

## Case Report

## Spiders, ladybugs and bees: A case of unusual sensations in a child with cingulate epilepsy



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## ABSTRACT

Cingulate epilepsy is a rare form of epilepsy. Seizures from the anterior cingulate may present with mood change, fear, hypermotor activity, and autonomic signs, while posterior cingulate seizures resemble temporal lobe seizures. We describe a child with cingulate epilepsy who experienced unpleasant/painful sensory phenomenon. The sensations were described as spiders crawling on his forehead/right leg, ladybugs causing right ear pain and bees stinging his head/right extremities. Unpleasant sensory phenomenon/pain are rarely reported in cingulate epilepsy. Recognizing the role of the cingulate in producing pain/unusual sensory phenomenon is important, and may have localizing value when evaluating children for epilepsy surgery.

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## 1. Introduction

Cingulate gyrus epilepsy is a rare and diagnostically challenging form of epilepsy, with a myriad of clinical manifestations [1–4]. The diagnosis is challenging given the location of the cingulate gyrus, capacity of scalp electroencephalogram (EEG) to record epileptiform discharges and ictal data from this region, as well as its overlap clinically with frontal lobe epilepsy [1,2,4]. Semiologically, anterior cingulate seizures are characterized by: fright, vocalizations, hypermotor activity, complex motor manifestations, automatism, autonomic signs and changes in mood/affect [1–4]. Gelastic seizures have also been reported to arise from the anterior cingulate gyrus [5–6]. Seizures from the posterior cingulate are less well described and may resemble temporal lobe seizures [1].

Overall, case reports of children with cingulate epilepsy are limited (Table 1) [1,5–13]. Here, we describe a child with drug-resistant focal epilepsy secondary to a left mid-cingulate ganglioglioma, who underwent invasive EEG monitoring. The child's seizures were uniquely associated with unusual sensations/pain in the right upper and lower extremity and head region. To our knowledge, there are limited case reports describing unpleasant sensations/pain as an ictal phenomenon in cingulate epilepsy [7].

## 2. Methods

Prior to compilation of this report, consent was obtained from the patient's family in accordance with the consent for publication of case reports policy at the Hospital for Sick Children, Toronto, Ontario, Canada.

## 3. Case description

A 3-year-old left-handed male with an unremarkable medical history and normal developmental history presented with new onset seizures. His neurological examination was normal. There was no family history of epilepsy, nor was there a previous history of central nervous system infection, febrile seizures, head trauma and/or previous cerebral insult. The initial seizures occurred mostly with sleep-wake transition, although intermittently were also seen during the daytime and were associated with; rapid blinking, breath-holding, grunting, smiling, and jerky limb movements. The seizures were under a minute in duration, but would cluster daily. Post-ictally, he would often sleep.

His epilepsy had an explosive onset and within weeks he began to have additional seizure types. There were seizures associated with forehead twitching, blinking and pedaling of the lower extremities as well as generalized tonic-clonic seizures with apnea. These seizures were brief and were seen during sleep-wake transition. Notably, he also began to have seizures with sensory phenomenon, which occurred during the daytime. First he experienced a feeling of spiders on his forehead

