CASE REPORTS

Anesthesiology
1996; 84:721–3

Fatal Paradoxical Cerebral Embolization during Bilateral Knee Arthroplasty

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NEUROLOGIC complications of knee and hip arthroplasty range from mild delirium to coma and death.[1] The pathogenesis and operative events that lead to acute neurologic injury during joint arthroplasty are not completely understood but are thought to be a consequence of the fat embolism syndrome.[1–3] The syndrome often is accompanied by pulmonary, circulatory, hematologic, and neurologic derangement. According to one hypothesis, procedures that increase intramedullary pressure promote the entry of marrow fat or other debris into the central venous circulation through the medullary veins.[3,4] These emboli accumulate within the lung, causing increases in the pulmonary vascular resistance and pulmonary artery pressure. The consequent increase in right atrial and pulmonary artery pressures favor right-to-left shunt flow *via* a patent foramen ovale (atrial septal defect) or intrapulmonary shunt increasing the risk of paradoxical cerebral embolization. In the following report, intraoperative hemodynamic monitoring, carotid artery ultrasonography, and electroencephalography (EEG) were used to detect the sequence of operative events that led to paradoxical cerebral embolization causing fatal neurologic injury during bilateral knee arthroplasty.

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Received from the Departments of Anesthesiology, Neurology, and Orthopaedics, University of Pennsylvania, Philadelphia, Pennsylvania. Submitted for publication September 15, 1995. Accepted for publication November 6, 1995.

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Key words: Brain: paradoxical embolization; stroke. Complications: fat embolism syndrome; paradoxical embolization. Surgery: complications; knee arthroplasty; orthopedics.

Case Report

An 84-yr-old, 51-kg woman underwent bilateral total knee arthroplasty for rheumatoid arthritis. Her medical history was notable for hypertension treated with pindolol and captopril. A preoperative transthoracic echocardiogram was notable for the presence of left ventricular hypertrophy.

General anesthesia was induced with fentanyl, thiopental, and pancuronium. Anesthesia was maintained with desflurane (1.4–1.8% end-tidal concentration), nitrous oxide (50–70%), epidural bupivacaine (0.5%), and epidural fentanyl (50 $\mu g \cdot ml^{-1}$). Extensive monitoring during general anesthesia was employed because of several recent incidents of hemodynamic and neurologic complications during single-stage bilateral knee arthroplasty. In addition to routine monitoring, a radial artery catheter, pulmonary artery catheter, and eight-channel scalp EEG (Grass model 9, Quincy, MA) in a longitudinal bipolar montage over both parasagittal regions were employed. The right common carotid artery and internal jugular vein were imaged transcutaneously by a 5.0-MHz phased array ultrasound transducer (Hewlett-Packard, Andover, MA).

Single-stage bilateral knee arthroplasty was performed sequentially on the right and left knees using Esmarch bandages to exsanguinate the limbs and pneumatic thigh tourniquets. After deflation of the first tourniquet following the first (right) knee arthroplasty, the pulmonary artery pressure, central venous pressure, and pulmonary vascular resistance increased (table 1), but there were no changes in the EEG waveforms or carotid ultrasound examination. After completion of the second (left) knee arthroplasty, deflation of the second tourniquet further increased the pulmonary artery pressure, central venous pressure, and pulmonary vascular resistance (table 1). This event was accompanied by the appearance of echogenic debris within the lumen of the right carotid artery and a decrease in high-frequency activity on the EEG waveforms (fig. 1). The amount of echogenic debris traveling cephalad in the carotid artery was maximum between 2 and 4 min after tourniquet release and persisted for more than 15 min after tourniquet release. EEG slowing was detected within 2 min and reached a nadir at 4 min after tourniquet deflation (fig. 2). The transient decrease in arterial blood pressure after release of each thigh tourniquet responded to treatment with 10 mg intravenous ephedrine and intravenous fluid administration. The decrease in oxygen saturation after the second tourniquet was released was treated by increasing in the inspired oxygen concentration to 100%.

After recovery from general anesthesia at the end of the operation, the patient's trachea was extubated when she resumed spontaneous ventilation and demonstrated the ability to obey simple commands. Postoperative laboratory tests were notable for an increased alveolar-to-arterial oxygen gradient (Pa_{O_2} of 217 mmHg breathing 100% O_2 from a nonrebreathing face mask), anemia (hematocrit of 30%),

