JOURNAL OF NEUROSURGERY:
Case Lessons

J Neurosurg Case Lessons 4(3): CASE2262, 2022
DOI: 10.3171/CASE2262

Delayed hemorrhage following deep brain stimulation device placement in a patient with Parkinson's disease and lupus anticoagulant syndrome: illustrative case

Robert B. Walker, BS, Audrey A. Grossen, BA, Christen M. O'Neal, BS, and Andrew K. Conner, MD

Department of Neurosurgery, University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma

BACKGROUND Treatment options for Parkinson's disease (PD) include both medical and surgical approaches. Deep brain stimulation (DBS) is a surgical procedure that aims to improve motor symptomatology.

OBSERVATIONS A 66-year-old White male with a 9-year history of PD presented to the neurosurgery clinic for DBS consideration. On the morning of scheduled surgery, preoperative laboratory test results revealed a prolonged prothrombin time of 50 seconds. Surgery was postponed, and further work-up revealed that the patient had a positive test result for lupus anticoagulant (LA). DBS implantation was performed 2 months later. The first stage of surgery was uneventful. The patient returned 1 week later for the second stage. Postoperatively, the patient exhibited a diminished level of consciousness. Computed tomography revealed left frontal intraparenchymal hemorrhage with surrounding edema, trace subarachnoid hemorrhage, intraventricular hemorrhage, and midline shift.

LESSONS The authors suspect that the hemorrhage occurred secondary to venous infarct, because LA is associated with a paradoxically increased risk of thrombosis. Although there is no documented association between LA and acute or delayed hemorrhage, this case demonstrates a possible relationship in a patient following DBS placement. More research is needed to confirm an association with coexisting LA with PD and an increased hemorrhage risk in neurosurgical interventions.

https://thejns.org/doi/abs/10.3171/CASE2262

KEYWORDS deep brain stimulation; delayed hemorrhage; Parkinson's disease; lupus anticoagulant; functional neurosurgery; magnetic resonance imaging

Parkinson's disease (PD) is a neurological disorder that is caused by a combination of genetic and environmental factors. An abundance of protein aggregates such as Lewy bodies and loss of dopaminergic neurons within the substantia nigra bring about the classic symptoms of PD.[1] Symptoms include resting tremor, bradykinesia, muscular rigidity, postural gait impairment, olfactory dysfunction, cognitive impairment, psychiatric symptoms, sleep disorders, autonomic dysfunction, pain, and fatigue.[2]

Treatment options for PD include both medical and surgical approaches. Deep brain stimulation (DBS) is a surgical procedure that aims to improve motor symptomatology. Stimulation of the subthalamic nucleus (STN) or globus pallidus internus has been recognized in alleviating the motor symptoms of PD.[2] Current practice involves delaying DBS after PD diagnosis for at least 4 years (average 10–13 years).[3] However, recent data suggest that DBS of the STN sooner after diagnosis (average 7.5 years or with motor fluctuations less than 3 years) may result in higher reported quality of life than other medical protocols.[3] DBS is considered a better option than thalamotomy and pallidotomy, which are both irreversible, destructive, and can be performed only in a unilateral fashion. In patients with PD, DBS is able to modulate the target region within the STN bilaterally or unilaterally.[4] This technique has been shown to decrease the need for pharmacological treatment and improve motor function, resulting in 39%–58% improvement in patients' Unified Parkinson's Disease Rating Scale scores.[2,5]

Complications of DBS include hemorrhage, infection, ischemia, device misplacement, battery misplacement, dyskinesias, seizures,

ABBREVIATIONS CT = computed tomography; DBS = deep brain stimulation; ICU = intensive care unit; IPH = intraparenchymal hemorrhage; LA = lupus anticoagulant; MRI = magnetic resonance imaging; PD = Parkinson's disease; PTT = partial thromboplastin time; STN = subthalamic nucleus.

