Unusual association of diseases/symptoms

A gut feeling about insular seizures

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Summary

A 43-year-old man presented to the Prince of Wales Hospital, Sydney, New South Wales, Australia, after experiencing his first tonic-clonic seizure. For the previous 2 years he had undergone gastroenterological investigation of episodes of gagging associated with hypersalivation and lachrymation, occurring three or four times per week. EEG showed epileptiform discharges in the right anterior temporal region; brain MRI revealed a lesion in the right insular cortex. Video-EEG telemetry demonstrated that the episodes of gagging were focal seizures. Antiepileptic drug therapy resulted in no further episodes occurring over the next 10 months.

BACKGROUND

This case highlights a neurological symptom masquerading as a gastroenterological problem. Although the manifestations of insular seizures have recently become more recognised, their unusual presenting symptoms can still often result in inappropriate referral and investigation.

Because of the rich cortical and autonomic nervous system connections of the insular cortex, patients with seizures emanating from this area are at higher risk of cardiac arrhythmias, which may result in sudden unexpected death in epilepsy (SUDEP).¹ Therefore, delay in diagnosis may have devastating consequences.

This case serves to remind clinicians that seizures occur in many guises and that gastrointestinal complaints may have a neurological basis.

CASE PRESENTATION

A 43-year-old man presented to the emergency department after his first generalised tonic-clonic seizure. The patient did not have any relevant medical history. There were no risk factors for seizures such as perinatal problems, febrile convulsions, central nervous system infections or head injury. Family history was negative. His only medication was a proton pump inhibitor for presumed

Figure 1 Interictal EEG demonstrating F8 spikes.

Figure 2 Unenhanced brain axial and coronal MRI showing a lesion in the right insular cortex with the typical features of a cavernous haemangioma: a reticulated core of high and low signal intensities surrounded by a hypointense rim.

gastro-oesophageal reflux. He had a smoking history of 20 pack years and consumed 40 g alcohol weekly.

For the previous 2 years he had had repeated gastroenterological assessment and investigation for sudden episodes of gagging, hypersalivation and lachrymation associated with dyspnoea, occurring three or four times per week. These events started as a subjective tingling sensation in his throat. They would last between 20 and 30 s, and occurred both in the daytime and at night, when they would wake the patient from sleep.

The patient maintained full memory and awareness during the episodes. Recovery was immediate. They would often cause embarrassment in social circumstances.

The symptoms were diagnosed as severe gastric acid reflux. Gastroenterological opinions were sought by his doctor on several occasions. One of four endoscopies revealed distal oesophagitis associated with *Helicobacter pylori* being detected in stomach washings. However, triple antibiotic therapy and daily proton pump inhibitor therapy had had no effect on his symptoms.

INVESTIGATIONS

Simultaneous scalp EEG recordings and 24-h video monitoring were undertaken over a 7-day period. Interictal F8 spikes were seen (figure 1), consistent with an area of potential epileptogenesis in the right anterior temporal region. Two episodes were recorded, comprising 10–20 s of choking, hypersalivation and lachrymation, associated with dyspnoea. The scalp EEG recording was obscured by electromyogram (EMG) and movement artefact. ECG monitoring showed no accompanying cardiac arrhythmia.

Unenhanced brain MRI revealed a lesion in the right insular cortex (figure 2) with the typical features of a cavernous haemangioma: a reticulated core of high and low signal intensities surrounded by a hypointense rim. There was no enhancement following contrast injection.

Positron emission tomography with fluorine-18-labelled fluorodeoxyglucose (FDG-PET) showed that this area was hypometabolic for glucose utilisation (figure 3).

Figure 3 Positron emission tomography with fluorine-18-labelled fluorodeoxyglucose scan with a 'punched out' region of glucose hypometabolism in the right insular cortex.

DIFFERENTIAL DIAGNOSIS

- ▶ Gastro-oesophageal reflux
- ▶ Laryngeal pathology – spasm/obstruction
- ▶ Oesophageal achalasia
- ▶ Diffuse oesophageal spasm
- ▶ Obstructive sleep apnoea.

TREATMENT

The patient was started on an antiepileptic drug, carbamazepine, with the dosage gradually increased to 400 mg twice daily. Proton pump inhibitor therapy was stopped.

OUTCOME AND FOLLOW-UP

The patient has been completely free of gagging spells and tonic-clonic seizures during 10 months of follow-up (video 1). He has returned to work and to driving (Australian law allows driving 6 months after first seizure, if free from seizure on treatment).

Video 1 Patient's typical seizure comprising gagging and ability to follow commands.

