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Case Report

# Enoxaparin as an Anticoagulant in a Multipara with a Mechanical Mitral Valve: A Case Report

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Patients who have undergone mechanical valve replacement require anticoagulation therapy with warfarin to prevent thromboembolism. However, administering warfarin to pregnant patients increases their risk of warfarin embryopathy or central nervous system disorders. Consequently, safer alternatives, such as heparin or low-molecular-weight heparin injection, are substituted for warfarin. However, limited research has been conducted on this subject, with no large-scale studies and particularly few investigations involving multiparous patients. A patient who had previously undergone mechanical mitral valve replacement for atrial septal defect and mitral stenosis received anticoagulant therapy with enoxaparin during 2 pregnancies. Upon confirmation of pregnancy, warfarin was replaced with subcutaneously injected enoxaparin with a dosage of 1 mg/kg at 12-hour intervals. The enoxaparin dosage was controlled using an anti-factor Xa assay, with a target range of 0.3–0.7 IU/mL. Intravenous heparin injections were administered starting 3 days prior to the expected delivery date and were continued until delivery, after which warfarin was resumed. No complications were observed during the deliveries.

**Keywords:** Multipara, Pregnancy, Anticoagulants, Heart valve prosthesis, Enoxaparin, Case report

## Case report

A 36-year-old woman presented to the cardiothoracic surgery outpatient clinic with a pregnancy plan. At 22 years of age, she had undergone atrial septal defect repair and mitral valve replacement with a 29-mm St. Jude mechanical valve at another hospital. Since then, she had been on anticoagulant therapy with warfarin.

The patient had a height of 167 cm, a weight of 58.5 kg, and no notable findings aside from cardiomegaly on a chest X-ray (Fig. 1). An electrocardiogram revealed atrial fibrillation and right bundle branch block, while transthoracic echocardiography demonstrated left atrial enlargement and mild aortic valve regurgitation. The prosthetic mitral valve function appeared normal, and the blood prothrombin time/international normalized ratio (PT/INR) was measured at 2.34.

The plan was to continue administering warfarin prior to pregnancy and switch to enoxaparin (Clexane; Sanofi, Paris, France), a low-molecular-weight heparin, once preg-

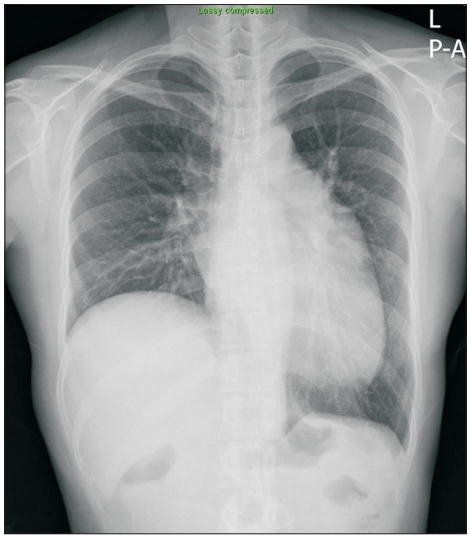


**Fig. 1.** Initial chest radiograph displaying cardiomegaly. L, left; P-A, posterior-anterior.

nancy was confirmed. While the patient was on anticoagulation therapy with alternating doses of 3 mg and 4 mg of warfarin, she tested positive on a urinary pregnancy test. An obstetric consultation confirmed a singleton pregnancy at 5 weeks of gestation, and an echocardiogram at the time showed an ejection fraction (EF) of 59%, a mean pressure gradient (PG) of 5.16 mm Hg, and a mean velocity (Vmean) of 1.04 m/sec. Subsequently, a standard dose of 60 mg of enoxaparin (1 mg/kg, provided at 12-hour intervals) was administered via subcutaneous injection twice daily. The dose was adjusted between 60 mg and 70 mg, targeting anti-factor Xa (anti-Xa) levels of 0.3 to 0.7 IU/mL, and monthly follow-up observations were conducted using an anti-Xa assay. At the 20th week of pregnancy, the patient experienced some vaginal bleeding; however, the amount was negligible, and only short-term follow-up observations were made without discontinuing enoxaparin. A transthoracic echocardiogram was performed monthly, and cardiac function was well maintained. No complications, such as valvular thrombosis, were observed. Prenatal ultrasounds were conducted monthly up to the 30th week of pregnancy, every 2 weeks from weeks 30 to 36, and weekly from week 36 onward. No abnormal fetal findings were observed. After consultation with an obstetrician, spontaneous vaginal delivery was determined to be the preferred method over cesarean section due to the risk of bleeding. Upon admission for delivery, enoxaparin was replaced with unfractionated heparin. This was discontinued 6 hours before delivery and reintroduced after confirmation that no major postpartum bleeding events had occurred. Warfarin was restarted the following day, and once the target PT/INR result of 1.8 was reached, heparin was discontinued.

The patient had a normal delivery on day 5 of the 37th week of pregnancy. Anticoagulant therapy was switched to warfarin starting on the evening following delivery. At that time, an echocardiogram revealed an EF of 53%, a mean PG of 7.6 mm Hg, and a Vmean of 1.45 m/sec.

However, on day 10 following the natural birth, the patient was readmitted to the emergency department due to postpartum hemorrhage. Warfarin administration was discontinued, and the patient received a blood transfusion. After a period of observation, she was discharged without complications.