INCLUDE WHEN CITING Published July 18, 2022; DOI: 10.3171/CASE2262.
SUBMITTED February 4, 2022. **ACCEPTED** April 25, 2022.

and psychiatric symptoms.[4] Most cerebrovascular complications occur during the procedure, but some cases can involve issues presenting later, including delayed hemorrhage. The likelihood of experiencing a delayed hemorrhage can be caused by the physical routing of the electrode, the number of electrode passes, and current presence of hemiparesis or hypertension.[2,6,7] The DBS-associated hemorrhage rate is 0.6%–3.3% per procedure, with the majority occurring in a delayed fashion.[8] In a meta-analysis of 272 patients undergoing multiple DBS procedures, a 4.77% hemorrhage rate per patient was reported, with 3.7% of total patients experiencing delayed hemorrhage.[9] Presentations of delayed hemorrhage may include hemiparesis and mental status change, but mostly patients are asymptomatic.[9]

Lupus anticoagulant (LA) disorders cause slower than normal clot formation due to antibodies attacking required clotting components. This error in immune response induces prolongation of the partial thromboplastin time (PTT).[10] These disorders are associated with a wide array of pathologies and accompanying diseases. Paradoxically, LA disorders increase the risk of thrombosis, as opposed to bleeding disorders that are normally associated with prolonged PTT.[10–12] Here, we describe a case of delayed hemorrhage in a patient following bilateral magnetic resonance imaging (MRI)-guided DBS lead placement for PD, and the patient was found to have LA preoperatively.

Illustrative Case

A 66-year-old White male with a 9-year history of PD presented to the neurosurgery clinic for worsening tremor, rigidity, and bradykinesia. His chief complaint was peak dose dyskinesias and on/off motor fluctuations. At the time, he was maintained on carbidopa/levodopa. He had previously received other medications, including rasagiline and pramipexole extended release. However, he had experienced hallucinations, so these medications were stopped.

After discussing available options and performing a preoperative evaluation (including preoperative MRI; Figs. 1 and 2), the patient was found to be an excellent DBS candidate. Risks and the two-stage procedural details of surgery were explained to and understood by the patient.

On the morning of the scheduled surgery, preoperative laboratory test results revealed a prolonged PTT of 50 seconds. Out of an abundance of caution, surgery was canceled, and the patient was referred to our outpatient hematology clinic. The patient had no reported family history of bleeding, although he did report occasional nosebleeds. Coagulation laboratory test results at this visit revealed a prolonged PTT. A mixing study and studies for LA were sent. The results were consistent with LA. Notably, the results of testing for anticardiolipin antibody and anti–β_2-glycoprotein 1 were negative.

Two months after the canceled DBS procedure, the patient was cleared to undergo surgery. Stage I DBS surgery involved the placement of bilateral STN electrodes and leads without complication (view the interventional MRI or ClearPoint technique shown in Figs. 3 and 4). Of particular note, patients undergoing DBS implantation via this method undergo immediate post–lead insertion MRI prior to the conclusion of the case.

One week later, the patient returned for stage II DBS placement. The patient had no preoperative neurological deficits based on examination on the day of stage II. He underwent an uneventful surgery, specifically from a hemodynamic standpoint. There was no manipulation of the intracranial leads. Postoperatively, the patient was noted to have trouble emerging from general anesthesia. It was noted that he had not received any PD medications for ~36 hours. A nasogastric tube was placed, and the patient was given his home dosage of

