Family Practice Grand Rounds

Postpartum Pulmonary Embolism

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DR. LARRY NOVAK *(Associate Professor, Department of Family Practice)*: Today we want to discuss a common medical problem, pulmonary embolism, in an uncommon host, a healthy postpartum family practice patient, and how hospitalization affects the maternal-child relationship. Dr. Enders and I have followed this family in the family practice center and hospital. He will present the case.

DR. GARY ENDERS *(Third-year Family Practice Resident)*: Nancy C. is a healthy 21-year-old, gravida 2, para 2, woman who had a normal, spontaneous vaginal delivery at term. She had a normal prenatal course and had no risk factors for thromboembolic disease. She is slender, gained only 29 lb with the pregnancy, had no varicosities, is a nonsmoker, and had an uncomplicated 16-hour labor. Nine hours later she complained of shortness of breath and chest pain while walking to the bathroom. On examination, her respiratory rate was 36/min, pulse 130 beats/min, and systolic blood pressure was palpable at 70 mmHg. There was no excess uterine bleeding or tenderness of her legs. Her hematocrit was unchanged at 38 percent. Arterial blood gases showed a pH of 7.43, PCO_2 of 30 mmHg, and PO_2 of only 46 mmHg. An electrocardiogram showed sinus tachycardia, and incomplete right bundle branch block, with a S_1Q_3 complex. Her chest roentgenogram revealed scoliosis with clear lung fields. A lung scan done immediately thereafter showed three perfusion defects in the left lung and one perfusion defect in

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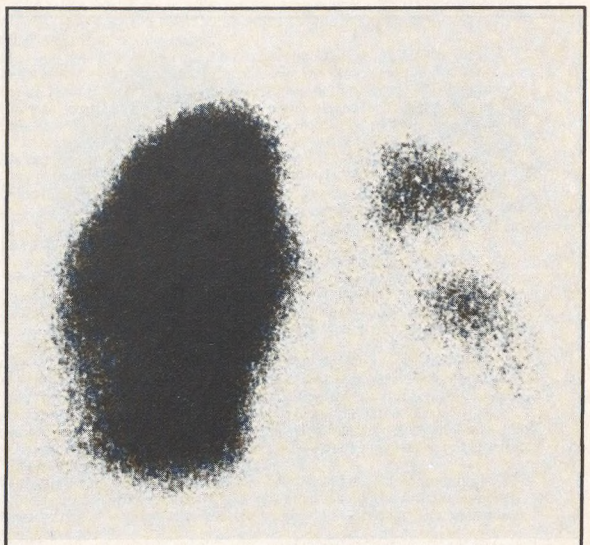

Figure 1. First lung scan, anterior view

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the right lung (Figure 1). A diagnosis of acute pulmonary embolism was made, and the patient was treated with an intravenous heparin drip. The patient was strongly motivated to breast feed, so she pumped her breasts for three days until the radiopharmaceutical used for the lung scan had decayed sufficiently.[1] Then she began breast feeding.

Three days later increased uterine bleeding was noted. The hematocrit dropped to 30 percent. She was treated with methylergonovine, and the bleeding decreased. Four days later an episiotomy hematoma formed that continued to bleed despite being drained, and she required two units of blood. Her heparin drip was discontinued until the bleeding stopped and then restarted at a lower dose.

On the eighth hospital day, she was begun on high-dose subcutaneous heparin, which was continued for six weeks. The doses were given each day at 8 AM and 8 PM, and adjusted to maintain the midpoint (2 PM) partial thromboplastin time (PTT) at 1.5 to 2.0 times control. She required 11,000 units of heparin per dose to accomplish this level of control.

