An Unusual Early and Persistent Symptomatic Presentation of Peri-Lead Edema Following Deep Brain Stimulation: Case Report and Literature Review
Running Title: Peri-lead edema after DBS surgery

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An Unusual Early and Persistent Symptomatic Presentation of Peri-Lead Edema Following Deep Brain Stimulation: Case Report and Literature Review

Running Title: Peri-lead edema after DBS surgery

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Conflicts of Interest: None

Abstract

Background:

Peri-lead edema (PLE) following deep brain stimulation surgery is apparently a common, self-limiting condition. PLE generally occurs within days to weeks, rarely occurring before postoperative day one. Majority of patients are asymptomatic, although a wide range of sings/symptoms may be present.
Case Description:

A 62-year-old female patient with Parkinson’s Disease underwent DBS of the subthalamic nucleus in November 2018. Asymptomatic, the patient presented bilateral PLE in the immediate post-operative CT. After two weeks, she developed a frontal lobe dysfunction and persistence of PLE in MRI. She underwent a three-week course of dexamethasone, with mild improvement. However, she subsequently fell at home in January 2019, sustaining an injury to the scalp over the connection site surgical incision. Due to persisting PLE, this was managed with a new course of Dexamethasone, and she was followed-up with CT scans. Two months later (March 2019) the patient presented with urinary tract infection and a lateral scalp erosion over the lead’s connection site. Debridement and primary closure of the skin were performed, followed by a four-week vancomycin course. A MRI at the stage showed marked improvement of the edema. The most recent MRI (May 2019) and CT scan (July 2019) showed resolution of the edema.

Conclusions:

We reported an atypical case of ultra early and persistent PLE presentation following DBS surgery, which improved with courses of steroids. It is unknown whether steroids have a role in the management of PLE.

Keywords:

Peri-lead; Peri-electrode; Edema; Deep brain stimulation; Magnetic resonance imaging;

Abbreviations List:

PLE – Peri-Lead Edema; CT - Computed tomography; MRI - magnetic resonance imaging; DBS – Deep Brain Stimulation, PD - Parkinson’s Disease

1. Introduction

Peri-lead edema (PLE) is a condition of unknown etiology, characterized as a hyperintensity in T2-weighted sequence of brain MRI and hypodensity in brain CT in the area surrounding the deep brain stimulation (DBS) leads.\(^2, 4, 5, 9, 13\) Previously thought as a rare complication, recent studies suggest that PLE is rather a common but underreported condition. Its appears to occur within days to weeks following DBS surgery, seeming unlikely to occur before postoperative day one.\(^2, 4, 5, 8, 9, 11, 13\) Available evidence also suggests that the majority of patients with PLE are asymptomatic.\(^2, 4, 8-10, 13\) When present, clinical features may vary widely, including altered mental status, gait disturbances, speech disturbances, seizures, and motor signs.\(^2, 4, 5, 13\) These, however, are unlikely to persist for over 44 days.\(^2, 4, 5, 7\) We report here an atypical case with ultra early and persistent symptomatic presentation of PLE, discussing its peculiarities in relation to the available literature.
2. Case report

A timeline with the case summary is presented in Figure 1. A 62-year-old female patient with Parkinson’s Disease (PD) diagnosis for 10 years showed progression of rigidity and bradikynesia, besides dyskinesia and predictable and unpredictable wearing off episodes despite optimized pharmacologic therapy. Past medical history included hypothyroidism, hypertension and history of right shoulder surgery and ulnar arthrodesis. She did not present dementia or any severe psychiatric condition.

A DBS of the subthalamic nucleus was indicated, which was performed in November 2018. No microelectrode recording was used. The surgical technique of placement was done in the usual fashion with awake patient to perform macrostimulation.\(^1\) The immediate post-operative CT scan (Figure 2A) showed bilateral PLE, while the patient was asymptomatic. After two weeks, she further developed a frontal lobe dysfunction, with MRI revealing persistence of the PLE (Figure 2B and 2C). No signs of infection were observed (MRI, acute reactant proteins, and, lumbar puncture). Then, she underwent a three-week course of dexamethasone.