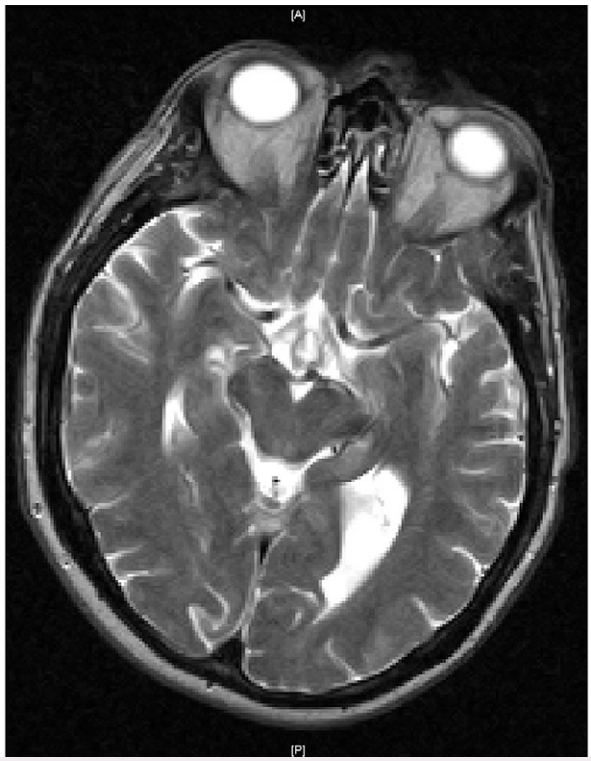

FIG. 1. Preoperative MRI scan shows the level of the STN near the most distal end of the intended lead location.

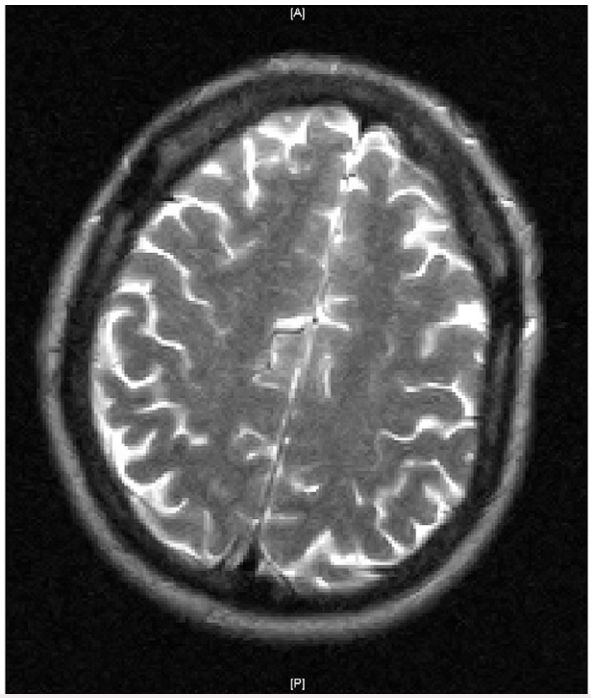

FIG. 2. Preoperative MRI scan shows area near the intended lead entry site.

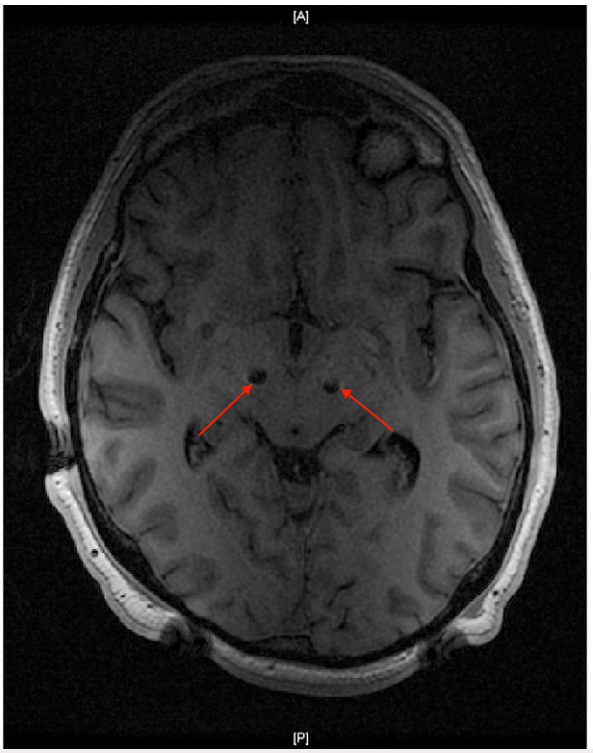

FIG. 3. Intraoperative MRI scan shows DBS lead placement (*red arrows*) at the level of the target.