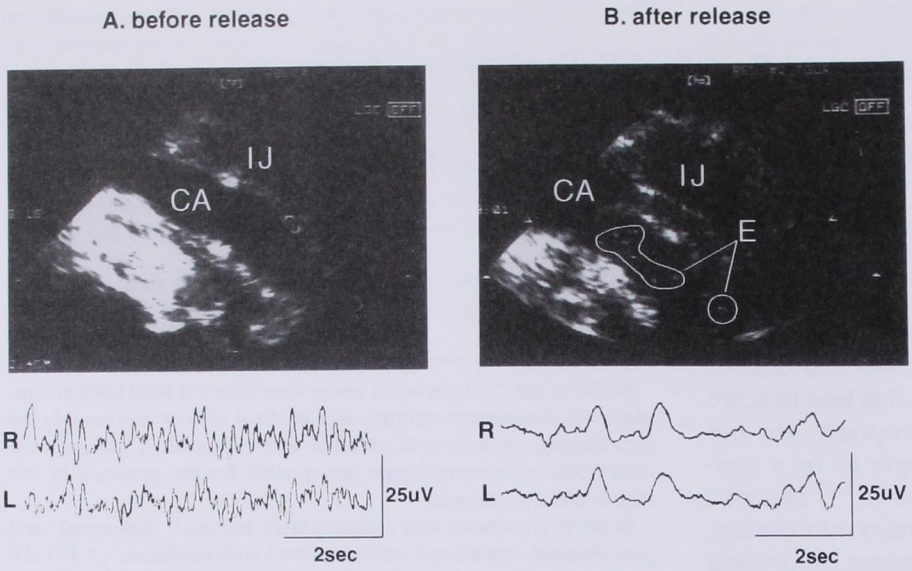

Fig. 1. Representative ultrasound images of the right carotid artery (*top*) and right (R) and left (L) prefrontal-to-frontal (Fp1-F3) electroencephalographic (EEG) waveforms (*bottom*) obtained shortly before (*A*) and after (*B*) release of the second tourniquet. After deflation of the second tourniquet (*B*, *top*), multiple intravascular emboli (E) were observed in the carotid artery (CA) but not in the internal jugular vein (IJ). Release of the second tourniquet was also associated with marked bilateral slowing and reduction of fast EEG activity (*B*, *bottom*) as compared to the EEG activity before tourniquet deflation (*A*, *bottom*).

thrombocytopenia (platelet count of $53 \times 10^9\ l^{-1}$), and coagulopathy (prothrombin activation time of 18 s, normal range 10–12.5 s; partial activated thromboplastin time of 80 s, normal range 23–34 s). The postoperative chest roentgenogram results were normal.

Six hours after the operation, the patient became progressively obtunded, and her trachea was electively reintubated to protect her airway. The neurologic examination was significant for responsiveness only to painful stimulation, absent corneal reflexes, and intermittent decerebrate posturing. The postoperative EEG showed severe diffuse slowing without seizure activity. Computed tomographic (CT) scans of the head demonstrated periventricular and subcortical lucencies that were consistent with multifocal regions of cerebral ischemia or infarction. Postoperative transesophageal echocardiography showed right ventricular and atrial dilation with moderate tricuspid regurgitation. A transesophageal echocardiography echocontrast and color flow Doppler study demonstrated the presence of an atrial septal defect and right-to-left intracardiac shunting. The patient's condition worsened, and the patient's family issued a "do not resuscitate" order. The patient died on the third postoperative day. The postmortem examination confirmed the presence of a patent foramen ovale and diffuse embolic infarcts throughout the brain.

Table 1. Hemodynamic and Respiratory Parameters in Relation To Tourniquet Release

	Release of First Tourniquet		Release of Second Tourniquet	
Parameter*	Before	After	Before	After
HR (beats/min)	54	53	50	58
BP (mmHg)	102/55	92/45	108/58	85/50
PAP (mmHg)	29/16	36/21	40/20	58/34
CVP (mmHg)	11	16	13	18
PAOP (mmHg)	14	15	20	21
CO (L/min)	3.39	2.36	3.42	2.30
PVR (dynes · s · cm^{-5})	149	372	156	730
SVR (dynes · s · cm^{-5})	1,408	1,514	1,442	1,518
Sp_{O_2} (%)	99	98	98	78
ET_{CO_2} (mmHg)	28	32	31	40

HR = heart rate; BP = radial artery pressure; PAP = pulmonary artery pressure; CVP = central venous pressure; PAOP = pulmonary artery occlusion pressure; CO = cardiac output; PVR = pulmonary vascular resistance; SVR = systemic vascular resistance; Sp_{O_2} = arterial oxygen saturation; ET_{CO_2} = end-tidal CO_2 tension.

* Values were recorded within 2 min before and after tourniquet release.

