A Case of Renal Failure Requiring a Renal Transplant Secondary to Lithium Treatment

To the Editor: Lithium is one of the most effective medications used in the long-term treatment of bipolar affective disorder as a mood-stabilizing agent. Lithium's renal toxicity is well documented in the literature: it causes renal side effects that vary from polyuria, polydipsia, and nephrogenic diabetes insipidus to end-stage renal disease (ESRD). Lithium-induced chronic renal failure is an uncommon but not rare complication of long-term lithium treatment. Until 2000, only 3 cases of lithium-induced ESRD were known in the literature.[1] We report an interesting case of lithium-induced renal failure requiring a renal transplant, which, to our knowledge, has never before been reported.

Case report. We are reporting a case of discontinuation of lithium therapy in Ms A, a 67-year-old woman with *DSM-IV* bipolar disorder who had developed chronic renal failure after long-term use of lithium (> 35 years) to manage her mood.

Ms A had her first episode of bipolar disorder at the age of 18 years, which required hospitalization. She was started on lithium treatment at that time and had been following up with her physician subsequently. She had been fairly stable on lithium at a dose of 300 mg 3 times a day. At the age of 56 years, she developed lithium toxicity. She had tremors and mild confusion, and the episode resolved without hospitalization. She continued her lithium treatment after the episode resolved.

Two years later, she again developed lithium toxicity following a bout of influenza that caused diarrhea and decreased fluid intake. Fortunately, due to changes in her mental status, she had unknowingly stopped taking her medications. She was hospitalized in a delirious state along with fever and headache, and her serum lithium level was found to be 1.59 mEq/L, with increased serum urea nitrogen (74 mg/dL) and creatinine (3.5 mg/dL) levels. She denied any history of dysuria, increased urinary frequency, or renal problems. She improved upon admission, and her confusion level subsequently declined. She was diagnosed with acute renal failure secondary to acute infection and lithium. She was recommended to avoid lithium due to its potential risk of toxicity. She was started on lamotrigine and aripiprazole to help control her mood.

She was referred to the renal physician, and a diagnosis of chronic renal insufficiency secondary to lithium toxicity was made on the basis of exclusion of other causes. Her lithium was finally stopped at that time. She was asked to follow up with her renal physician and was started on dialysis.

She was found to have had progressive renal dysfunction over the last 10 years. She had 10% of kidney function left with a glomerular filtration rate of 6 mL/min per 1.73 m^2. She was diagnosed with stage 5 chronic kidney disease and was considered for a renal transplant. Eventually, at age 67 years, she received a cadaveric renal transplant. Since then, she has been followed up by outpatient psychiatry on a regular basis and has been stable on treatment with lamotrigine and aripiprazole.

Studies during the 1980s showed a high prevalence of irreversible tubular and glomerular damage in patients treated with lithium for 15 years or more.[2] A potential subgroup of long-term lithium (> 15 years) users, suggested to be as high as 21%, was identified as at risk of developing renal impairment.[3] So it is to be expected that some lithium-treated patients will develop ESRD after long-term treatment. Two recent reports added further cases of lithium-induced ESRD, and 2%–7% prevalence of this adverse effect of lithium treatment was reported in ESRD populations.[4] Many patients on lithium therapy have to have lithium discontinued because of progression to renal failure and risk of lithium toxicity.[5] The duration of lithium therapy and the cumulative dose of lithium are the major determinants of nephrotoxicity. The UK National Institute for Health and Clinical Excellence guidelines recommend monitoring lithium levels every 3 months and monitoring thyroid and kidney functions every 6 months.[6]

Lithium is widely used for the prevention and treatment of mania, hypomania in patients with bipolar disorder, recurrent depression, and disorders of impulse control. It reduces both frequency and severity of relapses of bipolar affective disorder. Lithium causes a subtle decline in renal function. Duration of lithium treatment is a major risk factor. We found that renal failure is an uncommon but not rare end result of long-term lithium treatment. Most studies in earlier years reported only rare cases of lithium-induced chronic renal failure.[1,7] The latest research suggests that ESRD is a very rare complication of long-term lithium treatment, affecting ≈ 1% of patients who have taken lithium for more than 15 years.[8,9] The risk of renal failure as a consequence of long-term therapy may persist even after discontinuation of treatment.[8] Most of the enormous population of long-term lithium-treated patients will not develop chronic renal failure, and the risk for this outcome can be avoided by cautious monitoring. Monitoring of lithium levels every 3 months and monitoring of kidney functions and thyroid function testing every 6 months are recommended.

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