

EEG spikes resembling cardiac M-shaped waves in the EKG: the cerebral M pattern

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Received: June 14, 2016

Revised: September 3, 2016

Accepted: September 12, 2016

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Studies of interictal epileptiform discharges are essential for improving the diagnosis, classification, and management of epilepsy. In this case series we sought to identify the clinical and neurophysiological significance of bifid spikes, whose pattern bears a strong resemblance to the cardiac M pattern. We hypothesize that, analogous to the cardiac M pattern, the cerebral M pattern is generated by a conduction defect associated with asynchronous spatiotemporal averaging of electrical signals in the cortex, resulting in the signals reaching the scalp with different latencies. Unlike the cardiac M pattern, the pathology underlying the cerebral M pattern is unknown, although congenital CNS anomalies may be a culprit.

Key words: Interictal epileptiform discharges; Bifid spikes; Cerebral M pattern

Interictal epileptiform discharges (IEDs) in the electroencephalogram (EEG) are electroclinical patterns typified by sharp waves and spikes, and defined as waveforms that are distinct from the background activity due to their high amplitude (typically 2.5-fold higher than the background voltage). Their duration may vary from less than 70 ms (classified as spikes) to 70-200 ms (classified as sharp waves). There is a large body of literature on the characteristics of typical IEDs¹⁻⁵ but a paucity of data on atypical IEDs.

All scalp-recorded electrical activities are generated by postsynaptic potentials in cortical neurons. It is hypothesized that IEDs represent the summation of excitatory postsynaptic potentials (EPSPs) and inhibitory postsynaptic potentials in the cortex. IEDs in scalp recordings typically have a negative polarity that reflects the action of perpendicularly oriented neurons in the cortex. However, it is noteworthy that in certain types of cerebral insult (particularly congenital CNS anomalies), augmentation of the deep cortical EPSPs may

give rise to a prominent positive trough of the spike, which is recorded as positive sharp waves or spikes on the surface EEG that obfuscate the negative phase of the IED.⁶ Deep layers of the cortex may also be the source of other atypical IEDs (e.g., focal triphasic and sharp slow waves),^{7,8} where cortical deafferentation due to a subcortical pathology (e.g., heterotopias) may theoretically produce such patterns. Atypical IEDs are generally rare and probably underreported EEG patterns with focal and epileptogenic significance. Furthermore, their presence may indicate coexisting chronic or static CNS pathology, in particular congenital CNS anomalies.

Over the past year we have found a new variant of IEDs in the EEGs of 4 patients among a population of 980 patients who were studied in our laboratory at King Khalid Hospital, which is a tertiary-care facility in Ha'il, Saudi Arabia. This pattern consists of a succession of two negative spikes presenting in a bifid or conjoint morphology. This pattern bears a strong resemblance to cardiac M-shaped waves (M pattern) in the electrocardiogram (EKG) of individuals with right-bundle-branch block (RBBB) caused by various cardiac conditions. Bifid spikes were often followed by slow waves. They had a restricted electrical field, occurring either in isolation or, rarely, in brief bursts.

It is our opinion that studies of IEDs are essential for improving the diagnosis, classification, and management of epilepsy. In this case series we sought to identify the clinical and neurophysiological significance of the cerebral M pattern (CMP), taking into consideration other concurrent EEG abnormalities while attempting to draw an analogy between the CMP and the cardiac M pattern in the borderland of neurology and cardiology.

CASE

Case 1

Case 1 was a 30-year-old female with a diagnosis of moderate mental retardation (IQ = 55) and intermittent generalized tonic-clonic seizures (of unknown cause) that had occurred with an average frequency of one seizure per week since 1 year of age. She did not experience auras. Each seizure lasted 5 to 10 minutes and was followed by a postictal state. There were no known triggers for the patient's seizures. Her

prenatal, perinatal, and postnatal history was unremarkable. Her developmental milestones were delayed, in that she sat, walked, and talked at ages of 3, 5, and 6 years, respectively. She attended special education classes for the mentally retarded. Her family history was negative for mental retardation and seizures.

