A Case of Cerebral Infarction in Atrial Fibrillation Caused by Interruption of Warfarin Therapy for Colonoscopy

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ABSTRACT
A 75-year-old man was admitted to the emergency department with dysarthria. He had been taking warfarin because of atrial fibrillation and had a CHADS2 score of 5. The warfarin therapy was interrupted in preparation for colonoscopy and the patient developed a neurologic deficit 3 days after interruption of the therapy. Magnetic resonance imaging identified a cerebral infarction in the right frontal lobe. The patient was discharged after conservative management.

Key words: atrial fibrillation, cerebral infarction, colonoscopy, warfarin

Introduction
Warfarin is widely used in cases of atrial fibrillation (AF), venous thromboembolism (VTE), mechanical heart valve use, and stroke. Endoscopic procedures (e.g., esophagogastroduodenoscopy [EGD], colonoscopy, and sigmoidoscopy) are often used in Korea.

For AF with a high thromboembolic risk, bridging anticoagulation is used before such procedures. Because bridging therapy is expensive and time consuming, the procedure is instead performed with interruption of warfarin therapy in many cases.

We report a case wherein a patient with atrial fibrillation experienced a stroke when he temporarily stopped warfarin treatment in preparation for a colonoscopy.

Case
A 75-year-old man was admitted to the emergency room (ER) for dysarthria that was observed 4 hours earlier. When he arrived, body temperature was 36.0°C, pulse rate was 84 beats per minute with irregular beats, and blood pressure was 170/90 mmHg.
Figure 1. Twelve-lead electrocardiogram showed atrial fibrillation with non-specific ST-T wave change.

Figure 2. Brain computed tomogram showed an old left frontal infarction.

On neurologic examination, pupillary light reflex was prompt and he displayed isocoria. His eyes had a right–side deviation, visual field showed left hemianopsia, left facial motor tone had decreased, and peripheral motor tone was intact. His initial NIH stroke scale rating was 8 and his Glasgow coma scale score was 11.

Laboratory studies showed that the patient’s prothrombin time (PT) was 15.2 s (normal range 11.5~14.0 s), and PT international normalized ratio (INR) was 1.20, activated partial thromboplastin time (aPTT) was 30.6 s (normal range, 28.0~41.0 s); a random plasma glucose test showed that the plasma glucose level was 300 mg/dL (normal 70~110 mg/dL). The results of other laboratory tests were within normal limits.

Atrial fibrillation was detected in the ER (Figure 1). A computed tomogram (CT) (Figure 2) showed an old infarction in the left frontal lobe, but no sign of hemorrhage. Subsequent magnetic resonance imaging (MRI) (Figure 3 A, B, and C) identified an acute infarction in the right frontal lobe. However, because the symptom had occurred more than 3 hours earlier, thrombolysis was not performed.

The patient was under medical treatment because of a left middle cerebral artery (MCA) infarction that had developed 14 years earlier, as well as for
hypertension and diabetes mellitus. He had been taking warfarin as an outpatient and had a CHADS2 score of 5.

Interruption of warfarin therapy for colonoscopy had been recommended to the patient and the event occurred 3 days after this interruption of therapy.

His symptoms improved after conservative management and he was subsequently discharged.

Discussion

Many patients receive long-term treatment with warfarin because of AF, a mechanical heart valve, or VTE. Such patients frequently require warfarin therapy to be interrupted because of an upcoming surgery, tooth extraction, or invasive procedure.

The current European and US cardiology AF guideline1 recommends that bridging treatment should not be used in low-risk cases, but does recommend bridging in cases where the patient has a mechanical valve, a high risk of thromboembolism, or the therapy would need to be interrupted for more than 7 days.

It is uncertain whether such patients should receive bridging anticoagulation before and after a surgery or procedure. One study2 provided data on warfarin interruption in 492 patients (43% had AF) for surgery or a procedure. Bridging therapy was not used for 54% of the patients, while bridging with a therapeutic dose of heparin products was used for 33% of patients. Major bleeding occurred significantly less often when bridging therapy was not used (1.1%) than when bridging with a therapeutic dose of heparin products was used (6.8%); the difference was statistically significant. Thromboembolism occurred in 1.1% of cases where bridging therapy was not used and in 0% of cases where such bridging therapy was used; however, the numbers were too small for statistical comparison. The risk of major bleeding is strongly associated with the use of postoperative therapeutic doses of heparin products.