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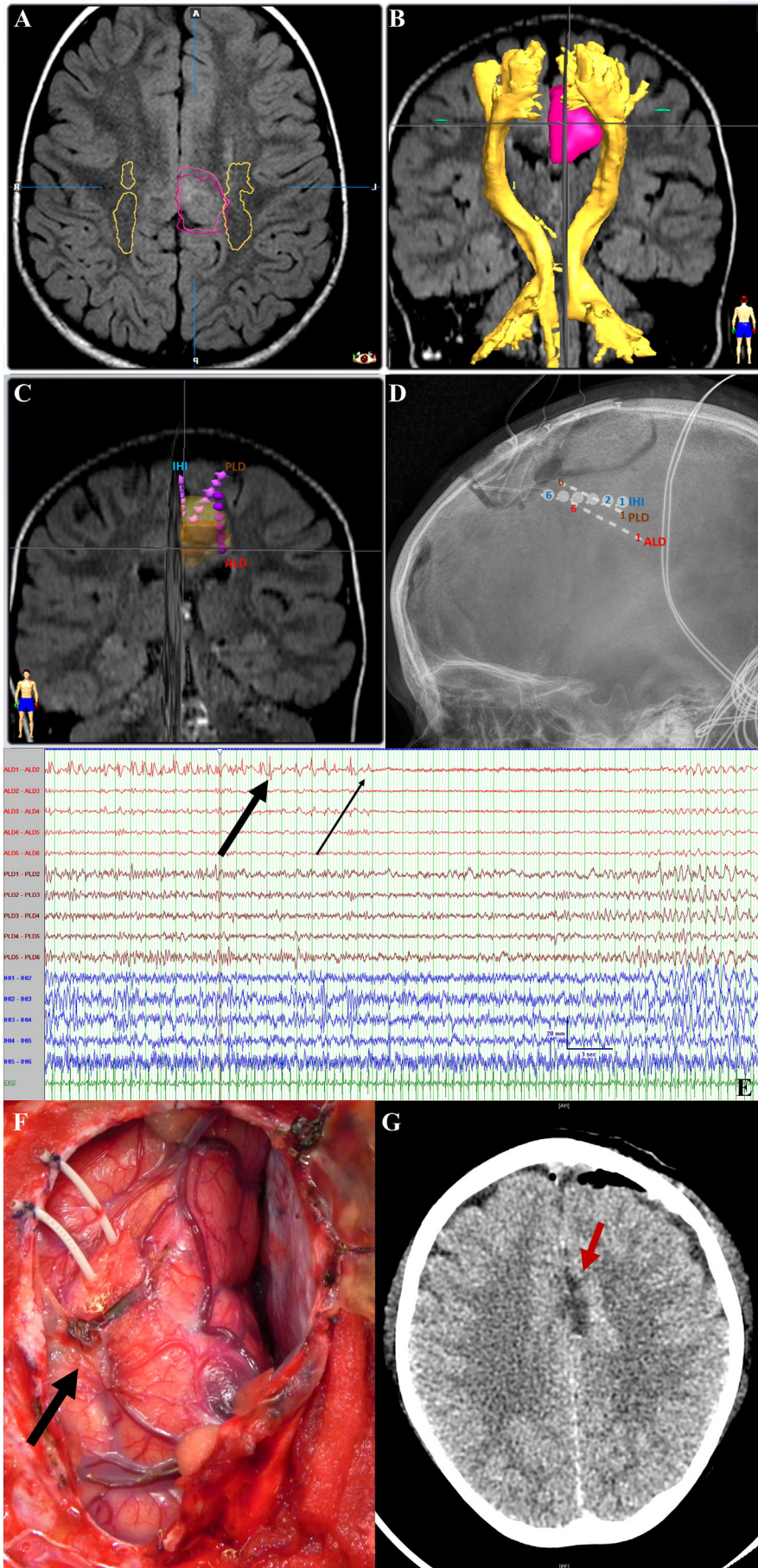
E-mail address: [blathnaid.mccoy@sickkids.ca](mailto:blathnaid.mccoy@sickkids.ca) (B. McCoy).

**Table 1**  
Summary of pediatric cingulate epilepsy cases:

Authors	Age of seizure onset	Seizure features:	EEG:	MRI:	Surgery/pathology	Outcome
Levin et al. 1991 [8]	2.5 years	1) Atonic (resolved) 2) CPS with bruxism, lip smacking, hair fixing & humming	Scalp: Ictal 3–4 Hz GEN SPW with buildup of delta activity over the right frontal polar region. Intracranial: 3–3.5 Hz GEN SPW that were preceded by 3–4 Hz monomorphic discharges from the right cingulate.	Normal	Resection of right anterior cingulate No pathology	Seizure freedom 15 months at follow up
McConachie et al. 1996 [5]	4 years	1) Gelastic 2) Hypermotor	Scalp: Right frontal IED Ictal onset right frontal central	FCD right cingulate	No surgery	Initial freedom with combination of 3 AEDs, then relapsed Seizure freedom 6 months at follow up
De Rose et al. 2009 [9]	20 months	1) GTCs 2) Hypermotor	Scalp: Slowing over left central head region Ictal delta/theta activity over the right frontal head region with contralateral spread	Tumor right mesial anterior cingulate	Lesionectomy Oligodendroglioma	Seizure freedom 6 months at follow up
Mohamed et al. 2007 [6]	10 years	1) Gelastic with bilateral hand, leg automatisms	Scalp: IED over left fronto-temporal Ictal 4 Hz theta over midline & bilateral frontal head regions	T2 heterogeneous mass with nodular enhancement & vasogenic edema.	Lesionectomy Pleomorphic xanthroastrocytoma	Seizure freedom 12 months at follow up
Alkawadri et al. 2013 [1]	12 years	1) Aura with fear, freezing & light headed + hypermotor + early loud vocalization	Scalp: No IED Ictal ipsilateral frontal central	Left anterior cingulate lesion	Lesionectomy Gliosis with cyst	Seizure freedom 1 year at follow up
Alkawadri et al. 2013 [1]	2.5 years	1) Hypermotor with bilateral tonic with right arm extension + ictal urination + personality changes	Scalp: Bilateral frontal central IEDS Ictal ipsilateral frontal central	Left anterior cingulate lesion	Lesionectomy FCD	Seizure freedom 5 years at follow up
Alkawadri et al. 2013 [1]	16 years	1) Stiffening of left arm + oral automatism, early loud vocalization +/- GTC	Scalp: No IED Ictal ipsilateral frontal	Right anterior cingulate lesion	Lesionectomy + adjacent superior frontal gyrus High grade astrocytoma	Seizure free for 2 years following surgery
Alkawadri et al. 2013 [1]	1 year	1) Head and eye version to right	Scalp: No IED Ictal obscured	Left anterior cingulate lesion	Lesionectomy + adjacent superior frontal gyrus Low grade astrocytoma	Seizure freedom 4 years at follow up
Alkawadri et al. 2013 [1]	13 years	1) Aura with depersonalization + left hand automatism > right version > GTC	Scalp: IED ipsilateral temporal	Left posterior cingulate lesion	Lesionectomy Gliosis	Seizure freedom 4 years at follow up

