CASE REPORT

Reflex anoxic seizures (RAS) in an adult patient: a separate entity from epilepsy

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Accepted 6 February 2018

SUMMARY

Reflex anoxic seizures (RAS) are essential in the differential diagnosis of non-epileptic paroxysmal seizures. They are precipitated by vagally mediated brief cardiac asystole, which in turn leads to transient cerebral ischaemia. RAS are usually seen in infants and preschool children, but in this case happened in a middle-aged man. Our patient is a 61-year-old man who presented with sudden, repeated contractions of his left upper arm and urine incontinence, followed by loss of consciousness for about 30 s. He reported a similar episode occurred 2 years earlier. He did indicate episodic confusion pointing towards possibility of more occurrences. In the emergency department, he developed a similar seizure, during which telemetry revealed sinus arrest lasted for 4–6 s that was followed by junctional escape. Implantation of a pacemaker resulted in total cessation of sinus arrest and seizure activity during the admission. On 1-year follow-up, patient and family members did not report episodic confusion or any seizure-like activity. RAS constitute a particular entity of seizures and need careful interpretation and management. They have a similar pathophysiology to cardiac syncope. Successful prevention of cerebral hypoperfusion with a cardiac pacemaker usually leads to complete resolution of symptoms in patients with RAS as demonstrated in this case

BACKGROUND

Reflex anoxic seizures (RAS) are predominantly seen in preschool children, and usually resolves by late childhood. In this case, however, RAS interestingly presented at an older age. With the appropriate workup and diagnosis, RAS can be successfully managed by controlling the underlying rhythm disorder. Additionally, this case points out that careful workup is needed on the part of neurologists, as anticonvulsants in this particular scenario may be harmful, and could expose patients to an unnecessary spectrum of side effects including cardiac arrhythmias.

CASE PRESENTATION

A 61-year-old man with a medical history of dyslipidaemia and gastro-oesophageal reflux disease presented with sudden, repeated contractions of left upper arm and urine incontinence, followed by loss of consciousness for about 30 s. He reported a similar episode occurred 2 years earlier. Evaluation with echocardiography and Holter monitor at that time was unrevealing. This time, the patient

and his wife stated that they were sitting watching TV and the wife noticed a strange look on his face; he was abnormally moving his arm, was profusely diaphoretic and became incontinent of urine. The patient thought he had drifted off to sleep. The patient denied having tongue bite, chest pain, shortness of breath, palpitations, headache or any focal signs of weakness.

His vital signs showed a temperature of 98.7°F, blood pressure of 105/78 mm Hg, heart rate of 65 beats/min and oxygen saturation of 98% on ambient air. On physical examination, patient was alert, awake and oriented. Head was normocephalic and atraumatic. Pupils were equal and reactive to light. Chest was clear to auscultation. Heart sounds were normal, with no rub, murmur or gallop. Abdomen was soft and non-tender. No peripheral oedema was detected.

Medication history: Ezetimibe–simvastatin 10–20 mg daily and omeprazole 20 mg daily.

Surgical history was significant for tonsillectomy at the age of 5.

Family history revealed that his mother had a pacemaker, his father had an open-heart surgery for unclear reason and his sister died of myocardial infarction in her 60s.

Social history was significant for current smoking and 45-pack-year smoking history. The patient uses approximately one pot of coffee daily. He denies any alcohol or drug use. He works on heavy equipment, and can conduct all of his daily activities without any limitation.

INVESTIGATIONS

Laboratory investigations, including complete blood count (CBC), lactic acid and urinalysis, were normal. Basic metabolic profile (BMP) was unremarkable except for a potassium of 3.3 mmol/L. Troponin I was 0.02 ng/mL (reference range is less than 0.05 ng/mL). Chest X-ray did not reveal any acute process. Brain CT was unrevealing. His initial ECG showed sinus arrhythmia (figure 1). In the emergency department, the patient developed four episodes of similar seizures, during which telemetry revealed sinus arrest lasting 12 s followed by junctional escape. The patient stated that he was resting before and during these episodes (figure 2).

DIFFERENTIAL DIAGNOSIS

The differential diagnosis considered included epilepsy, intracranial lesions causing seizures, psychogenic seizures and reflex syncope. Imaging

To cite: Cebe L, Singh H. *BMJ Case Rep* Published Online First: [please include Day Month Year]. doi:10.1136/bcr-2017-222389

Figure 1 Initial ECG.

as mentioned above ruled out intracranial lesions. Electroencephalography (EEG) was consistent with seizure-like activity, so psychogenic seizures and reflex syncope were ruled out. By definition of epilepsy, seizures should be unprovoked, but in this case were being provoked by preceding episodes of sinus arrest. Furthermore, cessation of seizure-like activity after pacemaker also helps rule out epilepsy.

TREATMENT

It was determined that the cause of patient's seizures was arrhythmia-induced drop in cardiac output resulting in reduced brain perfusion. Electrophysiology team recommended a pacemaker, and it was placed.