carbidopa/levodopa. He was also sent for computed tomography (CT) as a precaution. Postoperative CT showed left frontal intraparenchymal hemorrhage (IPH) with surrounding edema, trace right frontal IPH, trace subarachnoid hemorrhage), intraventricular hemorrhage, and 3-mm left-to-right shift as seen in Fig. 5.

Following ample recovery time from surgery, the patient was abulic with an upward, leftward deviated gaze. He withdrew to painful stimuli in all extremities and demonstrated purposeful movement of the left arm. He was also noted to have left facial weakness. He was admitted to the intensive care unit (ICU) for further monitoring. CT the following morning showed stability of the hemorrhage. At this time, a CT angiogram also showed an incidental 1.5-mm aneurysm arising off the superior aspect of the distal right M1 segment. Through the use of permissive hypernatremia, the patient's facial weakness and motor examination slowly improved and was transferred to stepdown after 2 weeks in the ICU. The following week, the patient was discharged to an inpatient rehabilitation facility.

At 2-month follow-up, the patient's condition had improved markedly since his hospital discharge. He was noted to have brief spells characterized by his eyes rolling back and his body becoming limp. These were determined to be syncopal in nature as opposed to epileptogenic. His cognition continued to improve, although he still had mild issues with word finding at times and some forgetfulness. At 8-month follow-up, the patient continued to improve. He still had some motor difficulties, including difficulty writing and apprehension about playing the guitar. He exhibited some speech difficulty, but his family reported that it had been slowly improving.

Discussion

Observations

To the best of our knowledge, this is the first reported case of delayed hemorrhage following DBS placement in a patient with concomitant PD and LA. We suspect that the hemorrhage occurred secondary to venous infarct, because LA is associated with a paradoxically increased risk of thrombosis.[10] It may be posited that the venous infarct occurred relatively quickly following stage I surgery

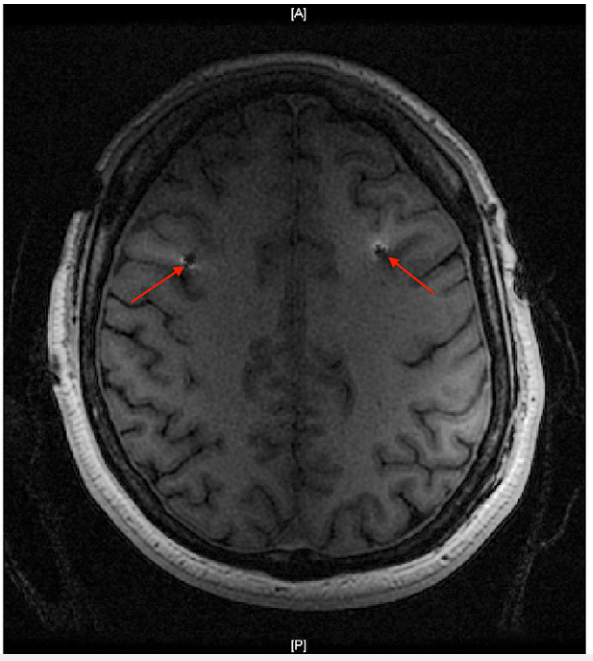

FIG. 4. Intraoperative MRI scan shows DBS lead placement (*red arrows*) near the entry site.

