CASO CLÍNICO/CASE REPORT

Peri-Lead Edema After Deep Brain Stimulation Surgery for Parkinson Disease: A Management Challenge

Edema Peri-Elétrodo Após Estimulação Cerebral Profunda na Doença de Parkinson: Um Desafio Diagnóstico e Terapêutico

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Abstract

Deep brain stimulation (DBS) is a well-established surgical treatment for Parkinson's disease. Peri-lead edema (PLE) is a poorly understood complication of DBS. We hereby report three cases of unilateral PLE after bilateral subthalamic nucleus (STN)-DBS and discuss its diagnosis and management.

Patient 1 reported a new-onset headache one month after his surgical procedure. Antibiotic treatment was administered. His complaint resolved two days later. Patient 2 presented in an acute confusional state on the seventh post-operative day. He was treated with corticosteroid. Within a few days clear clinical improvement was seen. Patient 3 developed PLE 56 hours postoperatively. He remained asymptomatic and the edema improved completely without any treatment. Two patients showed an abrupt change in impedance evaluation.

PLE is an underestimated complication of DBS. It is clinically heterogeneous and its management is still lacking. Impedance evaluation can help in its early recognition, avoiding unnecessary medical or surgical procedures.

Resumo

A estimulação cerebral profunda (ECP) é uma modalidade terapêutica eficaz na doença de Parkinson, sendo o edema peri-elétrodo (EPE) uma complicação pouco compreendida desta terapêutica. Reportamos três casos submetidos a cirurgia de ECP bilateral no núcleo subtalâmico, que desenvolveram EPE unilateral.

O doente 1 apresentou-se com um quadro de cefaleia um mês após a cirurgia. Foi tratado com antibioterapia, melhorando clinicamente após dois dias. O doente 2 apresentou um estado confusional agudo no sétimo dia após cirurgia. Iniciou corticoterapia e os sintomas desapareceram alguns dias depois. O doente 3 mostrou um EPE 56 horas após cirurgia. Permaneceu assintomático e o EPE desapareceu sem tratamento instituído. Em dois doentes, a avaliação das impedâncias encontrava-se alterada.

O EPE é uma complicação clinicamente heterogénea, cuja frequência, abordagem e tratamento permanecem desconhecidos. A avaliação das impedâncias poderá ajudar no seu reconhecimento, impedindo procedimentos terapêuticos desnecessários.

Introduction

Deep brain stimulation (DBS) is an increasingly applied, well-established surgery in patients with movement disorders including Parkinson's disease (PD).[1,2] Despite the significant benefits of this therapeutic modality, it is not free of surgical complications.[3,4] The most common complications include device-related failures, skin-erosions, infections and hemorrhage. Recently, peri-lead edema (PLE) has been recognized as a rare complication of DBS,[1,2,4–6] which can pose a diagnostic and management challenge.

Case Reports

We hereby report three new cases of patients who underwent bilateral subthalamic nucleus (STN)-DBS with micro-electrode recording (MER), intraoperative macrostimulation and implanted with Medtronic™ 3389 electrodes.

Case 1

A 47-year-old male with PD since his second decade of life underwent bilateral STN-DBS. The surgical procedure was uneventful. The postoperative head computed tomography (CT) scan (4 days after surgery) showed good placement of the electrodes and no abnormalities. One month later, the patient presented to the emergency room complaining of a new-onset headache. He described a bilateral frontal headache that would not go away with prescribed pain medications. Neurological exam confirmed good response to DBS and no other neurological signs were identified. Head CT scan revealed a right PLE (**Fig. 1A**). As he initially refused lumbar puncture, he was commenced on cefradine. All infective workup was subsequently negative. His symptoms subsided after two days and did not recur. A follow-up CT showed improvement of the edema 14 months after symptom onset (**Fig. 1B**).

