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CASE REPORT

Cerebrovascular infarction following bilateral total knee arthroplasty and tranexamic acid administration

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Tranexamic acid has been shown to reduce perioperative blood loss without increasing the risk of venous thromboembolism after total knee replacement. However studies to date were designed to assess efficacy as the primary outcome and were not powered to assess safety. We report the case of a 65-year-old male with a previously undiagnosed patent foramen ovale who suffered pulmonary emboli and cerebrovascular infarction after synchronous bilateral total knee replacement during which tranexamic acid was administered intravenously.

Keywords : cerebrovascular infarction ; bilateral total knee replacement ; tranexamic acid ; patent foramen ovale.

INTRODUCTION

Total knee replacement (TKR) is usually associated with marked perioperative blood loss and may necessitate allogenic blood transfusion. Potential complications of transfusion include acute and delayed haemolytic reactions, anaphylaxis, transfusion-associated acute lung injury, immunosuppression and disease transmission.

Antifibrinolytics such as tranexamic acid (TXA), epsilon-aminocaproic acid (EACA) and aprotinin have been used to reduce perioperative blood loss. Aprotinin was withdrawn form world markets in May 2008 because of concerns that it increased the risk of cardiovascular complications and death (*2,3*). Systematic reviews of randomised controlled trials have shown that TXA significantly reduces perioperative blood loss and blood transfusion requirements without increasing the risk of deep-vein thrombosis (DVT) or pulmonary embolism (PE) after total knee replacement and major surgery (*1,3*). However concerns have been expressed that the studies are underpowered to assess safety and that reporting of uncommon events in the small clinical trials included in the reviews may be inadequate (*1,3*).

We report the case of a 65-year-old male undergoing simultaneous bilateral total knee replacement in whom TXA was used to reduce perioperative blood loss.

CASE REPORT

A 65-year-old male was admitted to our elective orthopaedic unit for bilateral TKA in a single stage. He had a background history of bilateral knee osteoarthritis, ischaemic heart disease having suffered a

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myocardial infarction 8 years prior and having undergone triple coronary bypass grafting 3 years previously, and diet controlled type 2 diabetes mellitus. He had attended pre-operative assessment two weeks prior to his operation where routine investigations were performed (clinical examination, electrocardiogram (ECG), chest radiograph, full blood count and renal profile). The ECG showed a normal sinus rhythm. His haemoglobin was 13.8 g/dl and his haematocrit was 0.404 l/l. The prothombin time of 11.2s was within the normal range (9.7-11.3), as was the activated partial thromboplastin time (APTT) of 30 (23-31). His preoperative physical status was classified as American Society of Anesthesiologists (ASA) grade II.

The bilateral TKR was performed sequentially under the same spinal anaesthesia, beginning with the right knee. The tourniquet was sequentially inflated. The standard surgical technique was used for the fixed bearing, posterior-stabilized cemented prosthesis (P.F.C.® Sigma™). An intra-articular negative suction drain was inserted bilaterally. Each wound was closed prior to the release of the corresponding tourniquet. One gram of TXA was administered intravenously prior to deflation of the second tourniquet. The surgery took 1 hour 40 min from knife to skin until completion of dressings, with a 20 min preceding anaesthetic induction time. There were no unexpected events or immediate complications.

For thromboprophylaxis, 4500 IU of subcutaneous tinzaparin was given daily, commencing the evening prior to surgery. The second dose was given 10 hours postoperatively. Ankle pumps and early mobilization also formed part of the standard TKR thromboprophylaxis protocol.

On the morning following his surgery, the patient noticed that his speech was slurred. He was found to have a right facial droop and right upper limb weakness. He was promptly transferred for acute medial assessment at the neighbouring tertiary referral centre. At presentation he was alert and orientated. He had a marked dysarthria with an associated right-sided facial weakness. Eye movements and facial sensation were normal. There was significant weakness of his right upper and lower limbs but no sensory abnormalities. His right plantar reflex was upgoing. His calf muscles were not swollen. His chest was clear to auscultation but pulse oximetry revealed hypoxaemia (an oxygen saturation of 80% on room air). He was normotensive and an ECG showed normal sinus rhythm. A chest radiograph could not account for the hypoxaemia.