She was initially treated with valproic acid; this was later switched to lamotrigine, which controlled her seizures. A neurological examination showed no focal or lateralizing signs. Her speech was delayed and she needed assistance with activities of daily living. The MRI findings for the brain were normal.

Her EEG showed diffuse background slowing in the theta band. When she was drowsy or asleep, frequent and repetitive single sharp waves and spikes occurred in the left temporal-occipital, left frontal-temporal, left frontal, and right temporal-occipital regions. Especially notable was the presence of occasional, independent bifid spikes in the left and right temporal-occipital areas (Fig. 1).

Case 2

Case 2 was a 13-year-old male with a diagnosis of vitamin D deficiency and epilepsy. His birth history was unavailable, and he had achieved normal developmental milestones. At 5 years of age he began to experience generalized convulsive seizures at an average frequency of three seizures per month. There were no discernible triggers to the seizures. He would briefly appear frightened immediately before a seizure episode. His seizures responded favorably to carba-



Fig. 1. Nine-year-old female with partial motor (right-sided) seizures with secondary generalization. Patient asleep. The EEG shows quasi-periodic "bifid spikes" in the left occipital-temporal area. EEG, electroencephalogram.

mazepine. The findings of a neurological examination were normal. He was obese. Head CT showed moderate ventriculomegaly.

The patient was attending high school. He was able to perform day-to-day activities independently. His family history was noncontributory.

His EEG showed normal background activity while awake. When he was asleep, frequent, repetitive sharp waves and spikes occurred in the right temporal region, maximally in the right midtemporal area. This activity often exhibited bifid morphology (Fig. 2).

Case 3

Case 3 was a 9-year-old female with a history of multiple hospital admissions for generalized convulsive status epilepticus with a right-side onset and unknown etiology. Her first seizure occurred when she was 7 years old. These were right-side partial motor seizures with secondary generalization, with no known precipitating factors. When she presented to us she was taking a combination of phenytoin and valproic acid and exhibited only occasional seizure episodes. The findings of a neurological examination, head CT, and brain MRI were normal. Her birth history was unremarkable. She had achieved normal developmental milestones, and her family history was negative for seizures.

Her serum trough phenytoin and valproic acid levels were both subtherapeutic. We therefore elected to gradually increase the dosage of valproic acid while tapering phenytoin, which resulted in her becoming seizure-free.

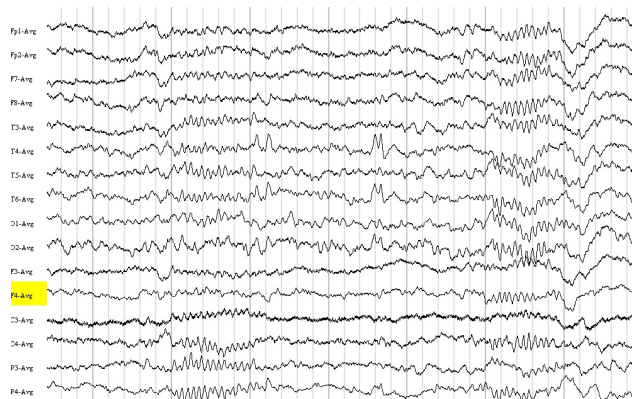


Fig. 2. Thirteen-year-old male with generalized convulsive epileptic seizures preceded by fear. Patient asleep. The EEG sample shows "bifid spikes" in the right temporal-occipital region. EEG, electroencephalogram.

Her EEG showed normal background activity. Several bursts of rhythmic notched delta waves occurred in the left temporal-occipital region both while awake and drowsy. Also, numerous sharp waves and spikes—often with bifid and occasionally with trifid morphology—occurred in the aforementioned topographic distribution (Fig. 3).

Case 4

Case 4 was a 2-year-old female with multiple handicaps, including congenital blindness and deafness, and psychomotor delay. Her birth history was significant for prematurity, which was complicated by intraventricular hemorrhage and hyaline membrane disease. She had experienced a single generalized convulsion at birth, which had not recurred. Her developmental milestones were globally delayed. In addition to the above handicaps, the neurological examination showed spastic quadriplegia, and choreoathetosis in all extremities. Head CT revealed a right hemispheric porencephalic cyst. Genetic studies were nonrevealing.