Case 2

A 61-year-old man with advanced PD, which started 11 years earlier, underwent bilateral STN-DBS. During the surgical procedure, a second cannula passage was performed to correct its deviation. The control head CT scan, on the 2nd postoperative day, was normal. Seven days later, he developed an acute confusion state. Neurological examination revealed only mild confusion, with no changes in clinical response to DBS. The impedance evaluation was lower in the right electrode (396Ω *vs* 834Ω). Head CT scan revealed a significant right PLE (**Fig. 1C**). He was given a low dose of dexamethasone (2 mg for 5 days, 1mg for 3 days, then 0.5 mg for 3 days). Symptom recovery took 5 days. Follow-up CT scan demonstrated improvement of edema 15 days after symptom onset (**Fig. 1D**). No further events were observed.

Case 3

A 60-year-old male with PD, which started a decade earlier, underwent bilateral STN-DBS. There were no intraoperative complications. During clinical evaluation after his surgical procedure, the impedance measurement was clearly asymmetric, showing marked decreased in the right electrode (550Ω *vs* 1709Ω). Head CT scan 56 hours postoperatively demonstrated a right PLE (**Fig. 1E**). Edema was still visible in a follow-up CT

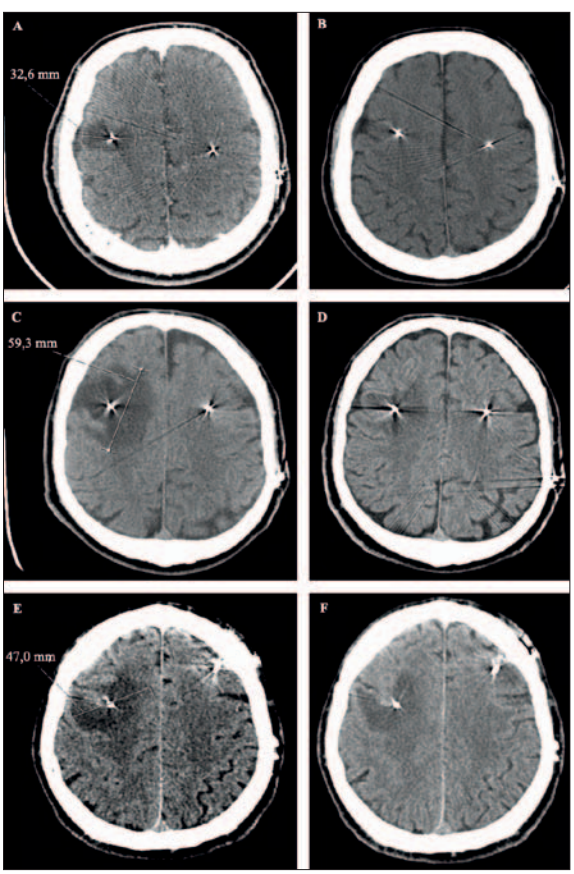


Figure 1. Neuroimaging findings. A. Brain CT scan with contrast one month after DBS of Patient 1 showing right cortical and subcortical hypointensity around the right electrode. B. Follow-up CT scan without contrast of Patient 1 showing dramatic improvement 14 months after symptom onset. C. Brain CT scan with contrast 7 days after DBS of Patient 2 showing right cortical and subcortical hypointensity around the right electrode. D. Follow-up CT scan without contrast of Patient 2 showing improvement 15 days after edema appearance. E. Brain CT scan with contrast 56 hours after DBS of Patient 3 showing bilateral cortical and subcortical hypointensity around the right electrode. F. Follow-up CT scan with no contrast of Patient 3 showing that edema is still visible 16 days later.

CT: cerebral tomography; DBS: deep brain stimulation.

Table 1. Demographic, clinical, radiological and treatment details of all three patients with peri-electrode edema.

