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CLINICAL REPORT

Suspected intraoperative formation of left atrial thrombus in a patient with atrial fibrillation receiving bridging anticoagulation therapy

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Abstract We present a patient with atrial fibrillation (AF) in whom a left atrial (LA) thrombus might have formed during laparotomy despite bridging anticoagulation therapy. No evidence of thrombus was detected by transesophageal echocardiography (TEE) at the start of surgery; however, a thrombus measuring 13 × 10 mm was found in the LA appendage by the end of the procedure, suggesting that thrombus might develop intraoperatively in patients with AF even when bridging anticoagulation is properly established. Intraoperative TEE can assist in detecting intracardiac thrombus in patients with AF regardless of their anticoagulation status and provides a tool for intervention to prevent systemic embolization.

Keywords Atrial fibrillation · Thrombus · Bridging anticoagulation therapy

Introduction

Atrial fibrillation (AF) is the most common perioperative cardiac arrhythmia. Its incidence increases with age, affecting 0.7 % of patients aged 55–59 years, increasing to 17.8 % in those aged over 85 years [1]. The incidence of first diagnosis or new onset AF in the perioperative period has been reported to be 2.3–12.3 % in non-cardiac surgery and 30–60 % in cardiac surgery [2–4]. Cardiogenic embolism is the cause of 42 % of perioperative cerebrovascular accidents (CVA), with AF present in 33 % of these patients at the time of the episode [5]. To reduce patients' risk of suffering a perioperative CVA, bridging anticoagulation therapy, in which heparin is given for 10–12 days around the time of the surgery when warfarin therapy is interrupted, is provided to patients with deep venous thrombosis, mechanical heart valve prostheses or AF [6]. However, the effectiveness of bridging anticoagulation therapy has not been well established [7]. Here, we report the case of a patient with AF in whom intracardiac thrombus might have formed during laparotomy even though bridging anticoagulation therapy was given. We suggest that screening for left atrial (LA) thrombus by transesophageal echocardiography (TEE) may offer an approach to lower the risk of CVA in high-risk patients undergoing surgery.

Case report

The patient provided consent for the publication of this case report.

A 77-year-old man (height 158 cm, weight 55 kg) presented for elective lower anterior resection for rectal cancer. At presentation he was taking warfarin 2.5 mg daily for AF associated with mitral valve stenosis (MS). Hypertensive nephropathy with an estimated glomerular filtration rate (eGFR) of 28.1 ml/min/1.73 m^2 and arteriosclerosis obliterans in both common iliac arteries were also diagnosed before surgery. A preoperative transthoracic echocardiography (TTE) showed normal biventricular systolic function, LA enlargement (LA diameter 62 mm) and moderate MS (mitral valve area 1.3 cm^2, mean pressure gradient 5.8 mmHg). In

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Table 1 Time-course of change in coagulation variables

Measurement	Day −3	Day −2	Day −1	Day 0	Day 1	Day 14
Prothrombin time (%)	44	83	70	Operation	77	32
PT-INR	1.76	1.12	1.27		1.18	2.3
APTT (s)	31.1	35.9	60.7		63.2	34.8
Platelet count (/μL)	138,000	146,000	136,000		130,000	308,000
Fibrinogen (mg/dL)	395	426	450		413	426
Antithrombin (%)		97	88			
Fibrin degradation products (μg/mL)		9.8	6.2			
D-dimer (μg/mL)		2.6	1.1			

PT-INR Prothrombin time-international normalized ratio, *APTT* activated partial thromboplastin time

accordance with the Japanese guidelines for management of anticoagulant therapy and the American College of Chest Physicians guidelines [6, 8], warfarin was withheld for the 3 days immediately prior to surgery and intravenous unfractionated heparin (UFH) was infused at a rate of 400 U/h. The patient did not have a genetic predisposition for hypercoagulability, such as antiphospholipid syndrome, cold agglutinin disease or deficiency in antithrombin III, protein C or protein S.