DISCUSSION

Each hemisphere of the adult brain has an insular (hidden) cortex (often called the insula), located deep within the lateral sulcus, beneath overlapping temporal and frontal lobe tissue. It has a perilimbic location; it receives and relays connections to all lobes of the brain except the occipital cortex. It has a highly dense surrounding vascular network, including the lenticulo-striate arteries. A recent study found it contained large, specialised neurons seen only in limbic structures, whose exact role is still under investigation.² As a consequence of this dense array of intercortical networks, the insula is involved in a wide variety of bodily functions. These range from somatic and visceral autonomic activity to processing of functions such as pain integration, language, drug cravings and emotion.^{3–5} Stimulation of various regions within the insula has also given rise to auditory

phenomena, speech arrest and reduced voice intensity.⁶ It is therefore not surprising that seizures arising from this area may have a wide semiology, which can deceive even the most astute clinician. Presentations can manifest as laryngeal discomfort, dyspnoea, perioral and somatic disturbances, including dysgeusia⁷; there are reports of insular seizures associated with obstructive sleep apnoea,⁸ piloerection,⁹ (ictal) flatulence,¹⁰ cardiac arrhythmias^{11 12} and SUDEP.¹

A literature search for cases similar to ours found an article describing a patient with a long history of nocturnal choking episodes, without loss of awareness, culminating in seizures after 4 years.⁸

Other articles concerning insular epilepsy have been published in specialist journals and have concentrated on four main themes: (1) unrecognised insular seizures as a cause of failed temporal lobectomy for complex partial seizures^{13 14}; (2) intraoperative stimulation for elucidation of function⁵; (3) intraoperative monitoring methods to determine ictal onset¹⁵; and (4) novel neurosurgical techniques to access this high-risk area.^{16–19} Intracranial electrode stimulation of the insula has evoked symptoms similar to those of our patient.^{4 6 20–22} Tumours located in the insula have occasionally been associated with laryngeal, perioral and visceral symptoms.^{23 24}

Cavernous haemangiomas ('cavernomas') account for approximately 15% of brain vascular malformations. In one study, 16 of 32 patients with multiple cavernomas had epilepsy.²⁵ Their epileptogenicity is thought to result from irritation of adjacent areas by the breakdown of blood products.²⁶ Cortical cavernomas are more epileptogenic than subcortical ones.²⁷

Surgical therapy is considered in patients with a history of partial seizures, with or without generalisation, deemed to be refractory to medical treatment. Video-EEG telemetry is mandatory to confirm partial seizures; MRI is required, especially to look for hippocampus sclerosis/atrophy, but also to detect other structural changes. Ideally, these studies are then followed by FDG-PET. If this demonstrates the area of interest to be hypometabolic to glucose, this is regarded as confirmatory evidence of epileptogenicity.²⁸ In a recent analysis, 16 of 22 patients (73%) who had a successful outcome to resection of frontal lobe lesions for intractable epilepsy showed FDG-PET hypometabolism.²⁹

Surgery in the region of the insula poses significant challenges due to the proximity of the internal capsule and the lenticulo-striate arteries. However, new advances in intraoperative MRI and frameless stereotactic navigation are improving operative morbidity and mortality figures.^{17–18 30} Furthermore, seizures arising from the insula may mimic temporal or frontal lobe epilepsy due to its proximity to these areas, their extensive intercortical connections and rapid intracortical electrical propagation. They may be very difficult to distinguish from each other, and undiagnosed insular seizures contribute to the 30% failure rate of anterior temporal lobectomy for refractory epilepsy.^{13 21 31 32}

Although we were unable to demonstrate an EEG seizure discharge during the events, this is not unusual with insular seizures. The distance of the insular cortex from the surface makes scalp recordings imprecise, and even subdural electrode grids overlying the cortex may not record the ictal

onset. In our case, the obscuring of the EEG scalp recording by EMG and movement artefact made demonstration of an accompanying cortical discharge pattern doubly unlikely. However, the presence of focal interictal epileptiform EEG discharges in the region of the lesion seen on MRI, the confirmation that this area was hypometabolic to FDG-PET and the response to antiepileptic therapy strongly support a diagnosis of insular seizures. The very sudden onset and termination of the episodes, their short duration and the repeatedly normal gastroenterological investigations make a primary gastrointestinal cause unlikely.

Learning points

- Unexplained episodic disturbances of almost any organ system should always raise the suspicion of epilepsy.
- Seizures may not involve loss of consciousness.
- Insular epilepsy should be considered if atypical gastrointestinal symptoms do not respond to therapy.
- Early recognition of a seizure disorder presenting in this manner is vital to prevent delay of diagnosis, especially given the risk of SUDEP.
- Epileptologists need to be aware of insular seizure semiology when contemplating epilepsy surgery, since it may mimic temporal lobe epilepsy.

Competing interests None.

Patient consent Obtained.

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