	Patient 1	Patient 2	Patient 3
Sex	M	M	M
Age, y	47	61	60
Disease	PD	PD	PD
Disease duration, y	29	11	10
Medical history	-	Hypertension, type 2 diabetes, dyslipidemia, benign prostatic hyperplasia	Recurrent urinary tract infections
UPDRS part III score before surgery	24 (on) 57 (off)	14 (on) 55 (off)	32 (on) 60 (off)
Procedure	Awake	Awake	Awake
Lead target	STN	STN	STN
MER *, no. tracks	R:3/L:3	R:3/L:3	R:3/L:4
Macrostimulation, no. tracks (no. tested positions)	R:3(2)/L:3(2)	R:3(2)/L:3(3)	R:3(3)/L:4(3)
Leads †	2	2	2
Lead model	Lead 3389, Medtronic	Lead 3389, Medtronic	Lead 3389, Medtronic
Order of implantation	L → R	R → L	R → L
No. total of brain penetrations	R: SP / L: SP	R: DP / L: SP	R: SP / L: DP
Subclavicular IPG	Activa RC, Medtronic	Activa RC, Medtronic	Activa RC, Medtronic
Normal postoperative CT	4 days	1 day	-
Edema appearance	30 days	7 days	56 hours
Symptoms at onset	Headache	Confusion	-
Laterality of PLE	R	R	R
Largest diameter of edema (mm)	32,6	59,3	47,0
Location	Cortical and subcortical	Cortical and subcortical	Cortical and subcortical
Stimulation at edema onset	ON	ON	OFF
Intervention	AB (ceftradine 1000 mg twice a day)	Steroids (dexamethasone 2 mg for 5 days, 1 mg for 3 days then 0.5 mg for 3 days)	Conservative
Recovery FU symptoms/ imaging (days)	2/420	5/15	-/n.a.
FU	5 years and 7 months	3 months	2 months

* During MER, three microelectrodes (anterior, central and lateral) were introduced simultaneously, except in Patient 3, in whom four microelectrodes (anterior, central, lateral and posterior) were performed.

† During surgical procedure, bilateral leads were implanted in one operation. All operations were performed by the same neurosurgeon (RP).

AB, antibiotics; CT, computerized tomography; DP, double passage; FU, follow-up; IPG, implantable pulse generator; L, left; M, male; MER, micro-electrode recording; n.a., not applicable; no, number; PD, Parkinson's disease; PLE, Peri-lead edema; R, right; SP, single passage; STN, subthalamic nucleus; UPDRS, Unified Parkinson's Disease Rating Scale; y, years

scan 16 days later (**Fig. 1F**). He remained asymptomatic and no treatments were given.

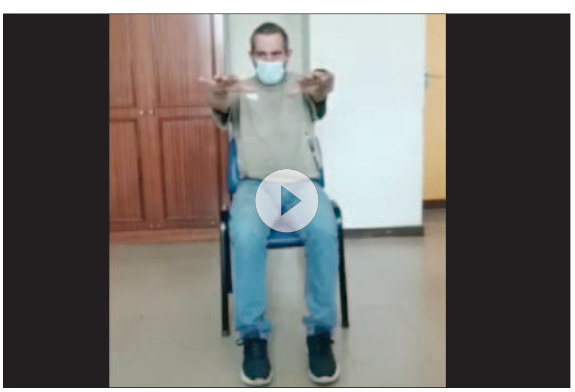
All 3 patients maintained good response to DBS (videos in Appendix). Patient 1 was the first reported case in our center, followed subsequently by patients 2 and 3. The detailed clinical features, surgical procedure and management of the patients are depicted in **Table 1**.

Discussion

Although the presentation of all patients differed in some aspect (time of onset, clinical symptomatology), the CT scan appearance, transient nature and benign course

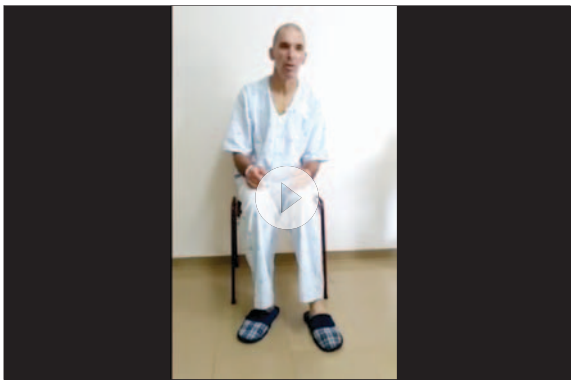
point towards an identical pathological process. PLE, as reported in previous studies,[2,4,5,7] occurs in the absence of hemorrhage, ischemia or infection in patients who initially did very well and had unremarkable brain imaging immediately following lead implantation. It has been recognized as a rare complication of DBS, although true incidence may be underestimated due to asymptomatic presentation, type of brain imaging performed and also because of the lack of routine brain scans in DBS patients.[2,4,7,8]