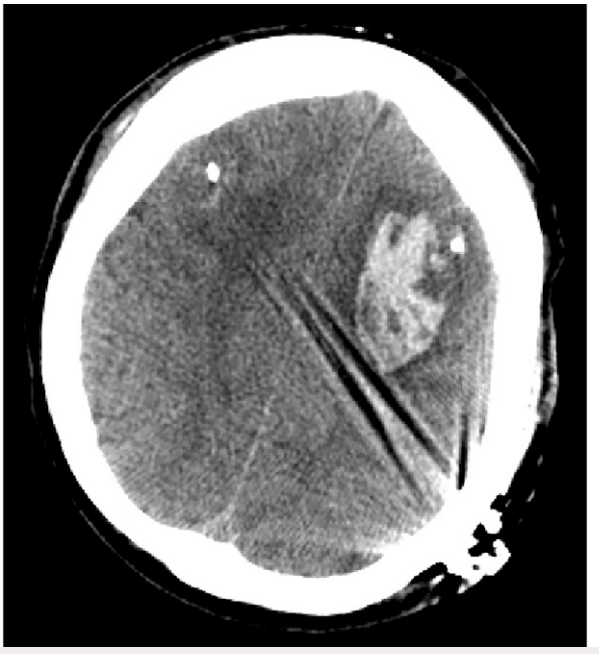

FIG. 5. Postoperative CT scan shows intracranial hemorrhage.

and that the delayed hemorrhagic conversion was related to hemodynamic changes during insertion of the implantable pulse generator. Because the patient underwent intraoperative MRI showing successful lead placement, he did not undergo postoperative imaging (e.g., CT on postoperative day 1) following stage I surgery. This could have potentially revealed the venous infarct earlier, and subsequent hemorrhagic conversion could have possibly been avoided.

In the perioperative management of patients diagnosed with LA, there is surprisingly little information regarding preoperative evaluation and postoperative protocols. Review of the literature yielded no established protocols within neurosurgical populations. Given that there was no precedent, treatment of the patient was unchanged from current protocol and standards. The outcome of treatment was mostly unaffected from normal conditions besides the hemorrhage occurring very soon after stage II surgery. It is also possible that LA had no effect on the presence of hemorrhage and the hemorrhage occurred by coincidence with LA.

Other etiologies of delayed hemorrhage in neurosurgery include arteriovenous malformation surgery, embolization, radiosurgery, flow diversion, microvascular decompression, and tumor resection.[13–16] Delayed hemorrhage can also be the result of minor head trauma in a state of anticoagulation.[13] The literature has illustrated a 5.8–72 per 1,000 incidence rate of delayed hemorrhage following minor head trauma in elderly individuals receiving warfarin.[13] It is well understood that an increased state of anticoagulation causes an increased risk of delayed hemorrhage, but LA places the patient in a state favoring thrombosis rather than anticoagulation. Interestingly, current literature has found that LA has no relationship with incidences of cerebral infarction following subarachnoid hemorrhaging.[16] However, some studies suggest a relationship between LA and incidences of cerebral infarction in individuals with cutaneous vascular changes and noninflammatory vascular thrombosis.[16] Although there is no documented association between LA and acute or delayed hemorrhage, this case demonstrates a possible relationship in a patient following DBS placement. More research is needed to confirm an association with coexisting LA with PD and an increased hemorrhage risk in neurosurgical interventions.

Lessons

We suspect that the hemorrhage occurred secondary to venous infarct in the present case, because LA is associated with a paradoxically increased risk of thrombosis. Although there is no documented association between LA and acute or delayed hemorrhage, this case demonstrates a possible relationship in a patient following DBS placement. More research is needed to confirm an association with coexisting LA with PD and an increased hemorrhage risk in neurosurgical interventions. In addition, this case serves as a lesson that standardized perioperative protocols in LA patients undergoing neurosurgical interventions may be warranted.

