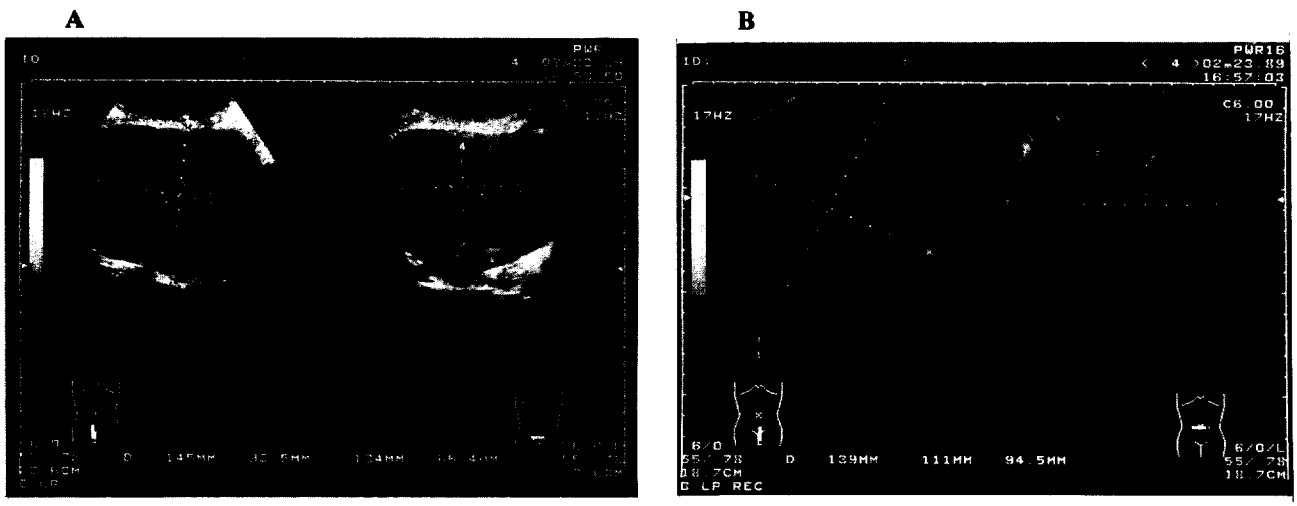

Fig. 3. Pelvic sonography revealed huge uterine myoma, measuring 145 × 93.5 × 104 mm in Case 1 (**A**) and 139 × 111 × 94.5 mm in Case 2 (**B**).

nal iliac veins (Fig. 2C and D). Pelvic sonography revealed a huge uterine myoma, measuring 139 × 111 × 94.5 mm^3 in size (Fig. 3B). Plasma levels of antithrombin III, protein C and protein S were within normal limits. Anticoagulation therapy was started. She became symptom-free after intravenous heparin followed by oral warfarin. Echocardiogram, performed one month later, showed normal ventricular size and minimal tricuspid regurgitation; pulmonary artery pressure was calculated to be 23 mmHg. One month later, the patient received laparoscopically assisted vaginal hysterectomy and the histopathologic finding showed adenomyosis and leiomyoma. Postoperative recovery was uneventful.

Discussion

Pulmonary thromboembolism usually is a complication of venous thrombosis. In approximately 70% of patients with pulmonary embolism, coexisting thrombi can be found in the deep veins of thighs or pelvis.[1,2] Deficiencies of antithrombin III, protein C, protein S and plasminogen are well-established inherited hypercoagulable abnormalities.[6-10] Acquired risk factors for deep vein thrombosis include increasing age, obesity, surgery, immobilization, trauma, cancer, chemotherapy, oral contraceptives, pregnancy, postpartum, stroke, spinal cord injury, indwelling central venous catheter and antiphospholipid syndrome.[6-10] It has been reported that there is a definite increase in the frequency of intravenous thrombosis, thrombophlebitis, and pulmonary embolus in women who have received hormone therapy containing estrogen.[11] For our two cases, inherited hypercoagulable states were excluded based on the normal values of plasma antithrombin III, protein C and protein S. Further clinical evaluation in our patients could not identify any of the significant, acquired prothrombotic conditions mentioned above. The effect of estrogen is also unlikely because our patients did not take high-dose hormone therapy for associated menorrhagia. The only possible causw of pulmonary embolismi our two cases is a a large uterine myoma.

Uterine myoma is a rarely reported risk factor that may precipitate deep vein thrombosis and pulmonary embolism. The pathogenesis of venous thrombosis may involve three interrelated factors ("irchow's triad"): damage to the vessel wall, slowing down of the blood flow and increase in blood coagulability.[6] The uterus is a pear-shaped muscular organ situated between the base of the bladder and the rectum. The size, location and orientation of uterine myoma determine the presence and the severity of symptoms. Compression of surrounding structures will result in urinary symptoms or hydroureter. Large posterior myoma may cause pelvic venous conges-

tion with edema of lower extremities and constipation. However, these symptoms are not often present in clinical situation. In our patients, bilateral common iliac vein compression by a mass (Case 1) and a cut-off lesion over the bifurcation of internal and external iliac veins (Case 2) were apparent on the venographic studies. It suggested that the large uterine myoma compressed iliac veins in the pelvis and the resulting venous injury and stasis caused deep vein thrombosis and pulmonary thromboembolism.[3-5,13]

