Paradoxical Cerebral Embolism After Total Knee Arthroplasty

BRIAN W. HILL, MD; HANWEI HUANG, MD, PHD; MENGNAI LI, MD, PHD

Abstract

Deep vein thrombosis is a frequent complication following total joint arthroplasty and other major orthopedic procedures. Pulmonary embolism occurs with or without a diagnosis of deep vein thrombosis, although infrequently (1.5%-10%). In patients with congenital cardiac defects, such as a patent foramen ovale, paradoxical cerebral embolism may also occur. This article describes a case of a 52-year-old woman who sustained a paradoxical cerebral embolism following total knee arthroplasty.

In the workup of a patient with a known murmur and stroke symptoms, paradoxical cerebral embolism should be included in the differential. The initial evaluation should incorporate transesophageal echocardiography because of its accuracy in the demonstration of the cardiac physiology. An abnormal intracardiac or intrapulmonary shunt is essential for paradoxical cerebral embolism, allowing the entrance of the thrombus into cerebral circulation from the venous system. No clear consensus has been reached on the management of patients at risk for paradoxical cerebral embolism prior to orthopedic procedures. However, when an embolic stroke is diagnosed acutely, ideal management includes thrombolytic therapy, but further research is needed to confirm that this is the correct management. Due to the risk of recurrence, postoperative thromboprophylaxis is recommended with or without closure of the foramen ovale. Most importantly, and as demonstrated by the current patient, who partially recovered but did not require walking assistance after 2-year follow-up, treating physicians should be prepared to counsel patients through a lengthened physical rehabilitative process.

Figure: Diffusion weighted axial (A) and coronal (B) magnetic resonance images of the brain showing restricted diffusion in the pre- and postcentral gyri, which is consistent with a moderate-sized embolic infarct in the right perirolandic area.
Deep vein thrombosis (DVT) has been recognized as a potential complication following arthroplasty procedures. Pulmonary embolism can also occur with or without a diagnosis of DVT, although infrequently. Cases of paradoxical pulmonary embolism are rare, with few published as case reports. This article describes a case of a patient with paradoxical cerebral embolism after a total knee arthroplasty (TKA) that resulted in hemiparesis.

CASE REPORT

A 52-year-old woman underwent elective right TKA with a diagnosis of degenerative joint disease and worsening knee pain that was recalcitrant to conservative treatment. Her medical history was significant for type 2 diabetes mellitus, hypercholesterolemia, carpal tunnel syndrome, depressive disorder, and a slight cardiac murmur since childhood. Her body mass index was 36.6 kg/m². Preoperative assessment and physical examination included an electrocardiogram, which showed a sinus rhythm with nonspecific T wave abnormality, no evidence of ischemia or infarction, and normal left ventricular function. Other laboratory results, including coagulation profile, were within the normal range. The patient had no apparent operative risk; thus, no intervention was given.

The TKA was performed under general anesthesia and a femoral nerve block. The total procedure was performed with a tourniquet time of 84 minutes at 300 mm Hg. The patient tolerated the procedure, and no acute perioperative complications occurred.

Thirty-three hours postoperatively, the patient began to experience episodes of transient tachycardia with a heart rate from 113 to 124 and concurrent hypotension of 80/61 mm Hg (systolic/diastolic). She reported shortness of breath and recorded drops in O₂ saturation (86% on a 6-L nasal cannula). Troponin levels elevated and calculated glomerular filtration rate dropped to 47.2/173 mL/min. An electrocardiograph showed a sinus rhythm but an incomplete right bundle branch block, indicating inferior ischemia. Pulmonary embolism was suspected; however, spiral computed tomography angiogram of the chest was negative. Five hours following this episode, the patient reported blurry vision with difficulty focusing. She also had left facial droopiness and hemiparesis with normal sensation and a flat mood. Stroke (most likely embolic instead of hemorrhagic) was the working diagnosis, and a head computed tomography scan 2 hours after the onset of the preliminary symptoms demonstrated a subtle low density in the posterior aspect of the right frontal lobe, indicating mild acute ischemia. Magnetic resonance imaging of the brain displayed an embolic infarct in the right periorolanclic area (Figure 1). A subsequent echocardiograph showed left ventricular ejection fraction of 55% but an inconsistent bubble. Transesophageal echocardiogram demonstrated a positive bubble study with a 2- to 3-mm patent foramen ovale. Doppler ultrasound of the lower extremities was performed due to edema and showed occlusive clotting in the right posterior tibial vein extending from mid-calf to the ankle, but no evidence existed of DVT in the left lower extremity. Because the patient had recently undergone TKA, the medicine team did not proceed with thrombolytic therapy.

