Case Report

Early postoperative seizures after vocal fold surgery attributed to shigellosis

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Summary

A 44-year-old previously healthy woman underwent surgery of the vocal folds and developed early postoperative seizures caused by an unusual aetiology. Clinical assessment and laboratory results revealed that the patient suffered from an acute-onset shigellosis infection which was thought to be the cause of her early postoperative seizures. The shigellosis infection was treated with azithromycin which resulted in rapid clinical improvement, and the seizures were successfully managed with benzodiazepines, sodium valproate and levetiracetam. To our knowledge, this is the first reported case of shigellosis-induced seizures in an adult in the peri-operative period. Early detection of the aetiology of seizures is crucial to ensure appropriate management and a safe patient outcome.

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Introduction

Peri-operative seizures may occur in both epileptic and non-epileptic patients. Postoperative non-epileptogenic seizures reported in the literature have been attributed to various causes, including metabolic disturbances (such as hyponatraemia and hypoglycaemia), hyperventilation, alcohol withdrawal, drug reactions, eclampsia, hypoxia, fever, brain injury (surgical, traumatic or disease related), psychogenic, local anaesthetic systemic toxicity and general anaesthesia [1, 2]. We describe a case of early postoperative seizures in a patient who had no previous history of epilepsy.

Report

A 44-year-old woman presented to our ear, nose and throat clinic with severe hoarseness, causing her difficulty with vocalising and speech. Her medical history revealed that she underwent several operations for hoarseness due to dysplasia of the vocal folds consisting of laser resection of scar tissue. She had no co-existing diseases except for morbid obesity. The patient did not take any regular medication, had no known allergies and consumed no alcohol.

The pre-operative stroboscopy image of her larynx showed irregular keratotic plaques on both vocal folds (Fig. 1), therefore she was scheduled for direct laryngoscopy and laser resection of the plaques.

General anaesthesia was induced with propofol and midazolam and was maintained with a continuous infusion of remifentanyl and propofol. Atracurium was used to facilitate tracheal intubation. Surgery performed under direct laryngoscopic-guidance consisted of removal of vocal fold pathological lesions with micro scissors, followed by laser resection

of scar tissue from both vocal folds. At the end of the procedure, the patient's trachea was extubated, and she was transferred to the recovery unit, awake and co-operative. Throughout surgery, her haemodynamic and respiratory measurements were normal (Table 1).

Ten minutes after arrival in the recovery unit, the patient developed tonic-clonic seizures, lasting for approximately 3 min, with loss of consciousness. Neither trismus nor urinary incontinence was noted. Her blood electrolytes and glucose levels were normal. The patient was given intravenous (i.v.) midazolam 5 mg and diazepam 5 mg. After administration of propofol, her trachea was re-intubated and mechanical ventilation of the lungs recommenced. An electroencephalogram (EEG) performed 1 h later revealed no epileptic activity and brain computed tomography (CT) scan was normal.

The patient was transferred to the intensive care unit (ICU) where, within 2 h she regained consciousness and her trachea was extubated. A few hours after tracheal extubation, the patient sustained another short episode of seizures without losing consciousness and was treated with i.v. diazepam. Intravenous sodium valproate was administered (900 mg bolus followed by 2100 mg over 24 h as a continuous infusion), together with levetiracetam 1000 mg twice daily. A second brain CT scan and another EEG performed later were again normal.

On the third postoperative day, the white cell count increased to $14,200 \mu\text{l}^{-1}$ with a pronounced neutrophilia (96%) with a temperature of 39.5°C . Physical examination revealed no signs of peritonitis. Transient, short-lasting hypotension was managed with i.v. boluses of lactated Ringer's solution. On the same day, the patient started having watery, green coloured

Figure 1 Trans-oral, strobo-laryngoscopic image of the patient's larynx. The vestibular (false) vocal folds are normal, as well as the ventricles. Irregular keratotic plaques are visible on both vocal folds (black arrows). The lesions emerge from a dense abnormal vascular bed on both sides. The subglottis and upper trachea are normal. The final histology report revealed the presence of keratosis, moderate squamous dysplasia and intra-epithelial neutrophilic inflammatory infiltrate.

Table 1 Vital signs at different stages of the patient's peri-operative care.

	Heart rate (beats.min ⁻¹)	Blood pressure (mmHg)	Oxygen saturation	Respiratory rate (breaths.min ⁻¹)	Body temperature (°C)
Pre-operative	80	112/70	99% on room air	Not measured	36.4 °C
Intra-operative	80–95	100/60–140/70	99% with FiO ₂ 0.3	12 (mechanical ventilation)	Not measured
Recovery unit	100–126	140/90–180/90	96–100% via facemask followed by mechanical ventilation with FiO ₂ 0.4	15–39	36.4 °C
Intensive care unit	86–120	75/40–166/80	95–100%	11–36	36–39.5 °C

FiO₂, fractional inspired concentration of oxygen.

