Case Report

Perioperative transient ischemic attack caused by the cessation of warfarin

Sing-Ong Lee, Min-Jia Li, Hsin-Ming Ho, Chih-Cheng Chien, Shu-Lin Guo*

Department of Anesthesiology, Cathay General Hospital, Taipei, Taiwan, R.O.C.

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A B S T R A C T

This paper describes the circumstances of a patient who had been receiving long-term warfarin treatment, but ceased it prior to surgical operation, sustained a transient ischemic heart attack post-operatively, which eventuated in delayed extubation and locked-in syndrome. For patients at low risk of perioperative bleeding, anticoagulation with oral vitamin K antagonist can probably be able to maintain the therapeutic range (INR $\leq 2.0$) extreme. For patients with a high risk of bleeding, the international normalized ratio (INR) should be kept $\leq 1.5$. Within this range, patients at low risk of thrombosis can discontinue warfarin treatment for 2–5 days pre-operatively; patients at high risk for thrombosis can stop warfarin but should probably be treated with intravenous or subcutaneous heparin when the INR is subtherapeutic.

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1. Introduction

Many patients undergoing surgery may have been receiving anticoagulant therapy, such as warfarin, because of atrial fibrillation, installment of mechanical prosthetic heart valves, or previous deep vein thrombosis or pulmonary thromboembolism. Although anticoagulation increases the risk of bleeding during the surgical procedure, the interruption of an anticoagulant therapy, on the other hand, increases the risk of thromboembolism. This article narrates the circumstances of a patient who has been receiving long-term warfarin treatment, ceased it shortly before operation, and this act eventuated in post-operative transient ischemic heart attack which entailed delayed extubation and locked-in syndrome.

2. Case Report

The patient under discussion was a 76-year-old woman with a 7-year history of hypertension, who received a prosthetic mitral valve replacement about 10 years previously. She had been under regular oral medication, with co-diovan (hydrochlorothiazide 12.5 mg; valsartan 80 mg) 1# QD, bisoprolol (5 mg) 1# QD, and warfarin (5 mg) 1# QD. Three days before admission, she was brought to a local urologic clinic by reason of gross hematuria with blood clots. Under the impression of urolithiasis, she was referred to our OPD of urology for further evaluation. Intravenous pyelography revealed suspicious filling defect of the left renal pelvis. A cystoscopy was also performed, which showed no evidence of any malignancy.

On the day prior to admission, she experienced a sudden onset of abdominal cramping pain over the left lower quadrant (LLQ), and the pain was severe and persistent. Cold sweating and vomiting also intervened, and the patient was brought to the emergency department (ER), where physical examinations revealed a prominent tenderness over the LLQ, and a knocking tenderness over the left flank. Bilateral renal sonography was undertaken, which showed left hydro-nephrosis and hydroureter, for which, the patient was admitted for a left ureteroscopy and a double-J stenting.

In fear of perioperative bleeding, the surgeon discontinued the warfarin 5 days before the operation, and the pre-operative coagulation profiles were PT/PTc = 16.8/11.9, international normalized ratio (INR) = 1.88, and APTT/APTTc = 41.6/310. On arrival at the operating theater, her blood pressure was 152/48 mmHg, heart rate was 58/min, respiratory rate was 18/min, and oxygen saturation (SaO2) was 95% with room air. Her Glasgow Coma Scale (GCS) was E4M6V5 with normal-sized pupils (3 mm in diameter) and normal light reflex.

Since regional anesthesia was contraindicated because of bleeding tendency, general anesthesia was decided. Anesthesia was induced with glycopyrrolate (0.2 mg), fentanyl (75 μg), lidocaine (50 mg), propofol (100 mg) and rocuronium (40 mg) and following smooth intubation, anesthesia was maintained with desflurane in O2. Positive pressure ventilation was applied to keep SaO2 of 100%...
and PaCO₂ of 30–40 mmHg. There was no hypoxia, hypothermia or hemodynamic instability to happen during the whole course of the anesthesia. Ureteroscopy and double-J stenting were performed smoothly without the need of additional surgical relaxation and completed in one and half hours. The total perioperative fluid supplement was 200 ml glucose saline. Residual muscle relaxation was reversed with neostigmine (3.0 mg) plus glycopyrrolate (0.6 mg). However, a prolonged intubation of 40 min was noted in spite of unmolested train of four (TOF) stimulation. Thus, the neurologist was consulted, and neurological examination demonstrated a GCS of E1M1Vt, quadriplegia, and both pupils were fixed and sized 7.0 mm, without light reflex. During this period, there were twice blinking of eyes in response to calls.