The patient began physical therapy on postoperative day 3 and was discharged 3 weeks later. She continued to work with physical, occupational, and speech therapy for 12 months. At 2-year follow-up, the patient was walking with no assistive device and recovered partially from left hemiparesis (Table 1). The patient reported slight weakness in hip flexion and extension but was able to attain 5 of 5 on all left lower-extremity muscle testing. The patient completed the stroke impact scale questionnaire developed to assess strength, hand function, mobility, activities of daily living, emotion, memory, communication, and social participation. Deficiencies were noted in strength and hand function (Figure 2). In addition, the patient completed the Western Ontario and McMaster Universities osteoarthritis index, with a score of 94.5.

DISCUSSION

Total knee arthroplasty has been a reliable surgical procedure for pain relief in patients with knee arthritis. Deep vein thrombosis is a well-known complication related to TKAs. The reported incidence is more than 50% in TKA, with approximately half of patients having no signs or symptoms referable to the limb. Stulberg et al studied 517 patients who underwent 638 TKAs and reported that 46% had venographic evidence of DVT in the calf and 11% had evidence of thrombosis in the thigh, popliteal vein, or both. However, less than 5% of these patients were clinically symptomatic. Few patients present with a pulmonary embolism (PE) (1.5%-10%) or fatal PE (0.1%-0.7%) after joint arthroplasty.
Among patients with PE, many had DVT on screening.\textsuperscript{14,15}

Conheim\textsuperscript{16} first described paradoxical cerebral embolism in 1877 as venous thrombosis causing systemic embolization through a right-to-left shunt. With a prevalence of 26\% in healthy patients,\textsuperscript{17} a patent foramen ovale can be detrimental in a patient with a traveling thrombus. In the current case, an occlusive thrombus was found in the posterior tibial vein of the operative side by Doppler ultrasound, likely the source of systematic embolus traveling through a congenital cardiac shunt.

Forty percent of cerebral infarcts are of undetermined causes despite comprehensive evaluation, and patent foramen ovale is believed to account for a significant fraction of cryptogenic stroke.\textsuperscript{18,19} An abnormal intracardiac or intrapulmonary shunt is essential for paradoxical cerebral embolism, allowing the entrance of the thrombus into cerebral circulation from the venous system. In a retrospective review of 4721 patients who underwent total joint arthroplasty, the incidence of stroke was reported to be 0.5\%; however, the cause was not determined.\textsuperscript{20} The exact incidence of paradoxical cerebral embolism remains difficult to determine, primarily due to its rarity and because it is often a diagnosis of exclusion. The diagnosis of paradoxical cerebral embolism is only definitive when made at autopsy or when a thrombus is seen crossing an intracardiac defect during echocardiography when an arterial embolus is present.\textsuperscript{21-23}

Despite the relatively high prevalence of patent foramen ovale, a paradoxical cerebral embolism is rare because the foramen ovale is closed by the pressure gradient of the left and right atria. An increase in right atrial pressure is required to create the right-to-left shunt. In the current case, before the onset of left hemiparesis on postoperative night 2, unexplained episodes of hypoxia, hypotension, and tachycardia occurred. Pulmonary embolus is the most common cause of acutely elevated right atrial pressure and right-to-left shunt in patients with patent foramen ovale or atrial septal defect, which occurs in at least 60\% of paradoxical cerebral embolism episodes.\textsuperscript{22} In the circumstance of combined paradoxical cerebral embolism and PE, the greatest danger of further paradoxical cerebral embolism seems to occur in the first few hours after the initial episode of PE.\textsuperscript{24-26} The current case had the characteristics of a PE episode before the paradoxical cerebral embolism. The onset of left hemiparesis happened 5 to 6 hours after episodes of unexplained shortness of breath and hypoxia, although a computed tomography angiogram of the chest revealed no pulmonary embolus.

Presumably, many factors were involved in producing DVT in the current case. Embolic materials, such as cement, blood clots, fat tissue, bone marrow, and surgical bone debris, could form during TKA.\textsuperscript{1,4,25,27,28} The surgical methods applied during TKA, such as limb twisting and knee flexion or application of a pneumatic tourniquet, is associated with the

### Table 1

<table>
<thead>
<tr>
<th>Function</th>
<th>Right</th>
<th>Left</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shoulder flexion</td>
<td>WNL</td>
<td>125\degree; improvement from 80\degree 6 months prior</td>
</tr>
<tr>
<td>Shoulder abduction</td>
<td>WNL</td>
<td>105\degree; improvement from 70\degree 6 months prior</td>
</tr>
<tr>
<td>Shoulder internal rotation</td>
<td>WNL</td>
<td>WNL</td>
</tr>
<tr>
<td>Shoulder external rotation</td>
<td>WNL</td>
<td>20\degree past neutral</td>
</tr>
<tr>
<td>Elbow flexion</td>
<td>WNL</td>
<td>WNL</td>
</tr>
<tr>
<td>Elbow extension</td>
<td>WNL</td>
<td>WNL; slow due to tone</td>
</tr>
<tr>
<td>Pronation</td>
<td>WNL</td>
<td>Able to move through full ROM</td>
</tr>
<tr>
<td>Supination</td>
<td>WNL</td>
<td>Able to move through partial ROM</td>
</tr>
<tr>
<td>Wrist flexion</td>
<td>WNL</td>
<td>Able to move through full ROM</td>
</tr>
<tr>
<td>Wrist extension</td>
<td>WNL</td>
<td>Able to move through partial to 30\degree</td>
</tr>
</tbody>
</table>

Abbreviations: ROM, range of motion; WNL, within normal limits.