Alkawadri et al. 2013 [1]	15 years	1) Aura with falling, gustatory, abdominal + bilateral asymmetric tonic	Ictal ipsilateral hemisphere Scalp: IED ipsilateral fronto-temporal Ictal bilateral diffuse, faster rhythms bifrontal	Left posterior cingulate lesion	Lesionectomy + adjacent frontal cortex Astrocytoma vs FCD	Seizure freedom 11 years at follow up
Alkawadri et al. 2013 [1]	9 years	1) Aura with déjà vu, jamais vu, abdominal + aura with frightened look or dialeptic	Scalp: IED posterior temporal Ictal ipsilateral temporal	Right posterior cingulate lesion	Lesionectomy Low grade astrocytoma	Seizure freedom 8 years at follow up
Roebing et al. 2009 [7]	17 years	1) Right thigh pain, stretching of knee and lower leg 2) Previous GTCs	Scalp: IED bifrontal theta Ictal bifrontal theta (L > R) with spike left frontal central	Lesion left middle cingulate cortex FCD	No surgery	Seizure free on lamotrigine at time of publication
Schrader et al. 2009 [10]	2.5 years	1) Spasms with subtle jerk and brief tonic component 2) Sudden jerk followed by tonic stiffening of all extremities, frightened expression, facial flushing, staring & automatism left hand	Scalp: No IED Ictal left midcentral sharp for spasm; other seizure with left central sharp followed by delta & attenuation	Lesion in midpart left cingulate	Lesionectomy	Seizure freedom 24 months at follow up
Schrader et al. 2009 [10]	11.5 years	1) Intense fear with desire to run away, dancing & confusion 2) Brief jerk or body or facial grimace 3) CPS with eye & head deviation to left, unresponsiveness, eyelid flickering	Scalp: Slowing right frontal, right frontal temporal IEDs Ictal	Lesion in right anterior cingulate gyrus	Lesionectomy	Seizure freedom 25 months at follow up
Enatsu et al. 2014 [11]	14 years	1) Seizures with automatisms	NA	Right posterior cingulate tumor	Lesionectomy	Seizure freedom 7 months at follow up
Glass et al. 2006 [12]	2 years	1) CPS with odd laugh, extension both arms + extension left leg 2) Reflex seizures with prayer & micturition	Scalp: Ictal onset 20–22 Hz from Cz spread to bilateral frontal SPECT hyperperfusion anterior cingulate & anterior lateral right frontal lobe	MRI normal	NA	Refractory seizures
Mirandola et al. 2015 [13]	13 years	1) Hypermotor 2) Psychogenic non-epileptic events	Scalp: Hypermotor ictal onset from right frontal; no EEG correlate non-epileptic	Right anterior cingulate gyrus FCD	Lesionectomy FCD type IIB	Seizure freedom 5 years at follow up
Imataka et al. 2008	2 years 8 months	1) Hypermotor	Intraoperative electrocortigram: Frequent spikes right cingulate gyrus	Cystic tumor in right cingulate gyrus	Lesionectomy DNET	Seizure freedom 4 years at follow up

Legend: GTCs = generalized tonic clonic seizures, GEN = generalized, SPW = spike wave, IED = interictal epileptiform discharges, FCD = focal cortical dysplasia, FS = focal seizure, DNET = Dysembryonal neuroepithelial tumor.



and/or right leg. Then he would giggle inappropriately. Following this, he described feeling ladybugs and bees. The ladybugs were painful like someone was hammering around the right ear. The bees were associated with a stinging sensation, which started at the top of his head and spread to his right arm and leg. Grimacing followed this. At times, he would fall during these seizures. There was no history of status epilepticus.

