



# Venous Thromboembolism in a Woman with Diffuse Adenomyosis and Heavy Menstrual Bleeding: Case Report

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## ABSTRACT

This is a case of 41-year-old Filipina, nulligravid with no known comorbidities, admitted due to 1 month history of easy fatigability. Work up revealed acute pulmonary embolism with underlying Protein C deficiency and with concomitant diffuse adenomyosis presenting as abnormal uterine bleeding. The patient was treated with anticoagulation therapy for pulmonary embolism and with GnRH analog for adenomyosis. She was discharged stable and was advised close follow up for monitoring. Pulmonary embolism with concomitant diffuse adenomyosis is uncommon. Few case reports have described the interesting combination of adenomyosis and venous thromboembolism which poses a challenging management dilemma. In this patient with underlying protein C deficiency who presented with pulmonary embolism and deep vein thrombosis, the appropriate management is the use of anticoagulation. However, considering that the patient was also diagnosed of diffuse adenomyosis and concomitant abnormal uterine bleeding, anticoagulation may worsen the patient's bleeding and anemia. Treatment of adenomyosis using combined oral contraceptive pills would aggravate thromboembolism and vice versa. This patient was managed successfully using a multidisciplinary approach with anticoagulation and GnRH analog injection with no adverse event noted. In conclusion, occurrence of venous thromboembolism in patients with adenomyosis is uncommon, however can be managed successfully with a multidisciplinary approach and careful planning. Management of these patients present with great challenges and requires timely intervention, including meticulous follow-up strategies after pulmonary embolism to prevent recurrence and untoward side effects of treatment regimen.

## INTRODUCTION

Pulmonary embolism with concomitant adenomyosis is uncommon. Few case reports have described the interesting combination of venous thromboembolism (VTE) and adenomyosis which poses a challenging management dilemma. Treatment of adenomyosis would aggravate thromboembolism and vice versa. Anticoagulation would predispose the patient to more bleeding, while hormonal or antifibrinolytic therapy for menorrhagia is contraindicated in active VTE.<sup>1</sup> This case report will review management options and surveillance among these patients.

## CASE

Presented is a 41-year-old nulligravid Filipina, no known comorbidities, admitted due to 1 month history of easy fatigability. At the emergency room, patient was weak-looking, not in distress, no active bleeding with BP of 110/80mmHg, tachycardic at 110bpm, afebrile and with no desaturation. Further physical examination showed pale palpebral conjunctiva, the rest were unremarkable. Pertinent blood examination findings were mild anemia Hgb 102 g/L (120-160g/L), low serum Iron 21 umol/l (40-58 umol/l), slightly elevated Troponin 12.3 pg/ml (0-pg/ml) and elevated NT-pro BNP of 1359. 12-lead ECG showed regular sinus rhythm with non-specific ST T-wave changes while chest Xray was unremarkable. Gynecologic history revealed menorrhagia using 5 to 6 sanitary pads per day with 8 days duration per menstrual cycle. This was associated with cyclic hypogastric pain relieved with NSAID. The patient denies history of oral contraceptive pills, previous pap smear or sexual contact. There were no changes in menstrual cycle, no palpable masses, no changes in bladder or bowel habits and no gynecologic consult in the past.

During admission, blood transfusion of 2 units pRBC was done to correct underlying anemia, she was also referred to OB-Gynecology service for co-management, wherein a transrectal ultrasound revealed an impression of diffuse adenomyosis, secretory phase endometrium and normal ovaries with no suspicion of malignancy, at this time planned treatment regimen was GnRH analogue intramuscular injections since oral contraceptive pills are contraindicated in venous thromboembolism. 2D echocardiogram showed mildly depressed left ventricular systolic function with anterior and inferior base to apical septal wall hypokinesia, dilated right ventricular dimension and depressed systolic function, dilated right atrium, pulmonary hypertension and minimal pericardial effusion. At this time, pulmonary embolism (PE) was considered, hence a stat venous duplex of the lower extremity was done which showed acute to subacute deep vein thrombosis of the left femoral, popliteal and peroneal vein. The patient was started on LMWH 1mg/kg subcutaneously twice daily. CT angiography of the pulmonary arteries (CTPA) was subsequently done which showed bilateral pulmonary artery embolism, thus anticoagulation was continued. The patient was also referred to Hematology service for evaluation, work up revealed within normal anti-thrombin, Factor V, Homocysteine and ANA levels; however, Protein C was low at 56.2% activity (70 – 140%). Anticoagulation with LMWH was continued and was overlapped with Warfarin 5mg/tab, 1 tablet once daily and was continued as outpatient. The rest of the hospital stay were unremarkable, the patient remained hemodynamically stable with no episodes

of bleeding and within target INR values. The patient was subsequently discharged.