![Figure 2: Summary report of Stroke Impact Profile. These 4 dimensions create the physical domain (asterisk). All scores are normalized values ranging between 0 (maximum dysfunction) and 100 (no dysfunction).](image-url)
formation of DVT.\textsuperscript{1,2,5,27,28} In the current case, the time of tourniquet application totaled 84 minutes. Studies have reported that the risk of DVT is significantly higher with a tourniquet application longer than 60 minutes.\textsuperscript{29,30} Occasionally, the transpulmonary passage of bone marrow fat dislodged in the course of intramedul- lary surgery could also cause neurologic deficits by an embolic brain insult.\textsuperscript{31} The current patient’s medical history, including type 2 diabetes mellitus, obesity, and age older than 40 years, contributed to the increased risk for the development of postoperative DVT.\textsuperscript{1,12,13}

No clear consensus has been reached on the management of patients at risk for paradoxical cerebral embolism prior to orthopedic procedures. Most paradoxical cerebral embolic events are associated with a patent foramen ovale of 0.6 to 1.0 cm, although some have been reported to occur with a patent foramen ovale smaller than 0.6 cm.\textsuperscript{34} The patent foramen ovale in the current case was between 2 to 3 mm as demonstrated with positive bubble study by transesophageal echocardiogram. Patients with a known patent foramen ova- le greater than 4 mm, atrial septal defect, or spontaneous passage of bubble contrast on transesophageal echocardiogram have been at higher risk for paradoxical cere- bral embolism.\textsuperscript{32,33} Preoperative percuta- neous closure of the patent foramen ovale was reported in a case report after a patient had symptoms of fat embolism syndrome after a long bone fracture and required further orthopedic procedures.\textsuperscript{34} In that report, the patient underwent intramedul- lary nailing of a femoral fracture after a positive patent foramen ovale was closed under angiographic and transesophageal echocardiogram guidance.\textsuperscript{34} Another case report documented a paradoxical cerebral embolism in a bilateral TKA.\textsuperscript{8} A transcatheater balloon was successfully used to close the patent foramen ovale after the patient became profoundly dysarthritic after tourniquet deflation. The cementing was deferred until 2 months later when the patient’s patent foramen ovale was closed with a transcatheter balloon, at which time the components were cemented.\textsuperscript{3}

In the current case, the medicine team did not use thrombolytic therapy although the diagnosis of a cryogenic stroke was confirmed less than 3 hours after onset. Although the reason for withholding the tissue plasminogen activator therapy was not documented in the notes, it was proba- bly withheld because the patient had recently undergone major surgery, which is 1 of the contraindications to tissue plasminogen activator therapy. Of note, infe- rior vena cava stent placement is reserved for patients with a contraindication to anticoagulation but is not believed to be helpful in patients with a patent foramen ovale.\textsuperscript{32} Filter placement does not prevent emboli smaller than 3 mm that may be as-ymptomatic as pulmonary emboli but can cause catastrophic arterial occlusion in the systemic circulation.\textsuperscript{23}

Although limited literature exists on the prevention of a paradoxical cerebral embolism in cases of a documented patent foramen ovale and high risk for DVT, few studies have reported the suggested follow- up. In 2 studies consisting of 140 and 132 patients, who had a paradoxical cerebral embolism, a 1.9% to 3.4% annual rate, re- spectively, existed of stroke recurrence or transient ischemic attack.\textsuperscript{36,37} Prevention depends on careful preoperative screening and postoperative thromboprophylaxis,\textsuperscript{37} and closure of the foramen ovale by less invasive techniques may be recommended in patients with documented large cardiac de- fects or increased right atrial pressures.\textsuperscript{8,38}

\textbf{CONCLUSION}

Paradoxical cerebral embolism following TKA is rare but potentially catastroph- ic. Paradoxical cerebral embolism should be included in the differential in the work- up of patients with known murmurs and stroke symptoms. Initial evaluation should include transesophageal echocardiogra- phy because of its accuracy in the demon- stration of the cardiac physiology. When an embolic stroke is diagnosed acutely, ideal management includes thrombolytic therapy; however, further research is needed to confirm that this is the correct management. Most importantly, treating physicians should be prepared to counsel patients through a lengthened physical re- habilitative process.

\textbf{REFERENCES}