Anticoagulation therapy is the classic treatment for acute pulmonary embolism, constituting secondary prevention rather than primary therapy. However, there is an increasing tendency to provide primary treatment of thrombolysis or mechanical intervention to pulmonary embolism patients with right ventricular hypokinesia. In our two cases, medical treatment with intravenous heparin was administered early and the clinical symptoms improved promptly so that thrombolytic therapy was not necessary. Oral warfarin was added to replace intravenous heparin for further prevention. Compression of the pelvic veins by an enlarged uterine myoma in patients with thromboembolic disease is an indication for hysterectomy, which is very important for long-term prevention of pulmonary embolism.[12] To reduce the surgical risk, hysterectomy was performed in our patient's after regression of tricuspid regurgitation and right ventricular hypokinesia was demonstrated by the follow-up echocardiography. However, it has been rarely reported[13] that emergent hysterectomy was performed to treat uterine myoma associated with acute pulmonary embolism and deep vein thrombosis under high surgical risk. Furthermore, several other reports suggested that insertion of umbrella filter over inferior vena cava just before hysterectomy might be effective to avoid aggravation of the thrombotic disease.[14,15]

In conclusion, patients with a large uterine myoma may develop deep vein thrombosis and acute life-threatening pulmonary embolism via the mechanism of venous stasis. Prophylaxis and early detection of deep vein thrombosis in high-risk patients should be attempted to reduce the morbidity and mortality of acute pulmonary embolism. It is also emphasized that a large uterine myoma should be recognized as a lethal predisposing factor for acute pulmonary thromboemolism and hysterectomy should be performed as the standard treatment following anticoagulation and/or thrombolytic therapy.

References

1. Moser KM.Venous thromboembolism. *Am Rev Respir Dis* 1990; 141:235-249.
2. Ryu JH,Rooke TW, Rosenow EC III. Venous thromboembolism. In: Giuliani ER, Gersh BJ, McGoon MD, Hayes DL, Schaff HV, editors. *Mayo Clinic Practice of Cardiology*. 3rd ed. St. Louis: Mosby, 1996: 1837-1851.
3. Nishikawa H, Ideishi M, Nishimura T, Kawamura A, Kamochi H, Tahara H, Tsuchiya Y, Shirai K, Okabe M, Arakawa K. Deep vein thrombosis and pulmonary thromboembolism associated with a huge uterine myoma. *Angiology* 2000; 51:161-166.
4. Chong YS, Fong YF, Ng SC. Deep vein thrombosis in patients with large uterine myomata. *Obstet Gynecol* 1998; 92:707.
5. Dekel A, Rabinerson D, Dicker D, Ben-Rafael Z. Thrombosis of pelvic veins associated with a large uterine myomatous ueterus. *Obstet Gynecol* 1998; 92:646-647.
6. Salzman EW, Hirsh J. The epidemiology, pathogenesis, and natural history of venous thrombosis. In: Colman RW, Hirsh J, Marder VJ, Salzman EW, eds. *Hemostasis and thrombosis: basic principles and clinical practice*. Philadelphia: JB Lippincott, 1993: 1275-1298.
7. Carson JL, Kelley MA, Duff A. The clinical course of pulmonary embolism. *N Engl J Med* 1992; 326:1240-1245.
8. Lensing AWA, Prandoni, P, Prins, Martin H, Buller HR. Deep vein thrombosis. *Lancet* 1999; 353:479-485.
9. Prandoni P, Lensing AWA, Cogo A. The long-term clinical course of acute deep venous thrombosis. *Ann Intern Med* 1996; 125:1-7.
10. Triplett DA. Antiphospholipid-protein antibodies: laboratory detection and clinical relevance. *Thromb Res* 1995; 78:1-31.

11. WHO Collaborative Study of Cardiovascular Disease and Steroid Hormone Contraception. Venous thromboembolic disease and combined oral contraceptives: results of international multicenter case-control study. *Lancet* 1995; 346:1575-1582.
12. Caprini JA, Arcelus JI, Hasty JH, Tamhane AC, Farbrega F. Clinical assessment of venous thromboembolic risk in surgical patients. *Semin Thromb Hemost* 1991; 17:304-311.
13. Ogawa N, Hyashi Y, Maechara T, Sato S, Tobe M, Ozaki T. A surgically treated-case of acute pulmonary embolism owing to deep vein thrombosis of leg mainly caused by uterine myoma. *Kyobu Geka* 1992; 45:631-634.
14. Greenfield LJ, Michina BA. Twelve-year clinical experience with the Greenfield vena cava filter. *Surgery* 1998; 104:706-712.
15. Decousus H, Leizorovics A, Parent F. A clinical trail of vena caval filters in the prevention of pulmonary embolism in patients with proximal deep-vein thrombosis. *N Engl J Med* 1998; 338:409-415.

巨大子宮肌瘤併發急性肺栓塞 —兩病例報告

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摘 要: 肺栓塞是臨床上造成死亡及罹病之常見原因。它通常是下肢深部靜脈栓塞的併發症。子宮肌瘤是深部靜脈栓塞罕見之危險因子。在此，我們報告兩病例皆因子宮肌瘤合併陰道出血來就診，入院後隨即被診斷有急性肺栓塞。臨床上，除了因子宮肌瘤導致骨盆腔及下肢靜脈淤積外，並未發現其他危險因子。我們以靜脈注射抗凝劑及子宮切除成功地治癒病人。我們必須確認子宮肌瘤是急性肺栓塞之重要誘發因子之一，並且在此強調子宮切除在治療這類病人之重要性。

關鍵詞: 急性肺栓塞、下肢深部靜脈栓塞、子宮肌瘤。

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