Her family history indicated that the parents were consanguineous. There was no family history of mental retardation or seizures.

An EEG recorded to evaluate the overall cerebral function exhibited depression of the background voltage on the left, and diffuse polymorphic delta waves on the right. There were spikes, polyspikes, and bifid spikes in the left occipital region. Independent spikes occurred in the right frontal and right posterior temporal regions. Positive sharp waves were



Fig. 3. The patient is a 30-year-old female with mental retardation and generalized convulsive epileptic seizures. Patient asleep. The EEG shows "bifid spikes" in the left temporal-occipital region. Intermixed are focal, at times "notched" delta in the left temporal region. EEG, electroencephalogram.

detected in the left occipital, right frontal-temporal, and right frontal-central areas. Trains of rhythmic notched delta waves occurred in the left parietal-temporal region. Occasional ripples were present in the right frontal and temporal-central areas. Occasional flattening of the background activity also occurred. Sleep spindles were depressed over the left hemisphere.

We decided against the administration of anticonvulsants, but we followed her closely in the outpatient clinic and scheduled long-term video EEG monitoring (Fig. 4).

DISCUSSION

In this case series (Table 1) we have reported on four patients with a history of chronic or static CNS disorders associated with either a history of epilepsy or a diagnosis of epilepsy.



Fig. 4. Two-year-old female with psychomotor delay and multiple congenital anomalies. The EEG shows trains of "bifid spikes" in the left occipital region. Note depression of left hemispheric background and sleep parameters. EEG, electroencephalogram.

Their EEGs showed a bifid epileptogenic pattern resembling the cardiac M pattern. Similar EEG patterns have been reported in association with acute neurological syndromes involving hyperexcitability of neuronal circuits (e.g., status epilepticus and postictal states, and periodic epileptiform discharges).

In attempting to explain the pathophysiology of the CMP it is important to consider factors that theoretically determine the morphology of IEDs in general. Such factors include the frequency, phase, and amplitude of waveforms that collectively generate various types of IEDs (e.g., sharp waves, spikes, and spike-wave complexes).⁹ On the other hand, when the spatiotemporal averaging of electrical signals in the cortex occurs asynchronously when they are projected to the scalp, they will reach the scalp with different latencies, resulting in the formation of peculiar patterns such as long duration (blunted) waveforms or perhaps CMP. This hypothesis is supported by the strong resemblance of CMP to the cardiac M pattern in the RBBB, where delayed right ventricular activation produces a secondary R wave (R') in the right precordial EKG leads.¹⁰ Epileptic activities in the cortex or within the subcortical tracks do not propagate in

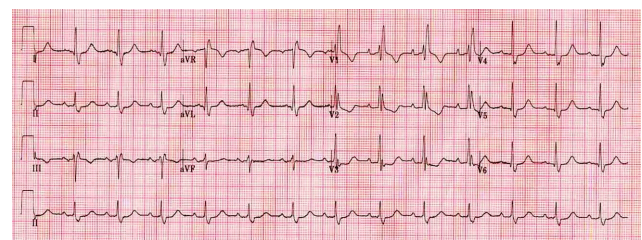


Fig. 5. EKG showing cardiac M-wave pattern which represent RBBB in the chest leads (V1-V2). EKG, electroencephalogram; RBBB, right bundle branch block.

