CASE REPORT

Deep brain stimulation complicated by bilateral large cystic cavitation around the leads in a patient with Parkinson's disease

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SUMMARY

Deep brain stimulation (DBS) is an approved and effective therapy for patients suffering from advanced Parkinson's disease (PD). Several clinical trials have indicated significant motor function improvement in patients undergoing subthalamic nucleus stimulation. This therapy is, rarely, associated with complications, mostly related to infections, seizures or stimulation-induced side effects. We report a case of a 71-year-old man with a 10-year history of PD who underwent bilateral placement of subthalamic nucleus DBS. As a complication, the patient showed subjective postoperative cognitive decline, and subsequent MRI showed peri-lead oedema, which progressed to large cystic cavitation around the leads without indication of infection. The patient received steroid therapy and the cavitations regressed without surgical intervention.

BACKGROUND

Since the inception of deep brain stimulation (DBS) for Parkinson's disease (PD), 2002^{1–2} multiple studies, including single centre, multicentre, retrospective, prospective, non-randomised and randomised trials, have been completed showing its efficacy in PD, with similar clinical results. The largest studies to date, comparing best medical management to DBS, showed statistically significant improvements in motor function in the stimulated group.¹ A recent multicentre study using a constant current device demonstrated similar stimulation results.² Only a few publications have focused on the various complications unique to DBS. Even fewer have concentrated on pure surgical complications. Of these studies, the complication rates varied extremely and were mostly collected in a retrospective manner. One prospective study suggested that complication rates were higher with this prospective mode of data collection and documented decline of mental status followed by motor problems, seizures and intracranial haemorrhage as the most common adverse events.³

Recent and yet to be understood postoperative transient imaging abnormalities include peri-lead oedema and intraparenchymal cyst formation. To date, only four publications directly discuss this DBS-related phenomenon of peri-lead oedema^{4–7} and three articles describe cyst formation.^{8–10} We present a unique case of a patient with PD who developed bilateral peri-lead oedema progressing into large cystic cavitations around the DBS leads

with sparing of the electrode tip. To the best of our knowledge, no other publication describes this progressive radiographic abnormality. Additionally, we reviewed the current literature and discuss the potential aetiologies, and propose a management algorithm for these findings.

CASE PRESENTATION

We present a case of a 71-year-old man who was diagnosed with idiopathic PD approximately 10 years prior to his DBS surgery. He reported progressive weakness and stiffness in the past 6 months. Several dopamine agonists and antagonists, including carbidopa-levodopa, Stalevo, Parcopa, pramipexole, Neupro, Azilect, entacapone and Apokyn were tried with initial improvement but eventually discontinued due to side effects and severe motor fluctuations. Overall, the patient's cognitive profile was indicative of mild frontosubcortical dysfunction, which is consistent with cognitive changes associated with PD. Specific testing using the Preoperative Unified Parkinson's Disease Rating Scale score (UPDRS) showed a 56% improvement on the left side and a 62% improvement on the right side on part III. The patient's UPDRS scores in conjunction with his neuropsychological evaluation indicated no contraindication to proceeding with DBS.

The patient underwent bilateral placement of subthalamic nucleus DBS leads (3389, Medtronic, Minneapolis, Minnesota, USA). The surgery was unremarkable with intended targets on both sides reached in a single pass. Intraoperative macrostimulation showed significant reduction of motor symptoms bilaterally as assessed by a movement disorder neurologist. During the procedure, the patient commented that he felt better than the best he has felt with optimised medication. After the surgery, the patient was discharged the following day and underwent pulse generator implantation 1 week later, without any complications.

During follow-up, the patient demonstrated improvement in his motor symptoms. However, approximately 4 months postoperatively, he sustained a fall and, at about the same time, the patient's family began to notice a severe decline in the patient's cognitive abilities. A CT of the brain was obtained, which demonstrated hypodensities surrounding both leads, with no abnormality at the level of the contacts (figure 1). Imaging was not suggestive of infection or haemorrhage and was

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Figure 1 Plain axial CT scan 4 months after implant of electrodes, showing hypodensities surrounding both leads, sparing the level of the contacts and absence of visible haemorrhage.

more consistent with oedema. The patient did not exhibit any systemic signs consistent with infection and the surgical site had healed well. No focal deficits or seizures were noted. Five months post-implantation, the patient underwent repeat neuropsychological evaluation due to subjective progressive cognitive decline, which revealed a decline from the previous evaluation (baseline: Mini-Mental State Examination (MMSE) 30/30, 3MS 96/100, 5 months post-implant: MMSE 28/30 and 3MS 83/100) especially noted in verbal fluency, visuospatial orientation, and verbal learning and memory. The patient's emotional well-being was also noted to be significantly affected. Turning off the device did not yield any improvement; on the contrary, the patient and his family reported a marked decline in his motor function leading to reactivation of stimulation.

