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Idiopathic delayed-onset edema surrounding deep brain stimulation leads: Insights from a case series and systematic literature review

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ABSTRACT

Introduction: Deep brain stimulation (DBS) is effective for some neurological and psychiatric conditions. Idiopathic delayed-onset edema (IDE) surrounding the leads has been anecdotally reported. The etiology, predisposing factors and prognosis of this complication are unknown.
We present a multicenter case series of patients with IDE, and a systematic literature review, aimed at defining the pathophysiology and identifying appropriate treatment strategies.
Methods: IDE was defined as edema along the DBS lead, occurring ≥72 h postoperatively, in absence of trauma, vascular events or infection. Information on patients with IDE was collected in a standardized way. A systematic search was performed in Pubmed.
Results: Twelve new patients presenting with 14 episodes of IDE are described. From the literature, 38 patients were identified. No common surgical aspects or patient-related factors were identified as risk predictors for the onset of IDE. Symptoms included deterioration of the stimulation effect, seizures and focal neurological signs. Although the condition is self-limiting, with symptoms resolution in 28.5 days on average, three patients underwent surgical revision and seven received antibiotics.
Conclusions: IDE is a rare complication of DBS procedures, presenting from few days to months after surgery. Symptoms can be mild and not-specific, and the condition is self-limiting. The diagnosis of IDE is made after exclusion of vascular events or infections. The pathophysiology is still unexplained. The

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recognition of this complication can help avoiding unnecessary surgical procedures (system explantation) and antibiotic treatment.

1. Introduction

Deep brain stimulation (DBS) surgery is an increasingly applied, well-established treatment for several neurological and psychiatric disorders [1]. DBS implantation is not risk-free, although intracerebral surgical complications are rare. A number of these, such as intracranial hemorrhage (ICH), ischemia and infectious cerebritis, may be associated with intracranial edema. In a few cases, idiopathic delayed-onset edema (IDE) surrounding the DBS leads has been reported [2–7]. At difference with edema associated with lead insertion, which is usually of small size, asymptomatic, and occurs in the perioperative period, IDE presents days to weeks after surgery, and can be fairly large and symptomatic. The etiology, predisposing factors and prognosis of this complication are still unknown.

We present a large multicenter case series of patients who developed IDE surrounding the DBS leads, and a systematic review of the literature, aimed at defining the pathophysiology and identifying appropriate treatment strategies.

2. Methods

Patients presenting with IDE were identified in the participating centers. Information was retrospectively retrieved from medical records and reviewed with standardized forms. Patient characteristics, surgical details, clinical and radiological details, and treatment strategies were recorded.

2.1. Definition of IDE

IDE was defined as edema along the DBS lead, occurring $\geq$72 h after surgery, in the absence of trauma, vascular events or signs of infection. Patients were not included if: a) postoperative imaging revealed abnormalities or symptoms presented in the first 72 h, b) imaging showed signs of hemorrhage or ischemia before or concomitant to edema onset, or c) patients showed signs of infection.

2.2. Search methods

A systematic search on English-language publications reporting edema after DBS was performed in PubMed using appropriate keywords (Supplementary file 1). Additionally, a cross-referencing check of relevant publications and a rough search were performed using the MeSH-term “Deep Brain Stimulation/adverse effects”. Data extraction was performed using the same definition of IDE and the same standardized form for data extraction applied to gather patient information from our study subjects.

2.3. Statistical methods

Descriptive statistics of retrieved data from medical records and reviewed publications are presented as mean ± standard deviation/range in case of continuous variables, or as frequencies/percentages in case of nominal variables.

3. Results

Of the referred patients, four were not included in this report because symptom onset or scan abnormalities were reported already on the first postoperative day, and thus they did not match the definition of IDE as defined above.

Twelve patients (10 males) from nine centers were included (Table 1). The approximate total number of DBS surgeries in the participating centers at the time of writing was >3000, which would suggest an approximate incidence of 0.4%. The average age at surgery was 51.7 years (range: 23–68). Indications for DBS included PD (eight patients), dystonia (2), ET (1), and chronic post-herpetic trigeminal neuropathy (1). Age at onset ranged from 6 to 56 years and disease duration from 4 to 24 years. One patient had a history of leukemia complicated by graft-versus-host disease and used antiaggregants, two patients had hypertension, and three had known allergies to antibiotics. (Supplementary file 2) Eleven patients underwent bilateral implantation, one with a staged procedure. Lead implantation was performed with local anesthesia in 10 patients. Nine patients received 3389 leads, connected to Activa (5), Kinetra (3) or Soletra (1) implantable pulse generator (IPG - Medtronic, Fridley, Minnesota, USA). The other three patients received the Vercise DBS System (Boston Scientific, Natick, Massachusetts, USA). Two patients underwent IPG implantation 5–8 days after lead implantation, while the others on the same day. Intra-operative microelectrode recordings (MER) were performed in eight patients, with 1–5 tracts per side. In four cases, an intraoperative stun-effect was observed. In seven patients plasma-derived fibrin sealant was used intraoperatively. Early post-operative imaging, available for nine patients, was normal.

IDE developed in 18 of the 23 implanted hemispheres, in 14 episodes (simultaneous bilateral IDE in four patients, unilateral in six, and staged bilateral in two). In these hemispheres, the target was the subthalamic nucleus (STN) for 12 leads, internal globus pallidus (GPi) for four, thalamic ventral intermediate nucleus (Vim) for two, and the periaqueductal grey matter for one. In approximately half of the cases the side with (larger) edema was the first implanted side. (Supplementary file 2) Symptoms presented, on average, 84.5 days postoperatively (range: 5–396 days), and included: dysarthria or aphasia (4), confusion (4), deterioration of stimulation effect (4), apathy/depression (3), seizures (3), hemiparesis (2), diminished level of consciousness, headache, diplopia, urine incontinence and agitation. One episode of unilateral IDE, documented four days after the second implant in a staged DBS procedure, was asymptomatic. The maximum axial diameter of edema was on average 35.7 mm (range: 16–100 mm), running along the whole lead track in some cases. (Fig. 1) Contrast-enhancement of small areas was observed in three patients. Bacterial cultures on blood (10 patients), cerebral spinal fluid (CSF – 7 patients) and surgical material (2 patients) were negative. None of the patients showed local or systemic signs of infection. At edema onset, stimulation was on in 14 leads, four of which showed decreased impedance.

4. Management and prognosis

Three surgical revisions were performed. One IPG was replaced in the hypothesis of a malfunction. In another patient, the lead and anchoring system were explanted; a new lead implantation performed 3 months later with perioperative steroid treatment, was

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