Two days before surgery, the patient complained of abdominal pain, nausea and vomiting. Abdominal contrast-enhanced computed tomography revealed an embolism in the ileal artery, a branch of the superior mesenteric artery. There was no evidence of intestinal ischemia, probably as a result of collateral arterial flow; however, this episode elevated his $CHADS_2$ score from 2 to 4. The $CHADS_2$ score is a validated method of estimating the risk of CVA in patients with AF, in which 1 point is awarded for a clinical history of congestive heart failure, hypertension, age >75 years, or diabetes mellitus, and two points are awarded for a history of stroke, transient ischemic attack or other arterial thromboembolism [9]. At this time, despite 400 U/h UFH, the activated partial thromboplastin time (APTT) value was only 35.9 s compared with a control value of 31.1 s. A vascular surgeon was consulted, and the infusion rate of UFH was increased to 600 U/h to achieve a target APTT ratio of 1.5- to 2.0-fold higher than that of control. The APTT value 20 h before surgery was 60.7 s (Table 1).

The heparin infusion was continued until 4 h prior to the patient being transferred to the operating room. General anesthesia was induced with propofol 70 mg and a remifentanil infusion of 0.5 μg/kg/min. Rocuronium 40 mg was administered to facilitate tracheal intubation. Anesthesia was maintained with sevoflurane 1.5 % and remifentanil 0.1–0.5 μg/kg/min. The heart rate was maintained between 70 and 90/min during anesthesia. After placement of a radial arterial cannula and a central venous catheter, TEE examination was undertaken using a Vivid I ultrasound system with a 6T-RS probe (GE Healthcare, Chalfont St Giles, UK). No thrombus was detected in the LA appendage (LAA) with careful observation by

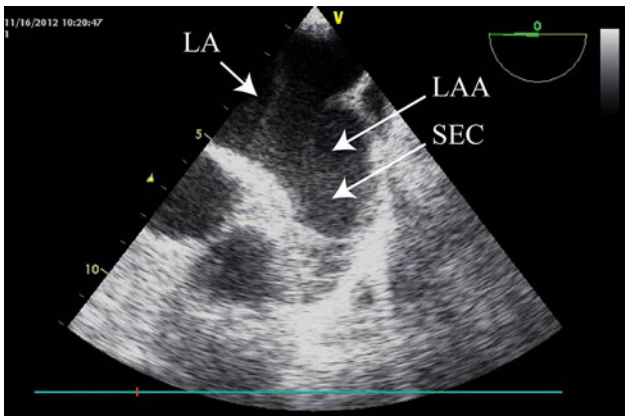

Fig. 1 An echocardiographic image of spontaneous echo contrast (*SEC*) of the left atrium (*LA*) and left atrial appendage (*LAA*) without evidence of thrombus

anesthesiologists experienced in TEE [Fig. 1; Electronic Supplementary Material (ESM) video 1]. The LAA had two lobes and the LAA Doppler flow velocity was approximately 15 cm/s. Activated clotting time (ACT) values were monitored hourly using a whole blood microcoagulation system (Hemochron Jr Signature; International Technidyne Corp, St Paul, MN). Intraoperative ACT values ranged between 171 and 199 s without administration of any additional anticoagulant.

The duration of surgery was 5 h and 12 min. The LA cavity was observed again at the end of surgery. Although no thrombus had been observed at the start of the operation, one measuring 13 × 10 mm was detected in the LAA at this time (Fig. 2; ESM video 2), leading to the resumption of anticoagulation therapy with intravenous UFH at a rate of 520 U/h within 1 h after surgery. In addition, warfarin 2.5 mg/day was restarted. The APTT value was 63.2 s on the first postoperative day. Two weeks later, the international normalized ratio of prothrombin time was 2.3. TEE examination revealed complete resolution of the LAA thrombus. The patient was discharged on the 25th postoperative day without evidence of arterial thromboembolism.

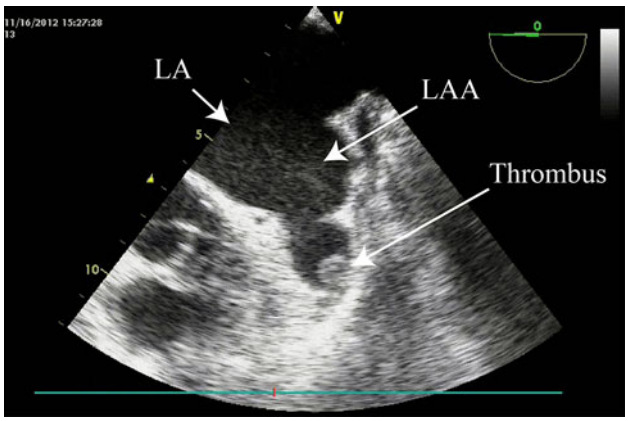

Fig. 2 An echocardiographic image of thrombus observed in the LAA

Discussion

We report the case of a patient with AF who might have developed LA thrombus during surgery despite perioperative anticoagulation bridging therapy.