The patient sought a second opinion since cognitive symptoms did not improve. MRI of the brain with gadolinium was performed, which revealed significant bilateral peri-lead oedema with large non-enhancing cystic cavities along the leads extending from the subcortical region to the deep white matter near the lateral ventricles (figure 2). There was no evidence of haemorrhage, assessed by subsequent CT imaging.

INVESTIGATIONS

After the patient developed neurocognitive impairment 4 months postoperatively, an axial CT scan without contrast was performed, which showed hypodensities surrounding both leads, interestingly sparing the level of the contacts, and absence of visible haemorrhage (figure 1).

Nine months postsurgery, axial fluid-attenuation inversion recovery (FLAIR) imaging was performed, which ultimately showed bilateral oedema around the DBS leads, with large non-enhancing cystic cavities resembling encephalomalacia,

extending from the subcortical region to the deep white matter near the lateral ventricles (figure 2).

DIFFERENTIAL DIAGNOSIS

- ▶ Microhaemorrhage
- ▶ Allergic reaction or hypersensitivity
- ▶ Infection
- ▶ Venous infarct
- ▶ Luxury perfusion from breakdown of the blood-brain barrier
- ▶ Microparticulate contamination
- ▶ Cerebrospinal fluid migration along the length of the electrode

TREATMENT

On the basis of the blood work up and the imaging studies, an infectious aetiology was ruled out as a source of peri-lead oedema and cavitation. The patient was further offered lumbar puncture to rule out infection but refused and underwent a course of steroid therapy. He subsequently underwent a skin allergy test supplied by Medtronic for components found in the Medtronic DBS leads and insulation, however, all results turned out negative. A neuropsychology test 13 months postoperatively showed that the patient's mental status was back to his pre-operative baseline.

OUTCOME AND FOLLOW-UP

The 18-month postoperative MRI revealed that peri-lead oedema and cysts had significantly regressed without medical or surgical intervention (figure 3) except for the course of steroid. Despite family and patient observations, a 1-year Movement Disorder Society's (MDS) Unified Parkinson's Disease Rating

Figure 2 Axial fluid-attenuation inversion recovery (FLAIR) imaging 9 months postsurgery, showing bilateral oedema around the deep brain stimulation leads with large non-enhancing cystic cavities extending from the subcortical region to the deep white matter near the lateral ventricles.

Figure 3 Axial fluid-attenuation inversion recovery (FLAIR) imaging 18 months postsurgery indicating significant regression of the peri-lead oedema and cysts.

Figure 4 Peri-lead oedema management algorithm. DBS, deep brain stimulation; ESR, erythrocyte sedimentation rate; CRP, C reactive protein; WCC, white cell count.

Scale (UPDRS) repeat examination performed with and without medication with DBS stimulation ‘on’ documented an improvement in motor scores part III of 15% on the left hemibody and 20% on the right indicating continued benefit from DBS 1-year postoperative compared to pre-DBS.

DISCUSSION

The success and safety of DBS for PD has led to its widespread use.¹¹ Likewise, DBS indications have broadened, and it is now being used to treat movement disorders,^{12–14} psychiatric diseases,^{15–17} chronic pain syndromes^{18–22} and epilepsy.²³ There are several reports of adverse events associated with DBS placement but there are very few descriptions of radiographic abnormalities around the DBS leads. Most radiographic abnormalities reported are peri-lead oedema or hypodensities of unknown aetiology in up to 39% of patients. Patients were either observed or treated with low-dose steroids.^{4–7} A correlation between the number of microelectrode passes and duration of resolution of the oedema was indicated by Deogaonkar *et al.*⁴ Aetiological factors discussed included infection, chemical irritation, allergic response and many others.

Another abnormality that might be in the same entity of complications but in a more severe form was described for the first time by Sarkar *et al.*¹⁰ as abstract in 2002 at the Congress of Neurological Surgeons. He described a unilateral cyst formation 4 months after DBS placement in a PD patient with neurological symptoms. The cyst was aspirated stereotactically and eventually resolved. In subsequent reports, Ramirez-Zamora *et al.*, in 2012,

and Baxi *et al.*, in 2014, also described intraparenchymal cyst development in patients after DBS placement. The former report included two patients who developed neurological deficits over a time period of 3–6 months, where the cyst formation was limited to the tip of the DBS electrode.⁹ The latter report described two patients who were incidentally found to have asymptomatic non-infectious cysts, also mostly located at the tip of the electrode lead.⁸ Patients with cyst formation were managed conservatively with observation if no symptoms were present or by removing the DBS electrode if symptomatic.

