

CEREBELLAR DAMAGE IN A PATIENT ON LITHIUM DEVELOPING ENTERIC FEVER: A CASE REPORT

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The effects of lithium on the CNS range from commonly observed mild effects to life threatening, irreversible brain damage in rare instances of severe toxicity (Moore 1972, Hartitzsch et al 1972, Reisberg & Gershon 1979, Kadgoanker et al 1981). Some of the common side effects include mild cognitive impairment, muscular weakness, tremors and EEG changes. Neurotoxicity usually presents with clouding of consciousness, abnormal movements, seizures and neurological deficits. According to Schou et al (1968) patients with lithium intoxication either die or recover completely with no lasting neurological sequelae. However, permanent cerebellar damage due to lithium toxicity manifesting as ataxia, tremors and dysarthria has been reported only recently (Sellers et al 1982, Hartitzsch 1972). Mostly, this neurotoxicity is associated with high serum lithium levels but it can occur even at low levels.

Cerebellar damage due to enteric fever is comparatively rare and there are only a few published reports (Joshi 1963, Scragg et al 1969, Kadgoanker et al 1985).

The present report pertains to a patient who was on lithium and developed enteric

fever and signs of cerebellar damage.

Case Report

R.G., a 42-years old male, developed psychotic illness for the first time at the age of 35 years. It was characterised by excitement; abusive, assaultive behaviour; grossly irrelevant speech; paranoid delusions; irritable and hostile affect without any evidence of elation or grandiosity. He was treated with phenothiazines and later put on maintenance doses. Over the next three years the patient presented with marked thought disorder of form and content, irrelevant talk, poor rapport as continuous disturbances punctuated at times by affective disturbances, both manic and depressive, suggesting a diagnosis of schizoaffective schizophrenia. Since the patient did not show any improvement on maintenance doses of Fluphenazine he was admitted and lithium was considered. Pre lithium assessment comprised a detailed physical examination including examination of the central nervous system, baseline investigations for renal functions (blood urea, serum creatinine, 24 hr urinary proteins and creatinine) and thyroid function tests. Since all were normal he was started on Lithium

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carbonate 600 mg per day on 8.7.1983. The dose was gradually built up to 1200 mg/day. His serum lithium levels done 12 hours after the last dose ranged from 0.40-0.85 mmol/L.

became unsteady. On the day of admission he developed a low grade fever which was not associated with chills or rigors. In the course of this his temperature increased. There was no history of clouding of

Table
Serial Serum Lithium estimations with corresponding Dosages

Date	Dose (mg/day)	Level (mmol/L)
26th July 1983	900	0.65
2nd August 1983	1200	0.85*
13th August 1983	1200	0.50
16th August 1983	1200	0.57
6th September 1983	1200	0.60
20th September 1983	1200	0.55
4th October 1983	1200	0.40
18th October 1983	1500	0.85*
8th November 1983	1500	0.45
12th November 1984 at 10.00 AM (Admission)	(Last dose on Lithium on 11th Nov. 84 was at 9.00 AM)	0.50
13th November 1983	Lithium stopped	0.119
14th November 1983	Lithium stopped	0.03

* Higher levels are temporally related to the increase in dose at first but are then followed by a decline.

The Table above shows the serum lithium levels and the corresponding dose of lithium. Since most of the estimations showed low levels (except one reading of 0.85 mmol/L) the lithium dose was raised to 1500 mg/day. With this there was an initial rise of serum lithium levels to 0.85 mmol/L done after 12 hours of last dose of lithium which fell again to 0.45 mmol/L after a month on the same dose.

The patient developed signs suggestive of lithium toxicity on 10th November 1983 and was hospitalized on 12th November. He complained of abdominal discomfort, anorexia and had two episodes of vomiting. He had excessive thirst and increased frequency of micturition. His speech became more slurred and his gait

consciousness. Meanwhile he remained stable in terms of his psychiatric state. General examination revealed a sick looking, pale man, febrile (39°C) with a pulse rate of 130/mt. CNS examination showed that there was no alteration of consciousness. He had dysarthria, titubation, bilateral intention tremors, inco-ordination, dysdiadochokinesis, and severe gait ataxia. There were no motor or sensory deficits. Deep tendon reflexes were normal and plantar responses were flexor bilaterally. The fundi were normal. The haemoglobin, total and differential counts, electrolytes, blood urea and blood sugar on admission were normal. Serum lithium level measured on that day was 0.50 mmol/L which decreased further on the two consecutive days as shown in Table.

Lithium and all other drugs were stopped and symptomatic management was started. The patient was transferred to the medical ward on 18th November 1983, and subsequently, his blood culture grew *Salmonella Typhi*. In the medical ward the patient had a stormy course developing multiple GI complications. At no time during the illness did he show signs of disorientation, confusion or memory impairment. However, cerebellar signs persisted with minimal improvement. He showed no psychiatric symptoms during this period. He gradually recovered and was discharged after 70 days of hospitalization. Follow-up every month for 12 months revealed no change in the severity of the cerebellar and his mental symptoms gradually reappeared 5 months after discharge.

Discussion

This patient presented initially with signs and symptoms suggestive of acute lithium toxicity in the form of gastrointestinal disturbances, increased thirst, polyuria, and cerebellar signs which preceded the development of fever by two days. However all other symptoms improved within 48-72 hours but cerebellar signs persisted. It may be that these signs were due to lithium toxicity and the enteric fever occurred later. More likely possibility is, that enteric fever occurred first and the dehydration and systemic derangement predisposed to lithium toxicity. However, it may also be that both the processes (lithium toxicity and enteric fever) developed simultaneously independent of one another.

Lithium has been known to produce irreversible, diffuse cerebellar damage (Hartitzsch et al 1972). This usually occurs at high serum lithium levels (1.5-2 mmol/L or more) but there are many individual case

reports of severe toxicity occurring below these levels (Shopsin et al 1970). In our patient apart from the toxicity appearing at low serum lithium levels, the lithium levels increased immediately on increasing the dose but fell later inspite of the same dose (Table). In such patients the concentration of lithium in RBC's may be more important as the ratio of RBC lithium to plasma lithium has been shown to be much higher in patients who become toxic compared to controls (Pandey et al 1979).

The lithium-sodium exchange pathway what controls the efflux of lithium from the RBC's is inhibited as toxicity develops. It is possible that similar mechanisms may be operating in our patient, since he presented initially with well established neurotoxic symptoms and signs of lithium in the presence of low serum lithium levels. The odd feature was that at no point in time he had clouding of consciousness, disorientation or confusion (toxic confusional state) as these have been reported in all cases of lithium neurotoxicity (Moore 1972). Agulvik, Alberto and Moore (1972) mentioned that the clinician should be cautious when serum lithium levels do not rise as expected with increasing lithium doses. It is quite possible that the development of enteric fever contributed to the precipitation of lithium toxicity at lower serum levels in this case.

With regard to enteric fever, although CNS involvement in enteric fever is quite common, cerebellar ataxia is rarely seen. A remarkable recovery in a short period is the hallmark of enteric induced cerebellar damage. The exact pathogenesis of the condition is not known but metabolic disturbances, toxemia, hyperpyrexia, and nonspecific changes such as oedema have been implicated (Scragg et al 1969).

The interaction between enteric fever and lithium is ill understood and worthy of further study. As there was no change in the severity of cerebellar signs after one year, it indicates that the damage has been permanent. The clinical course cannot confirm whether lithium is the cause of cerebellar damage in this case, although the development of enteric fever may have precipitated the onset of lithium toxicity in the first instance.

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