^aAccording to the Israel Society of Anesthesiologists (ISA) guidelines updated in 2019, intra-operative measurement of temperature is required in surgery lasting > 1 h and in at-risk patients such as premature babies, personal or familial history of malignant hyperthermia and whenever significant changes in body temperature are expected.

diarrhoea, with up to 10 episodes per day. Blood, urine and stool samples were sent for cultures, serology, virology and immunology investigations. Intravenous ceftriaxone 2 g was started every 12 h. Subsequently, the patient's stool culture revealed *Shigella sonnei* infection sensitive to azithromycin, therefore, oral azithromycin 500 mg was started and the ceftriaxone was stopped.

The patient's condition gradually improved and she was discharged home 6 days after surgery. The patient had no more seizures and an EEG performed one month after her discharge from the hospital was normal.

Discussion

Early postoperative seizures may occur in known epileptic patients [3], especially in those with inadequate drug treatment, in patients with new onset epilepsy, or it may be attributed to various other aetiologies [1, 2, 4, 5]. A considered differential diagnosis of the aetiology of peri-operative seizures is critical to ensure appropriate management and a good clinical outcome.

Anaesthetic drugs rarely produce true seizures. The possible epileptogenic effects of some anaesthetic agents are supposedly caused by an imbalance between their effect on glutamate receptors, gamma-aminobutyric acid (GABA) receptors and between different subtypes of GABA receptors [4]. The proconvulsant effects of anaesthetic drugs are enhanced by hypocarbia and are mainly manifested at the beginning or the end of anaesthesia, when the concentrations of anaesthetic drugs are lower. At higher doses, propofol has an anticonvulsant effect [4]. Prolonged administration of meperidine may induce seizures, ostensibly due to nor-meperidine accumulation [5]. The myoclonic activity of etomidate and muscle rigidity produced by some opioids can be confused with seizures [4].

In the acute phase, treatment of tonic-clonic seizures includes the administration of i.v. benzodiazepines [3] followed by specific anti-epileptic agents. The airway should be secured whenever compromised or endangered. We followed this protocol in our patient, who was effectively managed with benzodiazepines, followed by sodium valproate as a first line drug and levetiracetam as an adjuvant.

Our patient had no history of epilepsy and had two EEGs and two brain CT scans which were normal. Thus, the aetiology of her seizures was unknown. The patient did not have hypoglycaemia or hyponatraemia and maintained a normal body temperature during seizures. She had no alcohol or psychiatric history. The patient had another short period of seizures after fully regaining consciousness from anaesthesia, suggesting that anaesthetic agents were unlikely to be the cause.

A fever of 39.5 °C on her third ICU admission day, together with leukocytosis, extreme neutrophilia, elevated C-reactive protein and profuse, watery diarrhoea suggested the diagnosis of a severe, acute gastro-intestinal infection which was confirmed by stool culture that was positive for *Shigella sonnei*. After excluding other aetiologies, we conclude that the seizures were likely caused by the toxic effect of shigella infection on the central nervous system.

As well as the digestive manifestations of shigellosis (fever, watery or blood-stained diarrhoea, abdominal cramps), the enterotoxins secreted by shigella can cause extra-intestinal complications [6]. Encephalopathy with seizures is considered to be the most frequent extra-intestinal complication of shigellosis in children [6]. The presence of seizures increases the risk of death from shigellosis [6]. The mechanism of seizures in this setting is uncertain [7], however, in children it may be precipitated by fever or metabolic derangements [6].

Shigella-induced encephalopathy has been rarely reported in adults [8]. Schuster et al. described a case of an adult patient who presented to hospital with a 1-day history of diarrhoea, lethargy and fever, but without seizures. Similar to our patient, he had no signs of peritoneal irritation and treatment with ceftriaxone was initiated. Stool cultures revealed a *Shigella flexneri* infection [9]. We could find no reports of shigella-induced seizures in adults, possibly reflecting a less severe manifestation of the disease in adults. McCrickard et al. have analysed the US Foodborne Diseases Active Surveillance Network data for infections caused by shigella among adults between the years 2002–2014. No data were provided as to whether any of the patients suffered seizures [10].

In conclusion, we present a rare case of early postoperative seizures presumed to be caused by severe shigellosis. The differential diagnosis of the aetiology of peri-operative seizures may prove challenging. Early detection of the aetiology of peri-operative seizures is critical to ensure an appropriate management and a safe patient outcome.

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