



Case Report

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Recognising Acute Lamotrigine Induced Tourette's Syndrome in Adults

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Abstract

We report a woman with epilepsy developing acute reversible lamotrigine induced Tourette's syndrome. This rare reaction is important as lamotrigine is used widely in neurology, psychiatry and pain management.

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After six years of remission on carbamazepine, a 33-year-old woman with focal epilepsy of unknown cause had a seizure three weeks post-partum. Within 48 hours of starting lamotrigine (25mg twice daily), she developed severe complex motor tics and coprolalia. There was no personal or family history of tics or obsessional traits. Tourette's resolved within 72 hours of stopping lamotrigine. She declined re-challenge. There is no recurrence over nine years. Previous reports of Tourette's in patients treated with lamotrigine for epilepsy, bipolar disorders or refractory depression demonstrated a dose-dependent effect (Table). Our patient's symptoms occurred and resolved within 48 hours (compared to a mean 5 months and 72 hours respectively in all reports, see Table), more rapidly than previously reported. The severity of lamotrigine-induced Tourette's varies from mild to severe. In most patients, lamotrigine was withdrawn, but in 5/16 dose reduction resolved symptoms (Table). Several cases recurred on re-challenge, and 7/16 occurred in adults (see Table) in contrast to primary

Tourette's syndrome (commencing at mean 7 years), occurring in 0.5% of the population [1].

Carbamazepine, phenobarbital and phenytoin [2] as well as lamotrigine, are rare secondary causes of Tourette's. Only one previously reported patient had a prior tic disorder and 2/16 had pre-existing obsessional traits (Table). No predisposing or genetic factors have been identified, in contrast to primary Tourette's syndrome [1].

Tourette's syndrome is postulated to be due to basal ganglia and frontal dysfunction [3], along with genetic factors [1]. The mechanism of the reaction to lamotrigine is uncertain. Inhibition of voltage-gated sodium channels and subsequent attenuation of pre-synaptic glutamate release modulates basal ganglia circuitry and is postulated as the cause [3]. Lamotrigine-mediated nicotinic receptor agonism, mediating basal ganglia dopamine release, has also been suggested [3]. Neither hypothesis explains susceptibility in such a small percentage of patients.

Table 1: Reported lamotrigine-induced Tourette's syndrome.

First author, year	Age, sex	Indication	Past tics	Lamotrigine dose	Concurrent treatment	Tic severity	Time to onset	Time to resolve
	(years)			(total mg/day)		(YGTSSd-score)		
Angus-Leppan, 2019	33, F	focal epilepsy	nil	50mg	carbamazepine	severe (88/100)	2 days	complete, 3 days

Lu D, et al. [5]	15, M	bipolar disorder	nil	from 150mg	nil	mod (42/100)	NS	complete, 4 weeks
Musiek ES, et al. [6]	38, M	epilepsy, U	nil	200mg	nil	severe	7.5. months	9 months, incomplete
	28, M	epilepsy, U	nil	200mg	nil	mod	3-4 months	3 months, occasional tics
Alkin T, et al. [7]	49, F	major depression	nil	from 150mg	nil	NS	NS	2 months
Moreira B, et al. [8]	18, F	generalized epilepsy	nil	NS	valproate	not specified	NS	with 25mg dose reduction
Kim DG, et al. [9]	44, F	focal epilepsy	nil	200mg	nil	NS	NS	1 month
Seemuller F, et al. [10]	55, F	bipolar disorder	mild	200mg	nil	NS	NS	2 weeks
Sotero de Menezes MA, et al. [4]	12 F	focal epilepsy	nil	800mg	carbamazepine	NS	10 months	remained on Rx - acceptable tics
	5, M	behavioral disturbance	nil	325mg	nil	NS	10 months	2 weeks
	2.5, F	epilepsy	nil	62.5mg	nil	NS	4 months	3 months
	4, M	speech regression	nil	5mg/kg	nil	NS	6 months	1 month
	10, F	epilepsy, encephalopathy	nil	300mg	topiramate	NS	7 months	with unspecified dose reduction
Lombroso CT, [11]	7, F	focal epilepsy	nil	200mg	valproate	moderate	2 weeks	with dose reduction to 175mg
	12, M	epilepsy, U	nil	324mg	carbamazepine	severe	NS	with dose reduction to 225mg
	8, M	epilepsy, U	nil	275mg	gabapentin	severe	2 weeks	days, with reduction to 200mg

M=male, F=female

NS=not specified

mod=moderate

U=unclassified

Rx = treatment

a*plus ADHD, language dysfunction

b^hhistory of childhood ritualised behavior which resolved without treatment

c^mmild orofacial tics in childhood

d^YGTSS= Yale Global Tic Severity scale (0-100)

e^aafter reaching highest dose

In our secondary care cohort, lamotrigine induced Tourettes occurred in 0.3% of adults with epilepsy, and a previous report estimated 1.3% in children [4]. The reaction can be delayed up to 10 months after commencing Lamotrigine. A careful drug history is important in Tourette's syndrome, especially if atypical features, such as adulthood onset, or absent family history. Clinicians should be aware of this reversible cause of Tourette's syndrome.

Acknowledgement

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Conflict of Interest

None.

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