Discussion

Postoperative neurologic complications accompanied by pulmonary and circulatory derangements are known to occur as a consequence of joint arthroplasty.[1,4] In this report, a patient who underwent bilateral total knee replacements manifested a spectrum of pathophysiologic changes that culminated in fatal paradoxical cerebral embolization. The patient's final condition resembled the fat embolism syndrome as characterized by coma, hypoxemia, thrombocytopenia, hemodynamic instability, and coagulopathy. Intraoperative hemodynamic monitoring, electroencephalography, and direct ultrasound imaging of the carotid artery revealed several of the events and conditions that led to the neurologic injury. The increase in pulmonary vascular resistance, presumably caused by venous emboli from the arthroplasty site, was the primary event leading to paradoxical embolization of debris through a patent foramen ovale into the cerebral circulation.

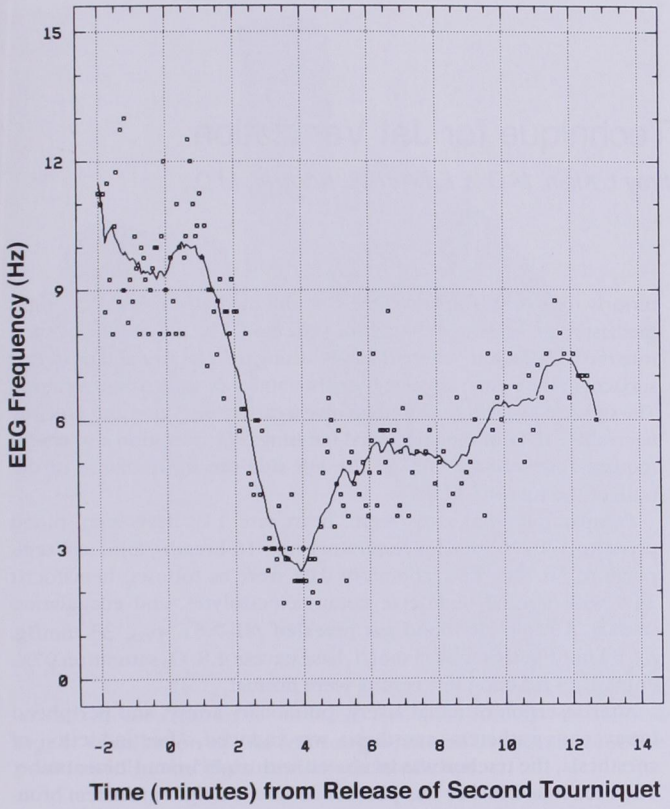

Fig. 2. The time course of the electroencephalographic (EEG) changes in relation to release of the second tourniquet (time 0). The EEG frequency is displayed as the zero crossing frequency of the left prefrontal-to-frontal channel (Fp1-F3). The decrease in EEG frequency was present bilaterally and began approximately 80 s after deflation of the second tourniquet.

The etiology of perioperative neurologic complications in this case was believed to be embolic in origin. It was unlikely that the depression of cortical electrical activity detected by EEG was caused by the transient hypotension. Although the arterial blood pressure decreased after the release of each of the tourniquets, significant EEG changes were observed only in association with the appearance of echogenic material in the carotid artery after release of the second tourniquet. The progressive postoperative neurologic deterioration could be explained by worsening cerebral edema as a consequence of the intraoperative injury. Finally, the postmortem examination verified the diagnosis of multiple cerebral infarctions caused by embolization.

Intracardiac and intrapulmonary shunting could explain the transit of venous emboli into the arterial circulation.[4] Although the presence of intrapulmonary shunting cannot be excluded, intracardiac shunting was the more likely source of paradoxical cerebral emboli in the presence of a patent foramen ovale. In a previous case report, fat emboli liberated during hip arthroplasty were visualized passing through the interatrial septum at the fossa ovalis.[2]

Embolization into the arterial circulation was temporally related to tourniquet deflation immediately after the second of two sequential arthroplasty procedures. Tourniquet deflation and limb reperfusion preceded increases in the central venous pressure, pulmonary artery pressure, and pulmonary vascular resistance that may have been caused in part by the accumulation of emboli within the pulmonary vasculature. Although the increased pulmonary artery pressure and pulmonary vascular resistance after release of the first tourniquet decreased slightly over time, they remained above baseline. Subsequent release of the second tourniquet was followed by a twofold increase in pulmonary artery pressure and a fivefold increase in pulmonary vascular resistance. The associated increase in right atrial pressure favored intracardiac shunting by increasing the pressure gradient across the interatrial septum or by distending the right atrium causing the foramen ovale to enlarge.

The findings described in this case report support the hypothesis that paradoxical cerebral embolization can be caused by the transit of venous emboli across the interatrial septum at the site of the fossa ovalis. Patients having a patent foramen ovale or atrial septal defect may be at increased risk of paradoxical embolization. Preoperative screening for this common abnormality, reported to be present in approximately 27% of people,[5] may be advantageous in patients for whom single-stage bilateral knee arthroplasty is considered.

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