Mrs. C. and her baby were discharged on the

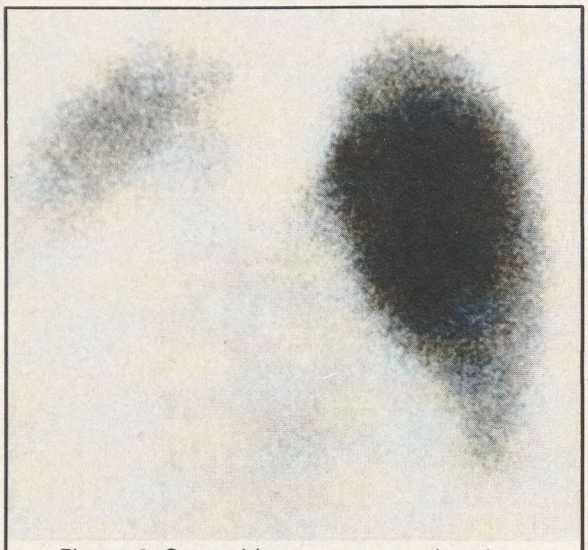

Figure 2. Second lung scan, anterior view

13th postpartum day. Mrs. C faithfully injected herself with heparin every 12 hours for the six weeks and did very well without dyspnea or other symptoms. At nine weeks of life, the baby was admitted to the hospital for two days with viral pneumonia. During the hospitalization Mrs. C. stayed overnight in a chair in her child's room. After discharge, Mrs. C. was carrying the child home when she suddenly developed shortness of breath and almost passed out. She was walking alone and barely managed to get home. She did not tell anyone about this episode until she brought her child in for a follow-up appointment a week later. At this time, Mrs. C. had a resting tachycardia of 150 beats/min and a respiratory rate of 30/min. A repeat lung scan showed almost complete loss of perfusion to the right lung (Figure 2). Cardiology and vascular surgery consultations were obtained, and further evaluation (angiography, venography) was considered, but it was felt to offer little information that would aid subsequent management. Because this second embolus was so large, intravenous streptokinase was used in an attempt to dissolve the clot rapidly. However, her thrombin time during streptokinase infusion remained baseline, and she was refractory to this therapy. Accordingly, streptokinase was discontinued and heparin begun. After six days, warfarin was started, and anticoagulation for at least six months was planned. An echocardiogram showed mitral valve prolapse and indicated possible pulmonary hypertension. She was discharged on the 12th hospital day. She slowly improved her exercise tolerance and proceeded to get back to normal. Because of her severe progressive scoliosis, she faces surgery in the future and probably will be in a body cast for six months.

The incidence of pulmonary embolism in the United States is estimated to be 650,000 per year.[2] Mortality is approximately 38 percent, and mortality is five to six times greater when the diagnosis is initially missed. Approximately 10 percent of those affected die in the first hour.

The risk of pulmonary embolism during pregnancy is only 1/100,000. In the postpartum state, hypercoagulability, loss of venous tone, and decreased physical activity place a woman at a somewhat greater risk—about 5/10,000.[3] Thromboembolism may stem from thrombophlebitis of pelvic or leg veins.

Heparin is the drug of choice for the treatment of pulmonary embolism during pregnancy. Warfarin is contraindicated, since it can cross the placenta and cause hemorrhagic complications in the fetus. The safety and effectiveness of adjusted-dose subcutaneous heparin for the long-term management of deep venous thrombosis has been documented by Hull et al.[4] In this study 106 patients with acute, proximal venous thrombosis confirmed by venogram and treated with conventional intravenous heparin were then randomized to either adjusted-dose heparin or warfarin for secondary prophylaxis. Two of the 53 patients receiving heparin, compared with 1 of the 53 receiving warfarin, had new episodes of thromboembolism. Nine patients taking warfarin had bleeding complications compared with one patient taking heparin. In the protocol described by Hull et al, heparin was given every 12 hours in adjusted doses, so the PTT taken six hours after a dose was 1.5 times control. After initial adjustments were made, there were no further changes in the heparin doses.