He was treated with multiple anti-seizure medications, initially including levetiracetam, oxcarbazepine and topiramate without seizure cessation. A combination of valproic acid, clobazam and lacosamide led to partial seizure control. On this combination, seizures occurred a few times per week, and consisted primarily of the daytime events of less painful sensory phenomenon, inappropriate laughter, grimacing and reduced responsiveness.

Given the explosive onset of epilepsy, the child underwent both routine and prolonged EEG monitoring, magnetic resonance imaging (MRI), as well as a baseline metabolic work-up. The metabolic work-up consisted of urine organic acids, acylcarnitines, ammonia and lactate, which were all normal.

Interictal electroencephalogram at seizure onset was normal. Prolonged EEG monitoring was completed at two and three months after seizure onset. Epileptiform discharges were appreciated over the left frontal, left temporal, midline and right frontal head regions during NREM sleep. Several seizure types were captured including those with: bicycling and left arm flexion/right arm extension followed by bilateral arm extension; seizures with brief cry and extension of the left extremity, seizures with right eye twitching and seizures with a brief cry, extension of the right upper extremity, flexion of the left upper extremity and left head version. The scalp EEG was not helpful in localizing the ictal onset, which varied from: the left frontal, bifrontal/midline, left central/midline or was indeterminate. Of note, ictal bradycardia was present, which was felt to represent an ictal autonomic feature. Magnetic resonance imaging (MRI) showed a lesion in the left mid cingulate gyrus, which was suspicious for focal cortical dysplasia (Fig. 1). Positron Emission Tomography was performed to elicit the extent of the disease and specifically determine whether there was any abnormality (i.e. hypometabolism) that extended outside the MRI visible lesion. The PET showed hypometabolic activity within the left cingulate gyrus.

Invasive monitoring was proposed to confirm the ictal onset zone and complete motor mapping, given the proximity of the lesion to the corticospinal tract. Prior to invasive monitoring, valproic acid was weaned to capture the events, and the seizures became more frequent. The sensory symptoms also became more pronounced and painful, and walking became difficult as a result. At 4 years, 7 months of age, the child underwent a left superior frontal craniotomy using an interhemispheric approach. Depth electrodes were placed using frameless stereotaxy to help confirm the epileptogenic zone and localize the suspected focal cortical dysplasia. Two 6-contact (5 mm inter-electrode distance) depth electrodes were placed into the MRI lesion in the left cingulate gyrus. One 6 contact (5 mm inter-electrode distance) strip electrode was inserted into the inter-hemispheric region in contact with the lesion (Fig. 1). Intra-operative cortical stimulation by trains of five using the two 6 contact depth electrodes and one 6 contact strip was performed for motor mapping. The depth electrode contact labelled ALD1 provoked wrist extensor muscle activity at the lowest threshold (60 V) and wrist extensor with tibialis anterior muscle activity at a threshold of 70 V. Depth electrode electrode ALD2 provoked wrist extensor activity with the threshold of 100 V. All other electrodes did not show any muscle activity with the stimulation  $\geq 100$  V. These findings were interpreted as the lesion residing adjacent (anterior) to

the motor cortex, but not directly involving the motor cortex, given the high thresholds obtained. The video-EEG was recorded using Natus NeuroWorks version 8.1 with a sampling rate of 2 KHz.

Interictally, frequent sharp-and-slow waves as well as high frequency oscillations (80–120 Hz) were seen from the lesion depths and inter-hemispheric head region. Ictally, 8 seizures lasting 3–7 min were captured associated with grimacing, staring, agitation, with or without sensory component of “spider and bee” feeling. Ictal bradycardia, an autonomic sign, to around 60 beats per minute was recorded. Ictal onset was confirmed from the lesion depth electrodes (Fig. 1). Given that the ictal onset zone, symptomatogenic zone and irritative zone were concordant, a lesionectomy was performed under continuous trains of 5 to monitor of the ipsilateral corticospinal tract. Although, focal cortical dysplasia was suspected based on MRI findings, the pathology was consistent with a ganglioglioma. Post-operatively, there were no neurological deficits.

Currently, the child has remained seizure-free on anti-seizure medication for 7 months since surgery (at the time of reporting).