The patient had a mild improvement but subsequently fell at home in January 2019, sustaining an injury to the scalp over the connection site surgical incision. Due to persisting PLE, this was managed with a new course of dexamethasone, and she was followed-up with CT scans. Two months later (March 2019) she presented urinary tract infection and a lateral scalp erosion over the lead’s connection site. Debridement and primary closure of the skin was performed, followed by a four-week vancomycin course. A MRI at the stage showed marked improvement of the edema. The most recent MRI (May 2019, Figure 3A to C) also shows progression on the recovery, while the most recent CT scan (July 2019, Figure 3D) was unremarkable.

3. Discussion

The exact incidence of PLE after DBS surgery is unknown. Initially, PLE was imagined as a rare and frequently symptomatic complication. However, the recent studies suggest that it is a common but underreported condition, appearing more often after a few days to weeks following DBS surgery. Major factors that may contribute to discrepancies among studies are: (1) study design (retrospective or prospective); (2) timing of the neuroimaging; (3) modality of neuroimaging (MRI or CT); and (4) reason for imaging (for screening or due to symptom onset). Studies that evaluated the incidence of PLE and their clinical presentation (symptomatic or asymptomatic) are shown in Table 1.

One pearl of the present case is the presentation of PLE in the immediate postoperative CT scan (Figure 2A). In fact, when considering three CT based studies that evaluated the incidence of PLE in immediate
postoperative or in postoperative day one, the incidence was 0% (0/443).\cite{2, 5, 7} In contrast, Nolt et al\cite{8} prospectively examined a series of consecutive postoperative MRIs (from day 1 to 7 weeks following the procedure) in 13 patients, showing that four patients (31%) developed PLE in postoperative day 1 (first scheduled MRI). Englot and his colleagues\cite{4} retrospectively analyzed the postoperative MRI of 133 patients for PLE. None of the fifteen patients who underwent MRI in the day of surgery and 1 of the 99 patients that underwent MRI in postoperative day one developed PLE.

In case series, the presence of symptoms was variable across studies.\cite{2, 4, 8-10, 13} Actually, studies that performed imaging out of the period with the highest incidence of PLE tend to demonstrate a higher proportion of symptomatic patients. When present, the reported symptoms included seizures, confusion, and transient speech or motor neurologic deficits.\cite{2, 4, 13} In the case series, the time for symptom resolution varied from a few days to 44 days.\cite{2, 4, 5, 7} The duration of PLE, in turn, is more difficult to assess, since radiological follow-up is much less frequent than symptom assessment. Despite, the PLE tended to persist for a longer period than symptoms (from a few days to several months) in MRI.\cite{2, 4, 8} In the present case, the last MRI available, performed after four months of surgery, revealed a remnant edema (Figure 3A to C). The patient showed complete symptom improvement.

No controlled studies evaluated whether and/or when PLE should be treated. While some studies demonstrated spontaneous resolution of symptoms and/or of PLE, others described improvement after the use of corticosteroids.\cite{2-7, 9, 10, 13} In a meta-analysis published by Tian et al, the authors suggest some theories for the occurrence of PLE, such as mechanical trauma to brain tissue, cerebrospinal fluid flow through the DBS pathway, or even immunological hypersensitivity to the implant materials. However, none of these theories convicingly explains such changes. Although hardware infection is relatively common, infection is not thought to be a cause of PLE, as infections in DBS lead are uncommon.

The incidence of PLE in the study was 35.8%, with only 3.7% of patients being symptomatic.\cite{12} Asymptomatic patients can recover completely without specific treatment, whereas symptomatic patients were mostly treated with corticosteroids.\cite{12} We suggest that corticosteroids should only be considered for symptomatic patients, avoiding overtreatment of this apparently frequent complication. Based on the benign course of this condition – as demonstrated by the literature so far - we also recommend against electrode revision or replacement due to isolated PLE. However, further studies are necessary to guide the optimal therapy.

4. Conclusion

PLE is not an uncommon complication. We reported an atypical case of ultra early and persistent PLE presentation following DBS surgery, which improved with courses of steroids. It is unknown whether
steroids have a role in the management of PLE. Further research seems imperative to better guide the management of this condition.

Acknowledgments:

None

Statement of Ethics:

The authors have no ethical conflicts to disclose. Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Conflict of Interest Statement:

The authors have no conflicts of interest to declare.

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Submission declaration:

This manuscript is a unique submission and is not being considered for publication, in part or in full, with any other source.

