

On the case...

Chest pain in a young woman

By Lisa Morrow, DNP, FNP, LAc

What is the cause of increasingly severe chest pain that developed in an otherwise healthy 23-year-old woman?

LT is a 23-year-old woman who presents to the clinic for the first time for contraception. She has never been preg-

nant, has regular menses, and has used only condoms in the past for birth control. Her body mass index is 22.5 kg/m² and she is physically active, engaging in 1 hour of

aerobic exercise 5 days a week. She has never smoked. At this visit, the nurse practitioner (NP) determines that LT's health history is negative for any cardiac disease, hypertension, thromboembolism, known thrombogenic disorders, diabetes, and malignancies. Her family history is negative for cardiac disease, thromboembolism, and known thrombophilias. LT's blood pressure (BP) is 100/70 mm Hg. She is taking no medications.

LT's only health history of note includes diagnoses for seasonal affective disorder and panic/anxiety disorder. She had been taking escitalopram (Lexapro®), a selective serotonin reuptake inhibitor (SSRI), to treat her panic/anxiety symptoms, but she discontinued the medication 2 months previously because she was feeling less anxious and was concerned about SSRI-related side effects. Her panic/anxiety symptoms had worsened when she began her graduate school program but improved when she met her current partner. She still experiences panic/anxiety symptoms (mostly chest tightness) when preparing for examinations. The chest tightness does not affect her ability to speak or exercise. Her



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most recent panic attack occurred 5 months ago.

LT expresses an interest in using the vaginal contraceptive ring. She has no known contraindications for use of a combined hormonal contraceptive (CHC).¹ The NP provides a prescription for the vaginal contraceptive ring and instructs LT on Quick Start.

One month after starting the vaginal contraceptive ring, LT presents to the clinic with a complaint of chest pain that has been increasing in severity over the past 3 weeks. She describes having a fever and body aches that started 3 weeks ago, accompanied by chest pain, a non-productive cough, and fatigue on exertion. The fever, body aches, and cough have subsided. She describes the persisting chest pain as tightness accompanied by a feeling that she has phlegm in her throat that she cannot dislodge by coughing and an inability to get enough air on inspiration. The chest pain became more severe the previous evening while she was cheering at a sporting event.

What other elements of LT's current health history would be useful to know now?

On further questioning, the NP finds that LT's chest pain worsens upon exertion. LT experiences chest pain and shortness of breath (SOB) when walking up hills on which she used to run without any problem. Whereas she used to be able to talk while sprinting, she now finds talking difficult even when walking because of the pain and SOB. She reports the ability to climb three flights of stairs without stopping but has decreased her exercise to twice a week and for only 30 minutes. The chest pain is not wors-

ened by deep breathing, coughing, or changes in body position.

The patient describes the pain as being localized bilaterally above each nipple, with the affected areas about the size of a dime. She points to the area above each nipple in the third intercostal space to indicate the location. She denies nausea or vomiting; diaphoresis; radiation of pain to the shoulder, back, neck, or jaws; palpitations; hemoptysis; leg pain or swelling; or any tearing sensation. She has had no trauma to the chest or legs and has not had any prolonged or confined travel or other prolonged immobilization recently. She has no history of respiratory conditions, including asthma. She denies having any increased stressors in her life, any intimate partner violence, or use of cocaine or other stimulants.

What differential diagnoses would you be considering at this point?

Emergent considerations that the NP wants to be able to exclude are myocardial infarction (MI), pulmonary embolism (PE), pneumothorax, and aortic dissection. Other diagnoses the NP might consider, given some of LT's symptoms, are pneumonia, myocarditis, pericarditis, and panic disorder.

What would you include in your problem-focused physical examination?

LT's vital signs are heart rate, 80 beats/minute; BP, 92/70 mm Hg; respiration rate, 12/minute; temperature, 98.2°F; and oxygen saturation, 99%. The NP immediately notices that LT has rapid speech and is fidgeting. Her skin is pink, with no rashes or bruising, and is

warm, without diaphoresis. Chest pain is elicited when she climbs three flights of stairs, but her oxygen saturation remains at 99%-100%. Bilateral chest pain is reproducible upon palpation in the area above the nipples. She experiences SOB, manifested as difficulty speaking, when she and the NP climb stairs together, but she does not try to slow down.