#### 4. Discussion

We have described an interesting case of cingulate epilepsy, which was associated with unpleasant sensory phenomenon and pain secondary to a left mid-cingulate ganglioglioma. The seizures were marked by a variety of clinical features including; hypermotor activity, pedaling, blinking, gelastic component with forced smile/giggling and GTCs, which are features that have been previously reported in pediatric cingulate epilepsy (Table 1) [1,5–13]. Importantly, ictal bradycardia was noted during prolonged video EEG monitoring and invasive monitoring which was felt to be reflective of the autonomic function of the cingulate [1,4,14]. The presence of ictal bradycardia is clinically important. Ictal asystole has been previously reported with stimulation of the cingulate gyrus, which has been postulated to produce bradycardia via the vagal pathway [15]. The variety of clinical features seen in our case is not surprising, given the diverse functions of the cingulate and its projection to several brain regions [1,4,14]. The cingulate gyrus has a cognitive component with connections to the parietal, lateral prefrontal, premotor and supplementary motor area as well as an affective component with connections to the amygdala, periaqueductal grey, anterior insula and nucleus accumbens [14]. Functionally, it has roles in emotion/affect, motor activity, pain perception, autonomic control, and motivational behavior [4,15].

The presence of unusual sensory symptoms with pain was unique in our case. Here, the child not only described dysesthesias such as the feeling of spiders crawling on this head, but also distinct painful sensations (i.e. stinging), which at times were so severe that the child could not walk. To our knowledge, we are aware of one other case of cingulate epilepsy associated with pain, reported by Roebing et al. (2009). They described a 17-year-old female with seizures characterized by pain in the right thigh associated with a focal cortical dysplasia within the left middle cingulate gyrus. It was postulated that the painful seizures might have arisen from the cingulate gyrus, although spread to the primary or secondary somatosensory cortex could not be excluded [7]. Ictal pain was originally postulated to arise from the primary or secondary somatosensory areas or temporal lobe [7,16]. Other areas postulated to be involved include the inferior parietal lobe and supplementary motor area [16].

Given the role of the cingulate gyrus in the perception, modulation and the affective aspect of pain, it is not inconceivable that seizures arising from here may be associated with painful phenomenon [1,4,14].

**Fig. 1.** Neuroimaging and EEG Findings. (A) Axial FLAIR MRI image and (B) Coronal FLAIR MRI image shows a lesion in the left mid cingulate gyrus (pink) with relation to motor tracks (yellow). (C) Coronal FLAIR MRI image and (D) Sagittal X-ray show placement of depth electrodes. Anterior lesion depth (ALD) was inserted deeper and angled targeting the inferior and lateral aspect of the MRI-visible lesion, with ALD in the lesion on fusion images. Posterior lesion depth (PLD) was inserted shallower and angled targeting the superior and mesial aspect of the MRI-visible lesion. Interhemispheric strips (IHI) were inserted through the inter-hemisphere to cover the MRI lesion in the left cingulate gyrus. (E) Ictal invasive depth EEG (sensitivity 20  $\mu$ V/mm; time scale 10 mm/s; low frequency filter, 1 Hz; high frequency filter, off) shows onset of seizure with initial rhythmic 2–2.5 Hz sharp and slow waves seen over ALD1 (thick arrow). This was followed by sudden attenuation at ALD with superimposed low amplitude fast activity at ALD 1–4 (thin arrow). (F & G) Post-operative resection and post-operative CT scan. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Recently, Montavont et al. (2015) demonstrated in 5 patients using stimulation from intracerebral electrodes that pain was reproduced by stimulation of the posterior insula or secondary somatosensory cortex, but not by the primary somatosensory cortex [16]. Interestingly, in 3 out of 5 patients, when the ictal discharges spread from insula/secondary somatosensory area to the anterior and mid cingulate cortex, there was no time-locked ictal pain [16]. Thus, it remains unclear what role the cingulate had in the generation of pain in our child, or whether it was due to spread to distant brain regions (i.e. insula, secondary somatosensory cortex).

## 5. Conclusions

In conclusion, cingulate seizures represent a rare and semiologically diverse form of epilepsy. The presence of sensory phenomenon, which manifested in our case as both unpleasant sensations and pain may represent a unique symptom associated with seizures arising from this area, or represent spread to distinct structures. The presence of such sensory symptoms may have potential localizing value when evaluating children for possible epilepsy surgery. However, given the small number of cases published, ongoing collaboration is necessary to further delineate this.

## Conflict of interest

None of the authors have any conflict of interest to declare.

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