OUTCOME AND FOLLOW-UP

The diagnosis of RAS was made. Implantation of a pacemaker resulted in cessation of seizure activity. On 1-year follow-up, the patient and his wife did not report episodes of confusion or seizures, and the patient was not hospitalised on this account. The patient is following up with the cardiology team.

DISCUSSION

Epilepsy is a disease predisposed by an underlying pathology leading to recurrent seizures. A seizure is a term referring to exhibiting a variety of a transient abnormal movement due to an abnormally high neuronal activity of the brain.

RAS should be considered in non-epileptic paroxysmal seizures.

In 1999, McLeod *et al* defined the term 'reflex anoxic seizures' to describe the non-epileptic motor seizure characterised by

stiffening and jerks which accompanies syncope secondary to cardiac asystole in response to a noxious stimulus or unpleasant circumstance.¹

We would like to mention the golden words by Fejerman² "Differential diagnosis between epileptic and non-epileptic paroxysmal disorders is fundamental not only to allow correct management of patients but also to avoid the burden of unnecessary antiepileptic medication."²

Although the exact pathophysiology of RAS is not precise, still it is mostly considered syncope secondary to severe cardiac inhibitory effect mediated by vagus nerve leading to anoxic seizure presentation. The parasympathetic outflow of vagus causes severe bradycardia/block that ultimately lead to a 'self-resolving' abrupt interruption of the blood supply to the whole body including the midbrain and cerebral cortex causing sudden cerebral ischaemia.³

The episode of RAS is usually brief, lasting between 15 s to a minute. Those events could be trivial and can pass unnoticed by the patients and witnesses.⁴ However, in rare cases, true generalised and even prolonged clonic seizures may follow the tonic episodes. These have been named anoxic epileptic seizures. The prevalence is estimated to be 1 in 1000.⁵ The patient may express upward deviation of eyes as well as urinary incontinence and usually recovers rapidly.^{6,7}

RAS have a sex preference for women more than men. RAS have a peak age of occurrence from the period of 6 months to 2 years as well; however, it can occur at any age.⁸ In our case, it happened in a middle-aged patient.

The usual trigger that cascades this event could be a physical or psychological hurt. A retrospective study that revealed bradycardia in ECG while performing ocular compression test with simultaneous RAS findings in EEG recording further supported pathophysiology of cerebral ischaemia during RAS.⁹ A junctional escape rhythm usually follows the block when the vagal outflow ceases. Ultimately sinus rhythm is restored.¹⁰

EEG is indicated as a baseline investigation for suspected RAS.¹¹ The chance misinterpreting epilepsy as RAS is minimal. The diagnosis of RAS primarily relies on excluding other causes by obtaining a focused but detailed history in association with a normal EEG. Cardiac event recorder (as NOVACOR that monitors and records cardiac activity for prolonged periods that can be correlated with clinical events) is a useful tool to document an episode.¹²

It is not recommended to treat RAS with antiepileptic drugs.

Stephenson studied RAS in children and reveals that "The most important treatment in children is to explain to the parents that the prognosis is excellent. Occasionally, however, a course of atropine has also been found to be necessary." He described its use in seven children with unusually severe or frequent episodes. The latter's results were impressive in reducing the number of attacks, with none of the side effects of atropine.¹³

McLeod *et al*, who run a prospective study, concludes that 'Permanent cardiac pacing provides an effective treatment for patients with severe reflex anoxic seizures especially to those with frequent and severe attacks in whom medical treatment has failed or is declined. Before pacemaker implantation, prolonged asystole should be demonstrated during an attack, ideally on more than one occasion. A cardiac event monitor or a tilt test can help with this determination. A ventricular system is as effective as dual chamber pacing for preventing syncope and seizures, although a dual chamber pacemaker with rate drop function is more effective at reducing overall symptoms.'¹

Kelly *et al*¹⁴ concludes that permanent pacemaker therapy for children with pallid breath-holding spells associated with severe bradycardia is safe, efficacious and warranted.¹⁴

Figure 2 Telemetry strips showing periods of sinus arrest followed by junctional escape rhythm corresponding to reflex anoxic seizures.

Our patient got a significant benefit from the pacemaker and he reported no more symptoms. With this case, we want to bring forward that RAS are essential in the differential diagnosis of non-epileptic paroxysmal seizures even in adult age group.

Learning points

- ▶ Reflex anoxic seizures (RAS) are important in the differential diagnosis of non-epileptic paroxysmal seizures even outside the peak age of occurrence, that is, children from the ages of 6 months to 2 years.
- ▶ Abnormal rhythm underlying seizure activity needs careful interpretation and management.
- ▶ Successful treatment of low cerebral perfusion caused by brief block with a pacemaker could lead to complete resolution of symptoms as demonstrated in this case.
- ▶ Always consider RAS before starting anticonvulsants as they do not help and can make the condition worse by potentiating arrhythmias.

Contributors LC wrote the report. HS prepared for submission and provided mentoring guidance on the case.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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