It has been reported that valvular AF, which is mostly caused by structural changes in the mitral valve, carries the highest risk of CVA. Compared with the general population, the risk of CVA for patients with valvular AF is increased by 17-fold [10]. Our patient's $CHADS_2$ score was 4. In patients with a $CHADS_2$ score of 4, the risk of suffering a postoperative CVA within the first 30 days following surgery is 3.62 % compared with 8.5 % per year in the non-operative setting [11], indicating that patients with AF are at a substantially increased risk of thromboembolism in the perioperative period.

The thrombus most often seen in AF lies within the LAA [12]. As TTE has a low sensitivity for detecting LA or LAA thrombus (<60 %), TEE is considered the "gold standard" tool for diagnosing a LAA thrombus with a sensitivity and specificity of 100 and 99 %, respectively [13]. The presence of spontaneous echo contrast in the left atrium or LAA, low LAA flow velocity, and MS are considered to be the main risk factors for LAA thrombus formation [14–16].

Although our patient's anticoagulation therapy with warfarin had been switched to UFH, the initial dose was subtherapeutic, resulting in the formation of an ileal arterial embolism 2 days prior to surgery. Following the administration of 600 U/h UFH, the APTT measurements taken 20 h before surgery and at the end of surgery were 60.7 and 42.9 s, respectively, whereas the control APTT value was 31.1 s. Therefore, it is likely that the LAA thrombus formed despite appropriate bridging anticoagulation therapy administered in accordance with the guidelines for the pharmacotherapy of AF [6]. The intraoperative ACT values ranged between 171 and 199 s, which were slightly longer than expected. Culliford et al. [17] found that several factors, such as platelet function abnormality or low temperature, can increase the ACT value. The temperature of the patient was kept in the range of 36.5–37.5 °C. It is also recognized that renal failure can depress platelet function [18]. Although we did not evaluate platelet function, it is known that hypertensive nephropathy is the most plausible factor causing platelet abnormality, thereby leading to increased ACT values.

It is possible that a small thrombus was not detected because our TEE views represent slightly different angles. In this case, the undetected small thrombus may have become larger than 10 mm during the operation. This possibility suggests that intraoperative evaluation of TEE is important. To prevent CVA in patient with AF, antiarrhythmic therapy should be continued perioperatively [19]. In addition, the correction of electrolyte imbalance and fluid volume is important because electrolyte disturbances and dehydration increase atrial activity and predispose the patient to the arrhythmia. Immediate anticoagulation therapy after confirmation of appropriate hemostasis is crucial when thrombus is detected intraoperatively. In our case, the surgeons confirmed hemostasis at the operative site 1 h after surgery; thereafter, intravenous UFH was administered. The utility of perioperative thrombolytic therapy is limited because of the risk of bleeding [20]. Surgical removal of the thrombus is another option if massive thrombus is formed.

Although the incidence of thrombus formation in patients with AF during non-cardiac surgery is not known, intraprocedural formation of LA thrombus may be detected in 10 % of patients during AF ablation procedures [21]. The use of perioperative TEE could detect pre-existing LA thrombus, perioperative LA thrombus formation and delayed development of LA thrombus. In patients with AF at a high risk of CVA, i.e. those with a $CHADS_2$ score of >2, LA dilatation (LA diameter >4.5 cm), low LAA flow velocity (<20 cm/s) or an ejection fraction of <50 %, intraoperative TEE might provide a means of detecting cardiogenic thrombus and thus allow the patient to receive treatment to protect against the potentially catastrophic consequences of embolism.

In conclusion, we have reported a case of a patient in whom LAA thrombus formed over a relatively short time during a laparotomy, even though appropriate bridging anticoagulation therapy had been administered. Intraoperative evaluation with TEE might afford a means of detecting new LA thrombus so as to prevent embolism in patients with AF in the perioperative period.

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