Since heparin does not pass into breast milk, it is safe for nursing mothers and was used in our

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patient. I felt that the use of warfarin while breast feeding was more risky. A British study, however, indicates that warfarin is probably also safe for nursing mothers.[5] In this study, warfarin could not be detected in the breast milk of 13 mothers taking it postpartum. Seven of the 13 mothers were breast feeding their infants; warfarin could not be detected in the serum of any of these infants. Three of these seven infants were measured for anticoagulant effect in their plasma; one of these infants was mildly affected at day 3 of life, but this improved slightly by day 7.

Warfarin is a weak acid (pH 5.0) and thus is present in ionized form at body pH. Warfarin is strongly bound to plasma proteins. Since warfarin is ionized, it has difficulty passing through the lipid barrier of the breast epithelium. The study concludes that warfarin is probably safe when given to breast-feeding mothers, but it would probably be advisable to monitor the prothrombin time (PT) of the infant.

DR. NOVAK: Did Mrs. C. consider switching to formula rather than breast feeding?

DR. ENDERS: She was very strongly motivated to breast feed. She did not breast feed her first child and had really anticipated breast feeding her second child.

RESIDENT IN THE AUDIENCE: Do you think it would be safer for the mother to take warfarin if the child was given a vitamin K preparation?

DR. ENDERS: Yes, that sounds like a good idea, since vitamin K counteracts the effects of warfarin.

DR. NOVAK: Are there any questions in regard to the home treatment?

THIRD-YEAR FAMILY PRACTICE RESIDENT: How did you decide to start with subcutaneous heparin in regard to dosage? Did you just pick a dose?

DR. ENDERS: One method is to total the amount of intravenous heparin given within 24 hours and then divide this into two doses. Dr. Hull and his colleagues found that the average dose of subcutaneous heparin required when given every 12 hours was 10,000 units. This is a good place to start.

FIRST-YEAR FAMILY PRACTICE RESIDENT: How did you follow up with laboratory testing?

DR. ENDERS: Six hours after the subcutaneous heparin injection, the PTT is measured and the dose is adjusted to make the PTT 1.5 times control. Once adjusted in the hospital, no further measurements are required. One benefit of twice daily heparin injections, as compared with warfarin, is that periodic anticoagulant tests are not needed, as shown in the study by Hull and colleagues.

Now I would like to discuss fibrinolytic therapy. The human hemostatic system is closely regulated and has the capacity of breaking down blood clots through the plasminogen-plasmin system (Figure 3). Plasminogen is an inactive proenzyme that can be activated to plasmin by certain endogenous stimuli. Plasmin is a very active enzyme that breaks down protein including fibrin clots. Both thrombolytic agents, urokinase and streptokinase, activate this endogenous fibrinolytic system. Urokinase is an enzyme derived from human kidney cells that cleaves two peptide bonds of plasminogen, forming plasmin.[6] Urokinase is much more expensive and less available than streptokinase. Streptokinase is a nonenzymatic protein produced by group C beta-hemolytic streptococci. Streptokinase forms an active complex with plasminogen, and this complex converts other plasminogen molecules to plasmin.

Most authors feel that thrombolytic therapy should be reserved for massive pulmonary embolism.[6,7] Our patient had a fairly large recurrent embolism in the setting of significant restrictive lung disease secondary to her scoliosis. She was probably not an ideal candidate for thrombolytic therapy, however, since her embolism was more than seven days old on admission to the hospital. After approximately five days, the fibrin clot becomes organized and somewhat resistant to lysis by plasmin.

DR. JAMES TUCKER *(Associate Professor, Department of Family Practice)*: Did you discuss future pregnancy with the family?

DR. ENDERS: Yes. Certainly she would be considered high risk for recurrent thromboembolic disease with future pregnancy. We discussed with her and her husband the need for subcutaneous heparin anticoagulation during the latter part of any future pregnancy. After her second embolus, however, Mrs. C. decided against future pregnancy and is now planning a tubal ligation, since she has two children already.