## DISCUSSION

Adenomyosis is a benign gynecologic condition, described as the presence of ectopic endometrial glands and stroma within the myometrium which commonly presents as cyclic menstrual pain, large uterus and abnormal uterine bleeding.<sup>2</sup> A causal relationship between VTE and adenomyosis has not yet been established and it is not known whether there is a direct link between the two conditions. In this patient with intermediate to high-risk severity of pulmonary embolism (sPESI score of 1), right ventricular dysfunction and positive troponin test, hospitalization and monitoring is needed due to the risk of early hemodynamic decompensation and circulatory collapse. Immediate anticoagulation is necessary with consideration of rescue perfusion if with clinical deterioration.<sup>3</sup> In the 2019 ESC guideline for Acute Pulmonary Embolism, it is reasonable to leave patients with intermediate-high risk PE on LMWH anticoagulation over the first 2 – 3 days and ensure the patient remain stable before switching to oral anticoagulation. Although warfarin was the traditional gold standard for anticoagulation among patients with pulmonary embolism, NOAC are now considered non-inferior to warfarin with lesser bleeding risk profile. The 2019 ESC guidelines, now recommends NOAC in preference to a vitamin K antagonist among eligible patients with no contraindications.<sup>3</sup> Considering that the more common risk factors for venous thromboembolism were absent in this patient, such as advanced age, major surgery, immobilization, cancer or a previous COVID-19 infection, work up for any hypercoagulable state was deemed necessary.<sup>4</sup>

In this patient with underlying protein C deficiency who presented with pulmonary embolism (PE) and deep vein thrombosis, the appropriate management is the use of anticoagulation, However, considering that the patient was also diagnosed with diffuse adenomyosis with abnormal uterine bleeding, use of anticoagulation may worsen menstrual bleeding and aggravate the patient's anemia. In a retrospective study of Hong et al in 2017, they evaluated the incidence of venous thromboembolism with concomitant adenomyosis. Of the 41 patients included in the study, five had associated venous thromboembolism (all five had pulmonary embolism). Three had worsening bleeding following anticoagulation which gonadotropin releasing hormone analogs were effective in controlling. Four of the five patients eventually underwent hysterectomy for long term management of adenomyosis.<sup>1</sup> Treatment of these patients remain challenging. In the setting of an active VTE, common management options for menstrual bleeding such oral contraceptive pills are usually contraindicated. All patients in the study of Hong et al were treated with GnRH analogs inducing a sustained period of amenorrhea, hence, preventing hemorrhagic episodes while ongoing anticoagulation treatment and until the thrombus has resolved.<sup>1</sup>

All patients with pulmonary embolism should receive at least 3 months of anticoagulation. Extended oral anticoagulation therapy reduces the risk for recurrent VTE by < 90%, but this benefit is partially offset by the risk of bleeding. However, in this patient with persistent risk factor for venous thromboembolism, extended duration of anticoagulation is recommended using

NOAC Apixaban or Rivaroxaban weighing the risk for increased bleeding.<sup>3</sup>

The patency of the pulmonary arterial bed is restored in the majority of PE survivors within the first few months following the acute episode; therefore, no routine follow-up CTPA imaging is needed. However, in some patients, thrombi become persistent and organized, which in rare cases may result in Chronic Thrombo-embolic pulmonary hypertension (CTEPH), a potentially life-threatening obstructing vasculopathy. The diagnosis of CTEPH is based on findings obtained after at least 3 months of effective anticoagulation, to distinguish this condition from acute PE hence the recommended follow up is after 3 months to assess symptom recurrence, bleeding risk and early 2D echocardiogram.<sup>3</sup> The aims of an efficient follow-up strategy should be to provide appropriate care such as exercise rehabilitation, treatment of comorbidity, behavioral education, and modification of risk factors and to ensure early detection of CTEPH for further diagnostic workup and specific treatment.<sup>3</sup>

In conclusion, occurrence of venous thromboembolism in patients with adenomyosis is uncommon and several treatment dilemmas may be encountered, however it can be managed successfully with careful multidisciplinary planning, timely intervention and meticulous monitoring. Efficient follow-up strategy after pulmonary embolism should be provided together with continuous gynecologic treatment and monitoring to prevent recurrence and adverse side effects of anticoagulation treatment.

## Keywords

Venous thromboembolism, Protein C deficiency, Pulmonary embolism, Adenomyosis

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