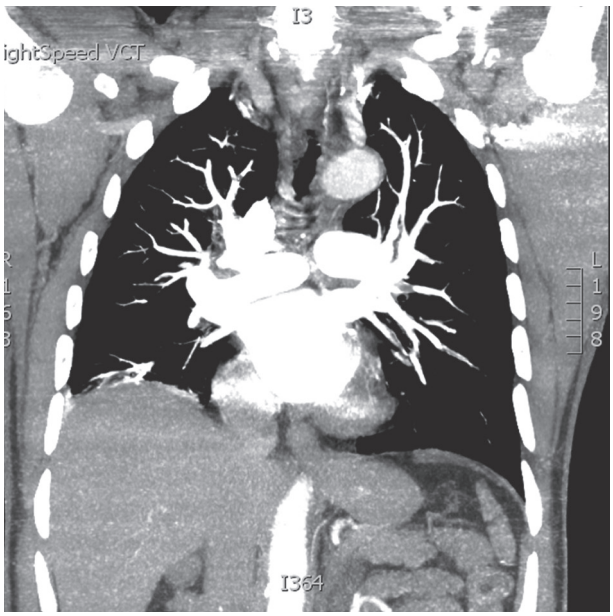

Fig. 1. — CT pulmonary angiogram showing bilateral filling defects.

A computed tomography (CT) pulmonary angiogram showed several filling defects arising from the first order branches of the left pulmonary artery and further smaller filling defects in the right upper lobe pulmonary arteries, consistent with pulmonary emboli (Fig. 1). An initial non-contrast CT brain was normal but a subsequent magnetic resonance (MR) brain scan without gadolinium showed an acute infarct of the basilar part of the left pons with smaller bilateral peripheral cerebellar infarcts (Fig. 2). There were no compelling radiological findings to suggest fat embolism syndrome. An MR angiogram of the neck showed only mild carotid bifurcation disease, with the right vertebral artery smaller than the left but patent, without an abrupt cut-off or tapering.

A transthoracic echocardiogram showed a mildly dilated left atrium and suggested a patent foramen ovale (PFO). Colour flow was suspicious for a PFO,