5. References


FIGURE LEGENDS

Figure 1. Timeline illustrating the main interventions and investigations of the case. APR: acute phase reactants; LP: lumbar puncture; DBS: deep brain stimulation; PLE: peri-lead edema.

62-year old female with Parkinson's Disease
Refractory side effects to antiparkinsonian medications

DBS of the Subthalamic Nucleus

November 2018

Immediate Post-operative CT: Bilateral PLE
Patient asymptomatic

Frontal lobe dysfunction after two weeks
Persistent PLE in MRI

Three-week course of dexamethasone

December 2018

Mild symptom improvement
No symptoms/signs of infection (APR, MRI, LP)

January 2019

Patient fell - scalp injury at lead's connection site
Persistent PLE in MRI

New course of dexamethasone

March 2019

Scalp erosion at lead's connection site
Urinary tract infection
Improvement of symptoms and PLE in MRI

Debridement and primary closure
Four-week vancomycin course

May 2019

Additional improvement of PLE in MRI

July 2019

Resolution of PLE in CT

Complete resolution of PLE and symptoms
Figure 2. (A) Control CT scan, performed within approximately 6 hours after the surgery, showing bilateral perilead hipodensity. With the onset of symptoms after 2 weeks, a MRI was performed, revealing a peri-lead high-signal in (B) T2-weighted and (C) FLAIR-weighted sequences.

Figure 3. Control MRI from May 2019 showing improvement of the edema in (A) contrasted T1-weighted (B) T2-weighted and (C) FLAIR-weighted sequences. (D) Control CT scan from July 2019 revealing resolution of the edema.
Table 1. Studies that estimated the incidence of perilead edema (PLE) following deep brain stimulation (DBS) surgery.

<table>
<thead>
<tr>
<th>Study Category, Author and Year</th>
<th>Imaging Modality and Timing (days) after DBS</th>
<th>PLE incidence - % (N/total of patients)</th>
<th>Percentage of Symptomatic Patients (N/total of patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Retrospective</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Borrelini et al, 2019</td>
<td>CT – immediate postoperative</td>
<td>0% (0/77)</td>
<td>N/A*</td>
</tr>
<tr>
<td>Kim et al, 2013</td>
<td>CT – immediate postoperative</td>
<td>0% (0/221)</td>
<td>N/A*</td>
</tr>
<tr>
<td>Fenoy et al, 2017</td>
<td>CT – one day</td>
<td>0% (0/145)</td>
<td>N/A*</td>
</tr>
<tr>
<td>Ryu et al, 2004</td>
<td>MRI – from 23 – 698 days (median of 35 days)</td>
<td>Overall: 39% (15/38)</td>
<td>&lt;30 days: 100% (7/7)</td>
</tr>
<tr>
<td></td>
<td></td>
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<td>30-90 days: 40% (8/20)</td>
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<td></td>
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<td>&gt;90 days: 0% (0/11)</td>
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<tr>
<td>Englot et al, 2011</td>
<td>MRI – from 0 to 13 days (mean of 5.1 days</td>
<td>11% (14/133)</td>
<td>29% (4/14)</td>
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<tr>
<td></td>
<td>when PLE and of 2 days when normal – p&lt;0.001</td>
<td></td>
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<tr>
<td>Saitoh et al, 2019</td>
<td>MRI – from 3 to 10 days</td>
<td>40% (6/15)</td>
<td>0% (0/6)</td>
</tr>
<tr>
<td><strong>Prospective</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Whiting et al, 2019</td>
<td>MRI – approximately 60 days (Mean of 59.1</td>
<td>15% (15/102)</td>
<td>47% (7/15)</td>
</tr>
<tr>
<td></td>
<td>days when PLE and of 72 days when normal – p=0.36)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Borrelini et al, 2019</td>
<td>MRI – from 7 to 20 days (mean of 10 days</td>
<td>100% (19/19)</td>
<td>32% (6/19)</td>
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<td></td>
<td></td>
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<tr>
<td>Nolt et al, 2021</td>
<td>MRI series – postoperative days 1, 14, 28, 42, and 70</td>
<td>85% (11/13)</td>
<td>0% (0/11)</td>
</tr>
</tbody>
</table>

Series that only performed neuroimaging due to symptom development and case reports are not shown.
*Perilead edema was observed in some cases when later additional neuroimaging was performed due to the development of neurological symptoms.
Declaration of Competing Interest

☒ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.