Under the impression of locked-in syndrome (a condition in which a patient cannot move or communicate due to complete paralysis of most voluntary muscles except for those of the eyes, largely resultant from a brain stem lesion in which the ventral part of the pons is damaged), an urgent computed tomography scan (CT) was immediately carried out, but no hemorrhagic lesions were noted (Fig. 1). In a transitory period, of 1 h the patient suddenly restored voluntary movements. A transient ischemic attack (TIA) of the brain stem was highly suspected, and she was transferred to the surgical intensive care unit (SICU) for further treatment. After a loading dose of 5000 U heparin, another 25000 U heparin was given in continuous infusion to keep the PTT > 2.5× for anticoagulation therapy. The patient fully recovered and extubated 2 days later. Fortunately, there was no major squeal attributed to this event.

3. Discussion

Warfarin is recommended for patients with prosthetic heart valves to prevent valve thrombosis and thrombo-embolic events. Systemic embolization (predominantly cerebro-vascular events) occurs with an incidence of approximately 0.7 to 1.0 percent in patients scheduled for surgery bleeding risk of under anticoagulation therapy has to be weighed against the increased risk of thrombo-embolism caused by stopping the therapy. The risk of bleeding occurring during surgery in patients taking an anticoagulant therapy depends upon many factors, namely the patient’s age, the presence of other diseases, the type of surgery to be carried out. Prolonged, complex, and major surgeries are much more likely to cause significant bleeding problems than those short, simple and minor surgical procedures. On the other hand, most patients with valvular replacement could tolerate a brief interruption of anticoagulation therapy without sustaining valvular thrombosis or thrombo-embolism, and this was illustrated in a report on 159 patients with prosthetic valves in 180 non-cardiac operations without molestation. The oral anticoagulants were discontinued 1–3 days before operation, and as long as 1 week following surgery, without inviting perioperative thrombo-embolic events.

In case of pre-operative preparation for patients with prosthetic valve replacement under treatment of oral warfarin, it is a usual doctrine to wait a few days for the INR to fall below 2.0 after cessation of treatment as it was done in our case. One study prospectively evaluated 22 patients with a baseline INR of 2.6 in whom this level was considered to be safe for discontinuation of warfarin. Their INR fell to 1.6 at 2.7 days and 1.2 at 4.7 days and, as we learn from the textbook “Anesthesia” by Miller, it is a common practice to cease anticoagulant therapy 3 days before surgery for patients undergoing non-cardiac surgery with installment of a mechanical prosthetic valve. An INR of 2.3 may be adequate to prevent venous stasis and a thrombo-embolism, but INR > 3 will increase the risk of hemorrhage.

For patients with mechanical prosthetic valves, the pre-operative INR should be maintained at around 2.0, and at such a level, surgery can be performed with relative safety. On the other hand, a slight elevation of the INR by 1.5 should theoretically provide partial protection against a thrombo-embolism. In our case, the INR was 1.88 after a 5-day cessation of warfarin. Although the INR was acceptable, the patient still suffered from a TIA of the brain stem post-operatively, with presentation of lock-in syndrome. One article suggests that pre-operative and post-operative prophylaxis against thrombo-embolism with heparin should be considered in high-risk patients, by which the prosthetic valve is placid in the mitral position with the INR less than 2.0.

Heparin is usually reserved for those who have had a recent thrombosis or embolism (within 1 year), and those who have previously sustained atrial fibrillation, previous thrombo-embolism, hyper-coagulable condition, and mechanical prosthesis. A lower threshold should be considered in recommending the use of heparin in patients with mechanical valves, and discontinuation of which could then be carried out 4–6 h before surgery with resumption shortly afterwards. We are reminded that the activated partial-thromboplastin time (aPTT) should be closely monitored during the use of intravenous heparin.

In conclusion, although there are no recommendations based on solid evidences for the use of heparin, we must observe the following guidelines. For patients at low risk of perioperative bleeding, oral anticoagulation with a vitamin K antagonist can probably maintain the therapeutic range at or below the lowest extreme INR ≤ 2.0. For patients at high risk of bleeding, the INR should be ≤ 1.5. In patients at low risk of thrombosis warfarin can be discontinued for 2–5 days pre-operatively; in patients at high risk of thrombosis, warfarin can also be discontinued with proviso that intravenous or subcutaneous heparin must be given while the INR is subtherapeutic. Warfarin and/or heparin can be restarted post-operatively when there is no contraindication for anticoagulation therapy.
References