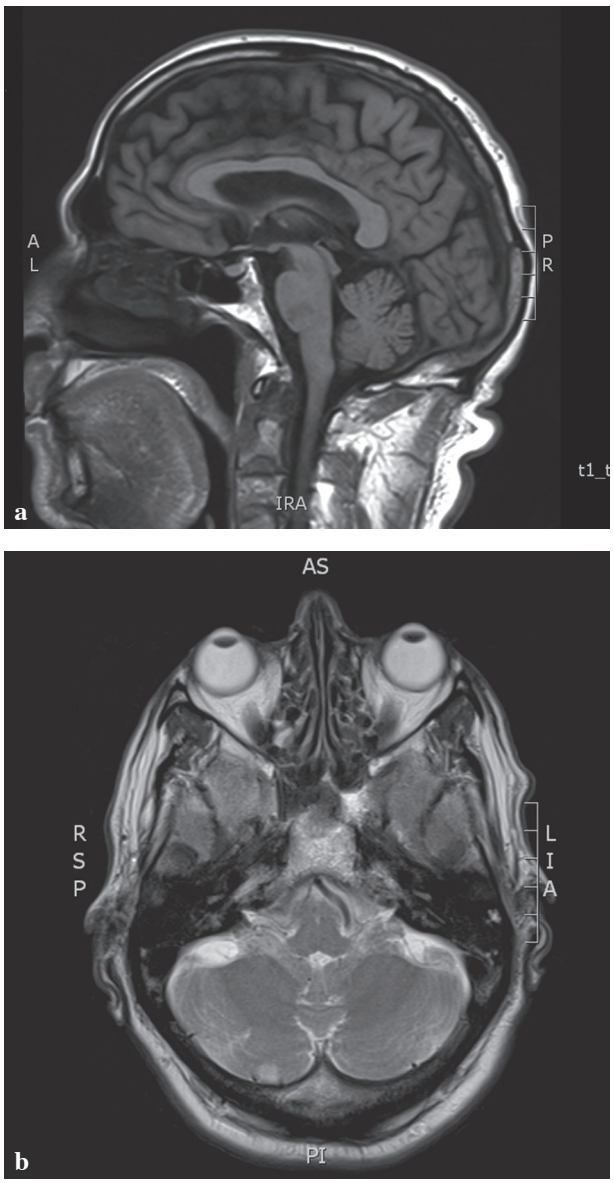

Fig. 2. — Magnetic resonance brain scan : (a) T1-weighted sagittal image and (b) T2-weighted axial image showing pontine and cerebellar infarcts.

while bubble echocardiogram was positive with significant increased bubbles noted in the left atrium after the Valsalva manoeuvre.

Blood pressure monitoring showed that he was normotensive during his admission (110-130/60-80 mmHg). Cardiac telemetry for 24 hours showed normal sinus rhythm with no evidence of atrial fibrillation.

The impression was that the patient developed contemporaneous pulmonary emboli and embolic posterior circulation infarcts, possibly paradoxical in nature associated with an underlying small PFO. Thrombolytic therapy was started using therapeutic doses of low molecular weight heparin. He made a very good recovery under treatment with all the neurological signs resolving over the following 5 days. Given that the brain MRI was otherwise unremarkable and that he had not had any other clinical thromboembolic events, short term (6 months) anticoagulation with warfarin was recommended rather than indefinite anticoagulation or PFO closure.

He was discharged home on the 13th postoperative day. At 4 months follow-up, he reported mild subjective residual dysarthria which was not obvious on examination, but which he said was prominent when he was tired. He was mobilizing well and was independent in activities of daily living. His neurological examination was normal except for hyper-reflexia throughout his right upper and lower limbs.

DISCUSSION

A recent systematic review and meta-analysis of the effect of TXA upon blood loss and transfusion in primary TKR showed that TXA led to significant reductions in blood loss and blood transfusion requirements (*1*). The review did not show an increased risk of DVT, PE or mortality. There were in fact fewer PEs in the TXA group than in the control group, although the difference was not statistically significant. However, the included trials were designed to assess efficacy as the primary outcome and were underpowered to assess the safety of TXA in TKR. There is also the potential for publication bias, where small negative trials are less likely to be published than small positive ones.

In this study, a patient with a previously undiagnosed PFO sustained both pulmonary emboli and cerebrovascular accident (CVA) within 24 hours of bilateral TKR during which TXA was administered intravenously. The embolic posterior circulation infarcts are believed to be paradoxical in nature, associated with right-to-left interatrial shunting across

a PFO. There is only one other published report of simultaneous PE and CVA in the presence of PFO after TXA administration, where a 46-year-old woman without thromboembolic risk factors developed an ischemic CVA after three days of oral tranexamic acid for the treatment of menorrhagia (*4*).

The role that TXA played in the genesis of the emboli in this study is uncertain. Other pertinent risk factors for thromboembolism include the bilateral nature of the surgery, the use of tourniquets, and the patient's cardiac history. A meta-analysis showed an increase in the incidence of PE in patients who undergo bilateral TKR compared to unilateral TKR, with an overall odds ratio of 1.8 (*5*).

Until results of studies adequately powered to assess the safety of TXA in TKR are available, it is prudent to avoid the use of TXA for patients with thromboembolic risk factors. A PFO may represent a contra-indication to the perioperative use of tranexamic acid.

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