References

1. Bo RX, Li YY, Zhou TT, Chen NH, Yuan YH. The neuroinflammatory role of glucocerebrosidase in Parkinson's disease. *Neuropharmacology.* 2022;207:108964.
2. Brontë-Stewart H, Louie S, Batya S, Henderson JM. Clinical motor outcome of bilateral subthalamic nucleus deep-brain stimulation for Parkinson's disease using image-guided frameless stereotaxy. *Neurosurgery.* 2010;67(4):1088–1093.
3. Campbell MC, Karimi M, Weaver PM, et al. Neural correlates of STN DBS-induced cognitive variability in Parkinson disease. *Neuropsychologia.* 2008;46(13):3162–3169.
4. Ortiz-Pérez S, Sánchez-Dalmau B, Molina J, Adán A, Candela S, Rumià J. Ocular tilt reaction as a delayed complication of deep brain stimulation for Parkinson disease. *J Neuroophthalmol.* 2009; 29(4):286–288.
5. Okun MS, Gallo BV, Mandybur G, et al. Subthalamic deep brain stimulation with a constant-current device in Parkinson's disease: an open-label randomised controlled trial. *Lancet Neurol.* 2012; 11(2):140–149.
6. Mikos A, Pavon J, Bowers D, et al. Factors related to extended hospital stays following deep brain stimulation for Parkinson's disease. *Parkinsonism Relat Disord.* 2010;16(5):324–328.
7. Panov F, Levin E, de Hemptinne C, et al. Intraoperative electrocorticography for physiological research in movement disorders: principles and experience in 200 cases. *J Neurosurg.* 2017;126(1): 122–131.
8. Morishita T, Okun MS, Burdick A, Jacobson CE 4th, Foote KD. Cerebral venous infarction: a potentially avoidable complication of deep brain stimulation surgery. *Neuromodulation.* 2013;16(5): 407–413.
9. Park CK, Jung NY, Kim M, Chang JW. Analysis of delayed intracerebral hemorrhage associated with deep brain stimulation surgery. *World Neurosurg.* 2017;104:537–544.
10. Chan EYH, Leung KFS, Soo ETL, Ma ALT. A Chinese boy with lupus anticoagulant-hypoprothrombinemia syndrome: a case report and review of the literature. *J Pediatr Hematol Oncol.* 2021;43(3): e445–e447.
11. Molhoek JE, de Groot PG, Urbanus RT. The lupus anticoagulant paradox. *Semin Thromb Hemost.* 2018;44(5):445–452.
12. Mueh JR, Herbst KD, Rapaport SI. Thrombosis in patients with the lupus anticoagulant. *Ann Intern Med.* 1980;92(2 Pt 1):156–159.
13. Miller J, Lieberman L, Nahab B, et al. Delayed intracranial hemorrhage in the anticoagulated patient: a systematic review. *J Trauma Acute Care Surg.* 2015;79(2):310–313.
14. Yang W, Hung AL, Caplan JM, et al. Delayed hemorrhage after treatment of brain arteriovenous malformations (AVMs). *World Neurosurg.* 2016;87:98–109.
15. Itazu T, Enomoto Y, Yamauchi K, Egashira Y, Iwama T. A case of delayed intraparenchymal hemorrhage due to hyperperfusion after flow diverter treatment. *J Stroke Cerebrovasc Dis.* 2020;29(8): 104869.
16. van Lier FATM, Urbanus RT, de Rooij NK, Rinkel GJE, Frijns CCJ. Lupus anticoagulant in patients with subarachnoid haemorrhage. *J Neurol Neurosurg Psychiatry.* 2012;83(1):89–90.

Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

Conception and design: Conner, Grossen. Acquisition of data: Conner, Walker, Grossen. Analysis and interpretation of data: all authors. Drafting the article: Conner, Walker, Grossen. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Conner. Administrative/technical/material support: Conner, Walker, Grossen. Study supervision: Conner.

Correspondence

Andrew K. Conner: University of Oklahoma Health Sciences Center, Oklahoma City, OK. andrew-conner@ouhsc.edu.