Another study3 was performed on 1,024 patients who underwent 1,293 interruptions of warfarin therapy for surgery or a procedure. Fifty-four percent of the patients had AF and 8.3% of the patients underwent bridging therapy with heparin products. The most common procedures were colonoscopy (25%) and oral or dental surgery (25%). More than 80% of patients underwent interruption

Figure 3. Magnetic resonance imaging findings. (A) Diffusion-weighted imaging (DWI) showed a high signal in the right frontal lobe, suggestive of acute infarction. (B) T2 weighted image showed high signal is seen in the left frontal lobe, suggestive of old infarction. (C) Magnetic resonance angiography showed occlusion of the superior branch of the right middle cerebral artery (arrow).
Table 1. Risk stratification for perioperative arterial and venous thromboembolism to guide the decision regarding whether bridging anticoagulation is required

<table>
<thead>
<tr>
<th>Thromboembolic risk category</th>
<th>Atrial fibrillation</th>
<th>Mechanical heart valve</th>
<th>Venous thromboembolism</th>
</tr>
</thead>
<tbody>
<tr>
<td>High risk (annual risk &gt;10%)*</td>
<td>CHADS$_2$ score of 5 or 6</td>
<td>Any mechanical mitral valve, older aortic mechanical valve (caged-ball, tilting disk)</td>
<td>Recent (within 3 months) VTE, High-risk thrombophilia</td>
</tr>
<tr>
<td></td>
<td>Recent (within 3 months) stroke or TIA, Atrial fibrillation, Rheumatic valvular heart disease</td>
<td>Older aortic mechanical valve (caged-ball, tilting disk), Recent (within 3 months) stroke or TIA</td>
<td></td>
</tr>
<tr>
<td>Moderate risk (annual risk 5-10%)</td>
<td>CHADS$_2$ score of 3 or 4</td>
<td>Bileaflet aortic valve prosthesis with ≥1 risk factor*</td>
<td>VTE within 3-12 months, Moderate-risk thrombophilia</td>
</tr>
<tr>
<td>Low risk (annual risk &lt;5%)</td>
<td>CHADS$_2$ score of 0-2 (no prior stroke or TIA)</td>
<td>Bileaflet aortic valve prosthesis without any risk factors†</td>
<td>VTE &gt;12 months prior</td>
</tr>
</tbody>
</table>

CHADS$_2$ score is based on cardiac failure (1 point), hypertension (1 point), age (1 point), diabetes (1 point), stroke (2 points). VTE: venous thromboembolism; TIA: transient ischemic attack.
*Additional patients who may be at high risk include those with prior thromboembolism during interruption of warfarin therapy.
†Age ≥75 years, atrial fibrillation, congestive heart failure, hypertension, diabetes mellitus, or stroke or TIA.
‡Deficiency of protein C, protein S, or antithrombin; antiphospholipid syndrome; homozygous factor V Leiden or prothrombin gene mutation
§Heterozygous factor V Leiden or prothrombin gene mutation
¶Cancer that is metastatic or was treated within the past 6 months

of warfarin therapy for 5 days or less. After 30 days of interruption, thromboembolism occurred in 0% of the patients who underwent bridging therapy and in 0.6% of patients who did not. Major bleeding occurred in 3.7% of the patients in the former category and in 0.2% of the patients in the latter. A brief (≤5 days) periprocedural interruption of warfarin is associated with a low risk of thromboembolism. The risk of major bleeding should be weighed against the thromboembolic risk for an individual patient before the administration of bridging therapy.

Because of thromboembolic risk and bleeding risk, the interruption of warfarin and the use of bridging therapy should be decided on a case-by-case basis. A randomized controlled trial (RCT), termed the BRIDGE study (bridging anticoagulation in patients who require temporary interruption of warfarin therapy for an elective invasive procedure or surgery), are being performed.

The BRIDGE study investigators' recommend the use of bridging anticoagulation therapy according to thromboembolic risk (Table 1). The 2010 Canadian guidelines' recommend that low bleeding risk for a surgery or procedure should not require interruption of warfarin therapy or consideration of bridging therapy. The 2009 American Society for Gastrointestinal Endoscopy (ASGE) guideline recommends not interrupting warfarin therapy for diagnostic tests (EGD, colonoscopy, or flexible sigmoidoscopy) including biopsy, as they are low-risk procedures.

However, these guidelines are not followed robustly in clinical situations. In a survey of
patients who temporarily stopped warfarin therapy, it was found that 57% had AF and 50% of the respondents had received at least 1 request for a periprocedural interruption of warfarin therapy during the prior 12 months. Nearly half (48%) of all requests to interrupt warfarin therapy were for guideline-discordant indications.

Because we expect a higher ratio in Korea, educational interventions may decrease the risk of periprocedural thromboembolic complications.

References