Similarly to the cases described in the literature,[2,4] the symptom onset range from the early to late post-operative period, mostly within the first 3 months after surgical procedure. Not all patients are symptomatic (Patient 3). Symptoms can be mild and non-specific, including headache (Patient 1), confusional state (Patient 2), seizures, new neurological deficits or worsening pre-existing PD signs.[2,6] A recent prospective MRI-study[4] found no correlation between edema volume and the presence of confusional state, which was more likely related to older age. Interestingly, our Patients 2 and 3 were the same age at the time of surgery and the clinical picture seemed to be more related to edema volume (**Fig.s 1C and 1E**).



Vídeo A. *Clinical follow-up of patient 1.*

Vídeo B. *Clinical follow-up of patient 2.*



Vídeo C. *Clinical follow-up of patient 3.*

Why PLE occurs in a subset of patients is still obscure. Considerations include possible blood-brain barrier (BBB) disruption secondary to mechanical trauma or micro-hemorrhages along the electrode, CSF tracking along the electrode, immune reaction, or predisposition.[2,4,5] No common patient-related factor, including disease duration and medical history, was identified in our patients. Because patients can often develop unilateral edema with bilateral electrode lead placement, as seen in all of our patients, an allergic reaction to the material and a complication of the stimulation itself do not fully explain this entitiy.[2,7,9] We hypothesized that the double passage of the cannula in Patient 2 may been responsible for local trauma, which then led later to ipsilateral PLE, while good response to steroids may support the hypothesis of an underlying inflammatory process secondary to BBB disruption. This is also supported by previous literature.[1–3,10] However, processes associated with traumatic brain damage are expected to start within hours and thus cannot explain the long delay to onset observed in some cases (Patient 1), as also reported in other reports.[6,7]

Regardless of the etiology, in order to define an appropriate management and provide a correct prognosis, PLE should be distinguished from other rare intracranial complications associated with edema, such as vascular events or infections, which might require specific treatment. Imaging can help distinguishing between these conditions.[2,6] On the other hand, CT scan may underestimate the presence and entity of edema due to lead-related artifacts.[4] Interestingly, in Patients 2 and 3, lower impedances were noticed at edema onset, which is supported by a recent multicentric retrospective study.[7] If edema surrounds the stimulating tip of the lead, impedance variations might occur. This highlights the beneficial role that impedance evaluation can play in recognizing this complication, in addition to brain imaging.

Considering the self-limiting nature of this complication, it appears that explantation of the DBS system and prophylactic antibiotic treatment are not recommended. This is an important point because any edema may resemble an infection and lead to hasty antibiotic treatment, as we showed in Patient 1. Moreover, there is insufficient data from the literature to draw firm conclusions regarding whether steroid treatment shortens symptoms duration, whilst no specific studies have looked at comparing treatment modalities. In our case report, the accumulated clinical experience from the first two patients enabled a more pragmatic approach to the management of Patient 3.

Therefore, PLE has been described in a limited few publications, its exact cause has not yet been established, and more cases are needed to elucidate its pathophysiology and risk factors. Further research is necessary to clarify two main paradigms: 1) the best clinical approach in order to reduce abroad variability, namely optimal timing between surgical procedure and subsequent neuroimaging; and 2) the most effective management: should we "wait and see" or perform an exhaustive workup in all patients?

Although PLE seems a rare complication, it may be more common than currently realized. It is clinically heterogeneous, and its management is still lacking. The impedance change can help in early recognition. All physicians involved in postoperative DBS management should maintain a high index of suspicion for this complication in order to avoid unwarranted surgical procedures or antibiotic treatment. ■

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