Unilateral mydriasis during temporal lobe seizures

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Received October 24, 2007; Accepted March 18, 2008

ABSTRACT – Autonomic signs and symptoms are a common feature of epileptic seizures. Although sympathetic activation responses are predominant, we can also find sympathetic inhibition and even an activation of the parasympathetic division of the autonomic nervous system, especially in partial seizures. These autonomic symptoms during seizures are thought to be the result of neuronal discharges arising from or spreading to cortical areas of the central autonomic network. Mydriasis, most commonly bilateral, is one of the most frequent findings. The patient described, a middle-aged man with a focal lesion in the right temporal lobe extended to the adjacent hypothalamus, presented with episodes of autonomic symptoms including prominent unilateral mydriasis, finally evolving into a state of decreased alertness. An ictal electroencephalogram and a simultaneous video recording supported the clinical impression of an epileptic aetiology. Unilateral mydriasis is a rare condition during epileptic seizures and very few cases have been reported in the past. [Published with video sequences]

Key words: temporal lobe seizures, autonomic symptoms, unilateral mydriasis

Autonomic symptoms are a common finding in seizures as a result of epileptiform activity arising from cortical areas of the so-called central autonomic network (CAN) (Devinsky et al. 2004). Its recognition is important for they are sometimes the only manifestation of seizure and might be involved in serious complications such as sudden unexplained death in epilepsy (SUDEP) (Baumgartner et al. 2001). Pupillary changes are among these autonomic symptoms, bilateral mydriasis being the most frequent by far. Although a very rare condition, unilateral mydriasis may also occur, as we demonstrate in this video recording (see video sequence). Our aim, like others, is to contribute to drawing attention to autonomic signs and symptoms in epilepsy, for they can certainly help to achieve a better knowledge of human brain functioning.

Case report

A 50-year-old, right-handed man was admitted to hospital because of a confusional state. At the age of 44, the patient had undergone a transurethral resection of a bladder neoplasm and posterior infusion of local chemotherapy, with no evidence of relapse. He also had a history of hypertension and brain haemorrhage in the right hemisphere 18 months prior to the current admission, with a left hemianopia and a severe, left spastic hemiparesis as sequelae.

On the day of admission, the patient had begun to suffer sudden episodes of fear, nausea and tachycardia. These symptoms recurred several times during the afternoon, so he was finally sent to the hospital by his family doctor. During his stay in the emergency room, he experienced a number of these episodes, during which the pa-
The patient showed a fearful face while complaining of “dizziness”, accompanied by a marked, right unreactive mydriasis, generalized sweating and tachycardia. Each bout lasted for about one minute, an ECG monitoring showing a sinus tachycardia of 150 to 200 with no other changes. On physical examination, his vital signs were normal.

Figure 1. Ictal EEG showing focal, rhythmic, delta activity with an increasing frequency in the right hemisphere (A) followed by fast spike and spike-wave discharges, with a maximum amplitude on the temporal area (B).
except for a blood pressure of 187/117 and a heart rate of 115. During the ictal episodes, oxygen saturation was between 91 and 93% while breathing ambient air, which normalized with the administration of oxygen by means of nasal cannulae. The rest of the general evaluation was normal.

On neurological examination, the patient was initially alert, with a mild temporal disorientation and a slight attention deficit; he was not able to remember any of three words after five minutes; while speaking, there were no aphasic errors but he answered some questions inappropriately; finally, he could not execute a drawing of two intersecting shapes. Interictally, he showed symmetric and reactive pupils (he had not received any kind of eye drops). There was a decreased blink reflex in response to threat on the left.

Motor examination revealed a spastic, left hemiparesis, comparable to that previously found, with ipsilateral hyperreflexia and the Babinski sign.

The haemogram, coagulation tests and serum levels of electrolytes and creatinkinase were normal, as were the renal and hepatic function analyses and a chest X-ray. A CT-scan of the brain showed a marked, hypodense area in the right temporal lobe extending into the ipsilateral hypothalamus and basal ganglia. A CSF examination revealed no abnormality.

During the episodes, an EEG and video recording was performed. The EEG showed rhythmic delta activity with increasing frequency in the right hemisphere, followed by fast spike and spike-wave discharges with a maximum amplitude on the right temporal area (figure 1A and B). These discharges coincided with the patient’s sense of fear and the right pupil mydriasis.

Eventually, one of these episodes was followed by an unresponsive state accompanied by a right gaze deviation and arrhythmic jerking of left hemifacial and upper limb muscles, with persistence of the fixed, dilated, right pupil. These symptoms subsided after a few minutes, the patient being then partially responsive with a reduction of speech, but returned intermittently every 10 to 15 minutes despite intravenous diazepam (40 mg) and sodium valproate (1200 mg) followed by a perfusion of clonazepam.

Finally, he was admitted to the intensive care unit, where phenytoin and midazolam were administered, instead of valproate sodium and clonazepam respectively, with the patient intubated. The EEG then showed a diffuse slowing of background activity, more intense in the right fronto-temporal region, with frequent sharp waves superimposed on this area. These paroxysmal discharges disappeared after the addition of levetiracetam. Three days later, an interictal EEG conducted in the neurology ward, showed an asynchrony of the background activity, consisting of a 6.5 Hz theta activity on the right and an alpha rhythm on the left side, with no epileptic activity (figure 1C).