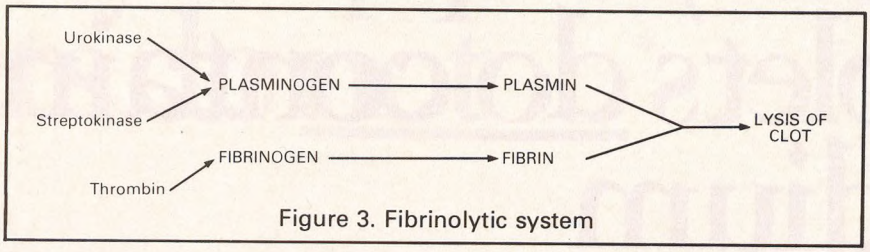

Figure 3. Fibrinolytic system

Although we assume that the changes in pregnancy and the postpartum period predisposed Nancy C. to thromboemboli, I would still consider her at greater risk in the future for nonpregnancy-related emboli than someone who had not had these problems. We would not suggest long-term coumarin therapy, and aspirin, dipyridamole, and sulfinpyrazone have not been shown to be effective in preventing recurrent pulmonary emboli. However, we would certainly not disagree with anyone who suggested long-term use of support stockings and avoiding prolonged sitting and external pressure to the legs.

DR. NOVAK: This brings up the problem of a hospitalized parent with a young child or children at home. Mary Studdiford will now discuss some things that can be done in the hospital or at home to try to keep families functioning during these difficult times.

MARY STUDDIFORD *(Family practice social worker)*: Concerns that come to mind when women with young children are hospitalized are bonding and child care. Many times these issues interfere with patient's compliance toward hospitalization. Mothers who are admitted, leaving an infant or young child at home, may feel inadequate because they are unable to care for their child. A certain degree of resentment toward the caretaker can occur as well as guilt for leaving a child or children at home.

Another recurring theme for women, particularly those with children aged under three years, is the fear that their children won't recognize them when they are reunited. Arrangements can be made during a lengthy hospitalization to enable the entire family to get together in a quiet corner of the lobby, waiting room, lounge, or even the patient's room.

It is common for women with dependent children to not have anyone who can provide child care, particularly for single parents or families with no relatives in the area. Social workers can help make child care arrangements. When family members are available, but will agree to help only if paid, we can arrange for the county Department of Social Services to reimburse that individual. We can also arrange for homemaker services to provide care in the home to supplement what the family can provide.

In those instances where there doesn't appear to be any alternative, parents have consented to place their children in foster care. Unfortunately, foster care carries negative implications because so many children have been placed as a result of child abuse. One of the advantages is that, when necessary, foster care can be arranged in a matter of hours. Many women would prefer to leave their children with an outside agency than depend on friends or relatives who may not be reliable, and there is never any trouble getting the children out of foster care when it is no longer required.

KATHY CAVANAUGH *(Family practice nurse practitioner)*: Do the foster parents bring the children to see the admitted parent?

MARY STUDDIFORD: Sure, and relatives are

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also strongly encouraged to visit the kids.

DR. NOVAK: Are there any additional questions?

DR. JAMES MARRON *(Assistant Professor, Department of Family Practice)*: Where was the site of the thrombosis?

DR. ENDERS: We don't know. On the first admission, we assumed it was of pelvic origin, so did not do any investigating. On the second admission, we did a phleborheogram, and it was negative. We elected not to do a venogram. We did do an echocardiogram to look for a possible thrombosis in the right ventricle. In addition, we wanted to confirm our suspicion of mitral valve prolapse.

QUESTION FROM THE AUDIENCE: Do patients with mitral valve prolapse have a higher incidence of pulmonary emboli?

DR. ENDERS: I don't think so. I am not aware of any such association. On examination she had an intermittent click and a systolic murmur, and my suspicion of mitral valve prolapse was confirmed on the echocardiogram.

DR. NOVAK: I want to thank all of you for a very interesting and informative discussion.

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