Further chest examination reveals equal expansion, normal cardiac rhythm with no extra heart sounds or murmurs, no diminished or abnormal breath sounds, and no extra lung sounds. LT's abdominal examination results are within normal limits. She has no tenderness, redness, or swelling of her extremities.

Can you rule out PE based on the history and physical exam findings?

The CDC estimates that 60,000-100,000 Americans die of venous thromboembolism (VTE), including deep vein thrombosis (DVT) and PE, each year.² Undiagnosed PE has a 25% mortality rate. VTE, although uncommon, is one of the most serious possible adverse events related to CHC use. To put the risk for this patient in perspective, the rate of VTE is 29/10,000 woman-years in pregnant women, 9-10/10,000 woman-years in CHC users, and 4-5/10,000 woman-years in CHC nonusers.³

LT does not present with the classic picture of a PE. The PE Wells rule lists specific clinical features and assigns points to each feature to predict the likelihood of PE based on clinical findings.⁴ Point values for clinical characteristics are as follows: clinical signs of DVT, 3; alternative diagnosis less likely than PE, 3; previous DVT or PE, 1.5; heart rate >100

beats/minute, 1.5; recent (within the past 30 days) surgery or immobilization, 1.5; hemoptysis, 1; and cancer (treated within the past 6 months), 1. The clinical probability of PE is “low” with a total score of 0-1, “intermediate” with a total score of 2-6, and “high” with a total score >6.

Using the Wells scoring system, the NP notes that LT has no signs or symptoms of DVT, her heart rate is <100 beats/minute, and she does not have hemoptysis. She has not had extended immobilization or surgery in the past 4 weeks, has no previous history of DVT/PE, and no history of malignancy, and it does not seem at this point that an alternative diagnosis is less likely than PE. The Wells score for LT would be 0, indicating a low clinical probability of PE.

Nevertheless, the NP recognizes that the Wells rule, in isolation, cannot be used to exclude PE. What other factors should the NP take into account? What should she do next?

The fact that LT’s respiratory and chest pain symptoms have persisted over a 3-week period and are worsened by exertion is troubling in this otherwise healthy young woman. A further concern is that the symptoms started after recent initiation of a CHC. Because the NP wants to rule out a potentially life-threatening condition, she sends LT to the emergency department for further evaluation. Of note, LT removed her vaginal contraceptive ring 4 days ago and is due to insert a new ring in 3 days. The NP instructs her not to insert a new ring until the reason for her chest pain is determined.

Which laboratory and diagnostic tests are indicated in this case?

The gold standard to diagnose or exclude a PE entails a plasma D-dimer enzyme-linked immunosorbent assay (ELISA), chest radiography, and/or helical computed tomography (CT) pulmonary angiography. A plasma D-dimer ELISA has a 0.95 sensitivity (0.85-1.00) for negative likelihood; a negative D-dimer can exclude PE when the chest

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radiograph is negative.⁵ A positive D-dimer alone is of little clinical value in diagnosing PE. PE has occurred in 1.5% of patients with a negative CT pulmonary angiogram at 3 months.⁶

LT’s chest radiogram is negative, but her D-dimer ELISA is elevated, indicating the need for CT pulmonary angiography. The diagnosis of PE is confirmed with the CT pulmonary angiogram. LT is admitted to the hospital to start

anticoagulation and is discharged to home 2 days later. Prior to her discharge, LT receives education about her oral anticoagulation therapy, the possibility that her PE was an adverse effect of CHC use, and the need to discuss other contraceptive methods with her primary care provider (PCP). She is advised to follow up with her PCP in 2 weeks and with the hematologist in 6 months.