Our patient presented initially with peri-lead oedema and was asymptomatic. We believe that this entity then progressed to large cystic cavitations bilaterally and therefore the patient ultimately became symptomatic 4 months after DBS placement. A difference to the previously reported cases was that our patient showed bilateral disease around the length of the DBS electrode with sparing of the electrode tip. His neurological function then continued to decline and low-dose steroid therapy was started, which resulted in significant regression of the cysts. Our patient had refused lumbar puncture required to further evaluate this problem, and the aetiology remained unclear. The possibility of haemorrhage would be hard to imagine going clinically unnoticed in an awake patient during and after surgery, as there were no focal or global deficits. In addition, there was no evidence of haemorrhage noted on the CT scans performed 4 months postoperatively (figure 1). In terms of microhaemorrhage, those patients undergoing MRI of the brain showed no evidence of haemosiderin in the affected areas. Ischaemia due to

venous injury is also unlikely as the radiographic findings are not characteristic of venous infarct and the asymptomatic presentation in some cases and complete resolution in others would imply other aetiologies.

Another aetiology could be a reaction to the lead material. Silicon as a biomaterial is extremely resistant to degradation and unless there is degradation, there is minimal possibility of adhesion of inflammatory cells to the insulation.²⁴ Several studies were conducted to assess the biotic–abiotic interface between the brain and the leads both through experimental animals (pigs) and autopsies of patients with DBS implants. The ‘lesion effect’, which is a transient improvement of symptoms, may be due to the oedema formation at the site of electrode implant.^{25–26} Macrophages and giant cells were noted adjacent to polyurethane insulation.²⁷ Fibrous tissue capsule (5–50 µm), glial fibrillary acidic protein (GFAP)-positive gliosis, mononuclear leucocytes, macrophages with haemosiderin ingestion (microhaemorrhage concept), and multinucleated giant cells (with engulfed fragments of foreign material), cell loss (60% in one patient on autopsy), collagen formation and tissue vacuolisation, were observed in the tract and surrounding tissue.^{25–33} There are reports of neurological disease and systemic inflammatory disease in patients with silicone breast implants but no statistical correlation was noted.^{34–35} All these findings and the resolution of the lesion with steroids point towards an inflammatory response of the leads, however, the presentation is very inconsistent and non-specific among different patients.

We presume that the reaction of peri-lead oedema and large pseudocyst formation around the leads both belong to the same spectrum of reactions.^{4–7} The imaging studies of our patient initially revealed peri-lead oedema followed by pseudocyst formation, which correlated with gradual functional decline. We consider the formation of the pseudocyst as a far more severe and advanced form of reaction. Although there were some functional changes noted in the neuropsychological evaluation, no life-threatening complications occurred. In addition, the patient continued to have a robust motor benefit from DBS, which was evident when the stimulator was turned off for a period of 24 h. At the request of the patient and his family, who noted significant deterioration in motor symptoms, the device was reactivated. This was an important finding that enabled us to save the leads.

Our particular case presented with subjective cognitive decline and is unique in that the peri-lead oedema progressed to large cystic cavitation around the leads bilaterally, sparing the electrode tip. However, consistent with the current literature, our patient’s symptoms and radiographic findings improved with time in the absence of any surgical intervention. Infection should be ruled out as false-negative cultures of intracranial implant material in the brain are common and can present with lack of systemic signs, maybe due to the low virulence of the organisms. Also important to mention is that radiographic findings in patients with infected DBS leads can present similarly to peri-lead oedema.³⁶ Our patient was symptomatic from these radiographic abnormalities, but never experienced any loss of motor improvement from stimulation. Likewise, similar to current reports, at no time did our patient exhibit any life-threatening symptoms. Thus, we chose a conservative therapeutic strategy with close clinical and radiographic observation and steroid therapy.

As treatment recommendation, we believe that asymptomatic patients with peri-lead oedema can be clinically observed without necessary intervention; symptomatic patients can undergo a short course of steroid therapy if there are no signs

of inflammation. **Figure 4** summarises our proposed management algorithm for DBS patients suffering from peri-lead oedema.

DBS seems to be a very safe and well-tolerated procedure, for example, in patients suffering from PD. Recent literature documents multiple cases with radiographic abnormalities around shunt catheters ranging from peri-lead oedema to cavity formation. We believe our bilateral case is a severe form of what has been described and believe the aetiological possibilities to be similar, suggesting a reactive process to the material used in the procedure. Further attention is needed to truly elucidate the cause of this relatively infrequent but possibly under-reported entity. Conservative therapy may be sufficient in most cases.

Learning points

- ▶ Recent reports have described temporary imaging abnormalities after deep brain stimulation (DBS) electrode placement, with unclear aetiology.
- ▶ The case described in this report seems likely to represent an extreme example of the previously reported reactions to DBS leads.
- ▶ Conservative management, including steroid therapy, may be successful, if there is not significant evidence of infection.

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