Thrombolytic Therapy During Active Menstruation: A Case Report

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The family physician is frequently the physician to whom a patient first presents when an acute myocardial infarction (MI) occurs. Early administration of intravenous thrombolytic agents decreases MI morbidity and mortality, and can safely be undertaken by family physicians even at community hospitals.[1,2] Accordingly, family physicians should understand the risks and benefits of thrombolysis in different settings. Because myocardial infarctions are more frequent in higher risk groups, clinical studies of thrombolytic therapy have primarily involved male and postmenopausal female subjects. We report a case dealing with a less frequent but nonetheless important situation: the use of intravenous tissue plasminogen activator (TPA) to treat an acute myocardial infarction sustained by a premenopausal woman during her normal menstrual period.

Case Report

A 29-year-old woman was admitted to the hospital 2 hours after the sudden onset of crushing substernal chest pain that radiated to her scapulae and was accompanied by dyspnea and diaphoresis. She had no previous diagnosis of coronary artery disease, but her cardiac risk factors were significant, and included a 16-year history of marginally controlled juvenile-onset diabetes mellitus, a history of heavy cigarette smoking, and the presence of premature coronary artery disease in several close relatives. She denied the use of cocaine or other illicit drugs. She denied upper gastrointestinal tract symptoms, hypertension, and any history of recent surgery, trauma, or bleeding problems. She had no history of stroke, brain tumor, or arteriovenous malformation. She had had two cesarean section deliveries and a miscarriage, none of which had occurred within the last 9 years. She denied a history of genitourinary tract problems, and was on the second day of her regular menstrual period.

The physical examination revealed a well-developed female patient in mild respiratory distress who was afebrile and had stable vital signs. Her lungs were clear. Her heart had a regular rate and rhythm, without murmurs, gallops, or rubs. Initial laboratory studies disclosed a hemoglobin level of 137 g/L (13.7 mg/dL). Her blood urea nitrogen (BUN) was 5.7 mmol/L (16 mg/dL), and her creatinine was 71 μmol/L (0.8 mg/dL). An electrocardiogram showed significant ST segment elevation in leads V_2 through V_6. Emergent echocardiography revealed significant hypokinesis of the distal septum and apex of the left ventricle, an ejection fraction of approximately 50%, and no mitral regurgitation or pericardial effusion.

A diagnosis of acute anteroseptal myocardial infarction was made. The cardiology service confirmed the diagnosis and assisted with patient management. The risks and benefits of the use of thrombolytic therapy in an actively menstruating patient were then considered. Specifically, the risk of uterine hemorrhage was weighed against the risk of progressive myocardial damage. After careful discussion with a cardiology consultant and an informed consent discussion with the patient, treatment was initiated.

Thrombolytic therapy was started 3½ hours after the initial onset of the patient's pain. One hundred units of TPA were given intravenously over 3 hours. Continuous infusions of intravenous nitroglycerin and heparin were started concurrently. About 2 hours after starting TPA, the patient noted some increase in her menstrual flow. She concurrently developed increased chest pain and nausea, and then vomited. The emesis contained a few flecks of blood. The chest pain resolved with a slight

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increase in the rate of her intravenous nitroglycerine drip, and she finished the thrombolytic therapy uneventfully.

Her chest pain did not recur and her ST segment elevation improved. She did not develop reperfusion arrhythmias. Cardiac enzyme studies supported the diagnosis of an acute MI, with her initial creatine phosphokinase (CPK) level of 78 IU/L followed 8 hours later by a peak of 1439 IU/L (7% MB). Her LDH_1 to LDH_2 ratio also increased from .55 to .89 in the first 24 hours.

Although the patient observed that her menstrual flow became heavier than usual during the TPA infusion, the duration of her period was decreased by about 1 day. Her hemoglobin level 12 hours after initiation of thrombolysis was 113 g/L (11.3 mg/dL), a drop of 24 g/L (2.4 mg/dL) from baseline. It gradually fell to a low of 91 g/L (9.1 mg/dL) by the 5th hospital day.