During the second pregnancy, which occurred approximately a year and a half after the first delivery, the anticoagulant therapy was switched from warfarin to enoxaparin upon confirmation of pregnancy. At that time, an echocardiogram revealed an EF of 59%, a mean PG of 3.6 mm Hg, and a Vmean of 0.82 m/sec. The dose was adjusted monthly, targeting an anti-Xa level of 0.3 to 0.7 IU/mL (range, 0.5±0.2 IU/mL). At the 18th week of pregnancy, the patient experienced vaginal bleeding equivalent to a medium-sized pad; however, the condition improved with conservative treatment and temporary cessation of anticoagulant administration. The second delivery, a natural birth, took place on day 3 of the 38th week. Post-delivery transthoracic echocardiography showed preserved cardiac function, and the anticoagulant therapy was switched back to warfarin and maintained. The echocardiogram indicated an EF of 53%, a mean PG of 5.9 mm Hg, and a Vmean of 1.07 m/sec.

The patient provided written informed consent for the publication of the research details and clinical images on March 6, 2023.

## Discussion

Anticoagulant therapy with warfarin is crucial for pa-

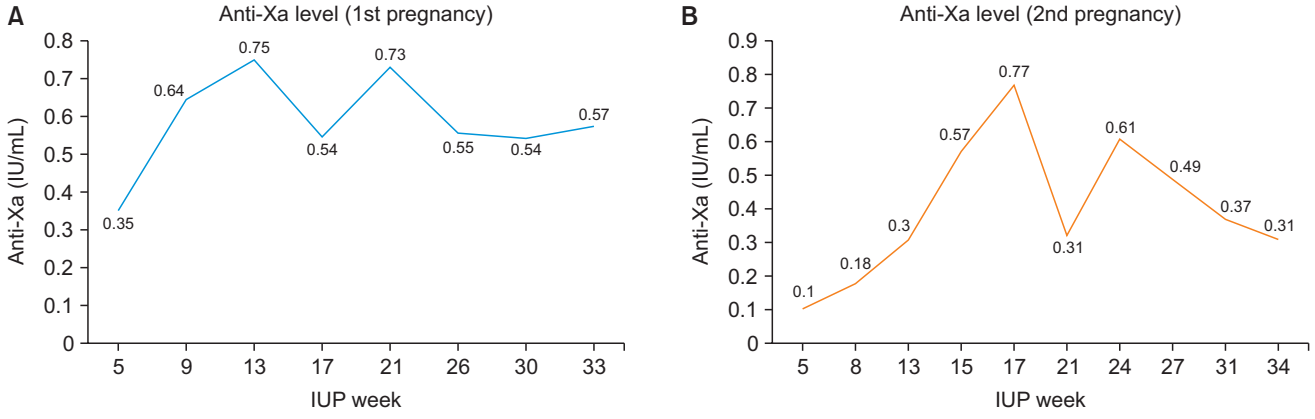


**Fig. 2.** Anti-Xa assay results. (A) Anti-Xa assay results in the first pregnancy. (B) Anti-Xa assay results in the second pregnancy. IUP, intrauterine pregnancy.

tients who have undergone mechanical valve replacement; however, its use in pregnant women is challenging due to the risk of congenital disabilities. Pregnant women experience an elevated incidence of deep vein thrombosis and pulmonary embolism because of increased coagulation levels, and the risk of thrombogenesis is even greater for those with atrial fibrillation. Consequently, anticoagulant therapy for pregnant women with atrial fibrillation and mechanical valves presents a meaningful challenge.

Anticoagulant therapy is frequently administered with heparin to pregnant women who cannot receive warfarin. Although numerous new anticoagulants besides heparin have recently become available, research on their use in pregnant women remains limited. Consequently, no definitive guidelines for anticoagulant therapy are available, especially in the context of multiple deliveries.

For the patient described in this case study, a comprehensive review of numerous journals was conducted, resulting in the selection of enoxaparin as a suitable alternative anticoagulant to warfarin due to its safety profile in pregnant women [1-6]. Minor differences in the reference range for anti-Xa levels were observed across various publications. Since Asian populations are known to have a higher bleeding tendency than Caucasians [7], a lower anti-Xa reference range of 0.3–0.7 IU/mL was chosen instead of the more commonly used range of 0.8–1.2 IU/mL [5,8-10]. The mean±standard deviation values of the anti-Xa results in the first pregnancy and second pregnancy were 0.584±0.127 IU/mL and 0.401±0.206 IU/mL, respectively. Although the results were slightly lower in the second pregnancy, the difference was not statistically significant.

Anticoagulant therapy with enoxaparin, an anti-Xa inhibitor, successfully prevented thrombosis and preserved cardiac function in a mother who underwent 2 deliveries without any fetal abnormalities. Enoxaparin was administered via subcutaneous injection twice daily at an initial dose of 60 mg (standard dose, 1 mg/kg; administered every 12 hours). Blood tests were conducted at 4-week intervals from pregnancy confirmation until immediately prior to childbirth, with dose adjustments made based on the test results (Fig. 2) [3,9-12]. Additionally, echocardiograms were performed to assess cardiac function and detect blood clots in the heart. Heparin bridging was administered before and after delivery to minimize the risk of perinatal complications and thromboembolic events [6,9,10].

Despite postpartum hemorrhage following the initial birth, the patient's condition was effectively managed through conservative treatment. Based on the current case, enoxaparin may be confidently employed as a safe alternative to warfarin in pregnant women with atrial fibrillation and mechanical valves, provided it is carefully monitored and administered according to a well-structured plan.

## Article information

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Conceptualization: YSL, JSK. Data curation: YSL. Investigation: YSL, JSK. Resources: JSK. Writing–original draft: YSL. Writing–review & editing: YSL, JSK. Final approval of the manuscript: YSL, JSK.

### Conflict of interest

No potential conflict of interest relevant to this article was reported.

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