Cranial MRI T2-weighted images showed a high intensity lesion in the right temporal lobe and adjacent deep areas, surrounded by a thin rim of marked hypointensity repre-
senting accumulation of hemosiderin, compatible with a chronic, focal haemorrhage (figure 2A and B).

Discussion

The autonomic nervous system (ANS), connected to every organ in the body in order to preserve corporal homeostasis by means of regulation of smooth muscle, heart and glandular functions, may be affected in different neurological conditions including epilepsy. Moreover, dysfunction of the ANS is quite common during seizures, especially in those arising from the temporal lobe, either accompanying other manifestations or as the predominant symptom. Autonomic symptoms can be divided into cardiovascular, respiratory, gastrointestinal, cutaneous and urogenital, and includes pupillary changes and visceral, emotional and sexual feelings. Sympathetic responses such as tachycardia, tachypnoea, increased blood pressure, pupillary dilatation, diaphoresis and facial flushing predominate. The intensity of these symptoms may vary from mild or subtle events to potentially life-threatening conditions thought to underlie sudden unexplained death in epilepsy (SUDEP) (Devinsky 2004). A very important fact is that they can not be considered just reactive, but have proved to be the result of electrical stimulation – or spontaneous seizures – arising from or spreading to areas of the so-called central autonomic network (CAN). This network comprises various cortical and subcortical structures fairly interconnected: the insular and medial prefrontal cortex, the central nucleus of the amygdala, the hypothalamus, the midbrain periaqueductal grey matter, the pontine parabrachial complex, the nucleus of the solitary tract and the intermediate reticular zone of the medulla (Liporace and Sperling 1997). Among these structures, the insula and the medial prefrontal cortex would be involved in higher order autonomic control, the amygdala would be responsible for integrating autonomic and motor responses to emotion and the hypothalamus would integrate autonomic, endocrine and behavioural responses. Their location could explain the prominence of autonomic symptoms in temporal lobe seizures.

Among pupillary changes, the commonest by far is bilateral, symmetric mydriasis during generalized tonic-clonic and complex partial seizures, particularly in medial temporal lobe epilepsy, although it may also appear in simple partial fits, even as a characteristic feature, for instance in seizures consisting of ictal fear due to amygdala atrophy (Cendes et al. 1994). Much less frequently miosis and hippus can also occur (Liporace and Sperling 1997).

Unilateral mydriasis, either contralateral or ipsilateral to the EEG focus, is a very rare condition (Baumgartner et al. 2001). Contralateral mydriasis has been observed in epilepsy due to frontal lobe involvement (Gadoth et al. 1981). Ipsilateral mydriasis, as seen in our patient, had been previously described in a patient with an occipito-temporal lesion with contralateral epileptic movements; experimental techniques performed in macaques also elicited unilateral mydriasis: while all clinical changes were contralateral in cases of frontal lobe stimulation, just mydriasis was ipsilateral to the stimulus when applied in the occipito-temporal region (Masjuan et al. 1997). However, its precise pathophysiology remains unclear.

In the past, some authors have suggested that contralateral miosis, a phenomenon described during occipital seizures, would be the result of the excitation of a predominantly crossed occipito-pretectal tract; supporting this theory, contralateral mydriasis was described as a negative ictal feature in a boy with parietal discharges (Lance 1995). Another possible explanation is that as hemispheric lesions extending to the paraventricular nucleus of the hypothalamus, affecting the sympathetic pathway, produce ipsilateral myosis in Horner’s syndrome, an abnor-
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to clarify the central representation of the ANS as well as seizure-induced, autonomic symptoms, as this could help recently, special interest has been paid in understanding the level of medial prefrontal cortex—with extensive efferent connections to diencephalic and brainstem autonomic nuclei (Ostrowsky et al. 2000). Furthermore, while stimulation of the right anterior insular cortex elicits tachycardia and pressor responses, the opposite occurs after left anterior insula stimulation, suggesting hemispheric-specific organization (Oppenheimer et al. 1992). Thus a hemispheric-specific representation of the CAN could result in certain autonomic symptoms providing lateralizing and sometimes localizing information on the seizure-onset focus.

Conclusion

Recently, special interest has been paid in understanding seizure-induced, autonomic symptoms, as this could help to clarify the central representation of the ANS as well as the origin of some seizure types, and the pathophysiology of certain conditions such as SUDEP. Pupillary changes are one of those autonomic symptoms during seizures. While bilateral mydriasis is a common and well-understood feature, a clear explanation for unilateral mydriasis does not exist, probably because of its rarity. Our patient’s symptoms correlate well with those previously reported in the literature for seizures arising from the amygdala. As for unilateral mydriasis, we speculate that it could be the result of the later spread epileptiform activity arising from limbic or paralimbic areas, or even the insula, to the ipsilateral hypothalamus, resulting in a sympathetic activation of the pupillary tract responsible for the changes described.

Legend for video sequence

– Resting state.
– Simple partial seizure: here we can see the conscious patient, responding adequately to questions about his name and how he feels. However, he is sweating, tachycardiac, with a frightened expression and with an intense right eye mydriasis.
– Complex partial seizure: here we can see that the patient is not relating to the interviewer, and responds to nothing. In addition to the previously mentioned signs, he presents gaze deviation to the right and sucking movements.

References