On the 5th hospital day, coronary angiography revealed a 90% mid-left anterior descending (LAD) artery stenosis, which was later successfully opened with percutaneous transluminal coronary angioplasty. She also had a 50% to 60% proximal LAD artery lesion, and 30% lesions of the proximal and mid-right coronary artery. The apical hypokinesis persisted, and 1+ mitral regurgitation was noted. She did well after the procedure, recovered rapidly, and was discharged from the hospital 9 days after admission.

After returning home, the patient was treated with insulin, aspirin, and metoprolol. She developed no further abnormal vaginal bleeding, and her hemoglobin returned to a normal level of 129 g/L (12.9 mg/dL). She also remained free of chest pain, and an exercise tolerance test 3 weeks after the MI occurred showed no signs of active myocardial ischemia. Unfortunately, she resumed her habit of cigarette smoking.

Discussion

Along with other types of internal bleeding, menstruation has been considered a contraindication to the use of thrombolytic therapy because of the risk of massive uterine hemorrhage. But physiologic control of uterine bleeding occurs primarily by contraction of endometrial vessels rather than by clot formation. It was decided that in this young woman uterine bleeding would be an acceptable risk compared with the possible morbidity that would be caused by a major anterior wall myocardial infarction.

A literature search revealed only one other report of the use of thrombolytic therapy in a menstruating woman.[3] After intracoronary administration of streptokinase, no increase in the subject's menstrual flow was noted. It is interesting that both TPA and urokinase occur endogenously in the human endometrium, which normally has plasminogen activator activity. In fact, Verstraete[4] reports that before cultured-cell lines were discovered that produced large amounts of TPA, the best source of TPA was the endometrium, from which about 1 mg of TPA could be produced per 5 kg of human uterine tissue.

Physiologically, plasminogen activator activity in the endometrium and uterine fluid appear to increase at mid-cycle, possibly to facilitate spermatozoa migration. Mid-cycle bleeding does not normally occur despite the peak activator activity. Most of the cyclic variation is due to urokinase, with the TPA activity contribution remaining fairly constant throughout the menstrual cycle. Overall activity levels remain relatively increased premenstrually, possibly facilitating normal menstruation.[5]

Although direct comparison of natural to pharmacologically obtained TPA levels may not be valid, it is interesting to note that the blood levels resulting from treatment with TPA are roughly 250 to 1000 times higher than the natural endometrial levels. Natural endometrial TPA levels range from 2 to 4 μg/L, while levels resulting from the administration of 60 mg of TPA over 1 hour are 1000 to 2000 μg/L. The clinical significance of this difference is not known.[5,6]

The reported patient noted an increase in volume but a shorter duration of menstrual flow, and there was a decrease in her hemoglobin. In the presence of adequate hydration, this decrease was likely due to combined blood loss from her minimal hematemesis, numerous blood tests, normal menstrual blood flow, and increased uterine bleeding caused by the TPA. Although difficult to quantitate, we believe that the TPA may have caused some increase in total menstrual blood loss. The increase in menstrual flow that was noted in our patient, as opposed to the patient of the earlier case report,[3] could be explained by the use of a different thrombolytic agent, by the route of administration (intracoronary vs intravenous), or by individual variation.

Although the number of myocardial infarctions sustained by menstruating women is small, such cases do occur and may be more common as a result of the increased prevalence of cocaine abuse. Family physicians should be prepared to consider the use of thrombolysis in the menstruating patient who presents with an acute MI.

This case demonstrates that intravenous TPA can be used in a menstruating woman without causing dangerous hemorrhage. Menstruation is not a pathologic cause of bleeding, and we believe that it should not be considered an absolute contraindication to the use of thrombolytic agents. Although this case report should not serve as a sole guide to therapy, it can stimulate investigation into the relative importance of the established contrain-

dications to the use of thrombolytics. Such study may provide further insight into the relative contributions of clotting and vessel contraction in menstrual hemostasis.

Key words. Fibrinolytic agent; menstruation; myocardial infarction.

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