Table 1. Pertinent data in four patients with EEG bifid spikes

Patient no.	Age (years)	Birth history	Family history	Seizure type	Neurology	Medications	Neuro-imaging	EEG
1	30	Neg.	Neg.	GCS	MR	VPA	N	MTF
2	13	Neg.	Neg.	PCS+GCS	N	CBZ	Ventriculomegaly	IED (RT)
3	9	Neg.	Neg.	SPS+GCS	N	DPH+	N	IED (L-OT)
4	2	Prematurity+	Neg.	One GCS at birth	MR, spasticity quadriplegia	None	Right hemispheric porencephaly	MTF

EEG, electroencephalogram; Neg., negative; GCS, generalized convulsive seizure; MR, mental retardation; VPA, valproic acid; N, normal; MTF, multifocal; LMT, lamotrigine; PCS, partial complex seizure; CBZ, carbamazepine; IED, interictal epileptiform discharge; R, right; T, temporal; SPS, simple partial seizure; DPH, phenytoin; L-OT, left occipital temporal region.

the same way as signals from the heart, although the cardiac M pattern and CMP may have a common pathophysiological mechanism; namely, a conduction defect in projection fibers (Fig. 5).⁶

Our case series does not reveal the type of pathology that is selectively conducive to CMP. A particularly interesting observation in two patients (cases 3 and 4) was the occurrence of CMP concurrently with notched delta waves, which constitute a poorly defined and rare EEG pattern that is believed to occur primarily in genetic disorders. The coexistence of these two patterns suggests that CMP and notched delta have a common pathophysiological mechanism. The presence of a psychomotor delay in two of our patients (cases 1 and 4), and the discovery of ventriculomegaly in head CT of case 2, which may have been caused by genetic factors or neonatal asphyxia, tend to support this theory. Furthermore, the preponderance of occipital-temporal bifid spikes in our series resembles that of the IEDs in occipital focal cortical dystrophy (FCD), an intrinsically epileptogenic focal pathology in which MRI abnormalities are often subtle.¹¹ The heterotopia of gray matter in FCD typically induces architectural anomalies of the cortical layers that could influence the morphology of the FCD-related IEDs. Furthermore, subcortical white-matter heterotopias could interrupt cortical-subcortical connections (producing a conduction defect) so as to result in the emergence of bifid spikes. It is hypothesized that the genesis of FCD-related IEDs depends on excitatory amino-acid receptor-mediated mechanisms. Other EEG abnormalities in FCD include intermittent or continuous, focal and high-frequency, stereotyped rhythmic epileptiform discharges with variable frequencies and durations.¹² When continuous, these discharges may be caused by the recurrent excitation and decreased inhibition of neuronal circuits within the epileptogenic zone, leading to prolonged trains of epileptiform activity. The absence of high-frequency IEDs in our patients does not necessarily rule out the presence of FCD, where an underlying congenital CNS disorder may coexist.

The small number of the patients in this study means that conclusions cannot be drawn regarding a possible role of anticonvulsants in the pathogenesis of CMP. All four patients in our series had either a history of seizures or a diagnosis of epilepsy, and all but one of them experienced generalized convulsive seizures. The sole patient with partial seizures

(case 2) experienced ictal fear preceding a generalized convulsive seizure.

Bifid spikes, as an expression of epileptiform discharges, showed a limited projection ipsilaterally, and little or no projection contralaterally. This limitation to a single epileptogenic zone presumably reflects the preserved integrity of the inhibitory restraint (also known as surround inhibition) that interferes with regional as well as transcallosal synaptic transmission.^{13,14} These inhibitory mechanisms are believed to be due to the intrinsic structures of most cortical circuits.

The prevalence of bifid spikes in our patients was extremely low (0.4%). However, since the study was conducted at a tertiary-care facility, referral bias could have been present during patient recruitment. It is therefore difficult to determine the actual prevalence of this pattern and its pathological significance in the general population.

In summary, CMP is a rare and probably underreported EEG pattern that is of epileptogenic significance. It is probably generated by asynchronous spatiotemporal averaging of electrical signals in the cortex (theoretically caused by a conduction defect in projection pathways), resulting in the signals reaching the scalp with different latencies. Unlike the cardiac M pattern, the pathology underlying CMP is poorly understood, although congenital CNS anomalies may be a culprit. Larger studies are necessary to elucidate this.

Acknowledgments

The authors wish to thank Michael K Janati for editing the paper. We also thank Jeffrey F. Ricablanca, Fareed Ahmed Anees, Rashid Eissa Alshubrumy, and Valerie Cerna for their technical contributions.

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