At her 2-week follow-up visit, LT states she has had no chest pain or difficulty breathing since her hospitalization. She is taking her oral anticoagulant without difficulty. She expresses concern about her future risk for another PE and reports that she read on the Internet about genetic predispositions to getting blood clots. The NP reviews measures that LT can take to reduce her risks for DVT and PE, which include not smoking, maintaining a healthy weight, and using strategies during prolonged confined travel such as taking breaks to stretch and exercising her legs to avoid venous stasis. She advises LT that she should not use hormonal contraceptives that contain estrogen.¹ LT chooses to use a nonhormonal intrauterine contraceptive, which is placed at this visit.

Should LT be tested for inherited or acquired thrombophilias?

An unrecognized acquired thrombophilia such as antiphospholipid syndrome or an inherited thrombogenic mutation (e.g., factor V Leiden; prothrombin mutation; protein S, protein C, or antithrombin deficiency) may contribute to a first VTE in a CHC user.¹ A retrospective cohort study of 160 women with a first VTE while using a combina-

tion oral contraceptive (COC) showed that the cumulative incidence of recurrent VTE was 5.1% after 1 year and 14.2% after 5 years.⁷ Significant factors associated with recurrence were renewed COC use (hazard ratio [HR], 8.2 [2.1-32.2]), antiphospholipid syndrome (HR, 4.1 [1.3-12.5]), and protein C deficiency or factor II prothrombin mutation (HR, 2.7 [1.1-7]). Use of a progestin-only contraceptive (HR, 1.3 [0.5-3.0]) and factor V Leiden (HR, 1.3 [0.5-3.4]) did not increase recurrence.

The genetic framework underlying VTE is complex and likely interplays with risk factors such as recent hospitalization, smoking, obesity, and CHC use. Decisions regarding duration of anticoagulant therapy and the need for thromboprophylaxis during pregnancy are best considered in terms of clinical risk factors. Testing for inherited thrombophilias provides an uncertain estimate of risk and is not recommended in most circumstances.^{8,9}

LT has a follow-up appointment with a hematologist in 6 months. She will discontinue the anticoagulant 2 weeks prior to this visit so that the workup will not be affected by the medication. The hematologist will reassess LT's risk factors and the need for further testing.

Reflection on this case

LT's only identified risk factor for VTE when she presented with chest pain and SOB was the use of a CHC. Results of studies looking specifically at the vaginal contraceptive ring and risk for VTE are mixed.^{10,11} However, several cases of VTE have been reported in women with no other identi-

fied risk factors besides vaginal contraceptive ring use.^{10,11}

Other diagnoses such as MI, pneumothorax, myocarditis, pericarditis, and pneumonia were unlikely given LT's history and physical exam findings. The history of panic/anxiety could have led the NP to initially consider panic attacks as the origin of LT's chest pain. The patient's rapid speech and fidgeting were a clear indication of anxiety, which could have been related directly to pain. Anxiety (sense of doom) and restlessness are also common findings with PE. The NP was correct to maintain heightened suspicion for PE in this otherwise healthy young woman presenting with chest pain and SOB who had recently initiated a CHC.

Recommendations for practice

Nurse practitioners should always conduct an appropriate workup to rule out VTE risk factors prior to prescribing a CHC for a given patient. All women using a CHC should be advised of symptoms of VTE that must be immediately reported to their provider. Routine screening for thrombogenic mutations is not appropriate because these conditions are rare and the cost of testing is high.¹ NPs should re-evaluate CHC users for risk factors at regular visits. NPs should always initiate testing to rule out or confirm PE if another cause of chest pain and/or SOB in a CHC user is not apparent. An elevated D-dimer indicates the need for urgent chest radiography, and, if inconclusive, a CT pulmonary angiogram.

A helpful tool to use when considering contraceptive options for patients seeking family planning

guidance is the **Medical Eligibility Criteria for Contraceptive Use^B**, published by the World Health Organization and most recently updated in 2010.¹² Tables in this document include recommendations for the use of contraceptive methods by women and men with particular characteristics or medical conditions.¹³ Each condition was defined as representing either a person's characteristics (e.g., age, history of pregnancy) or a known pre-existing medical/pathologic condition (e.g., diabetes and hypertension). NPs should check the CDC's **MMWR website^C** for up-to-date information regarding medical eligibility criteria for contraceptive use. ●

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