Nonadherence to Medication in Hypothyroidism: A Case Report

Rajeev C. Kandukuri, MD; Mehnaz A. Khan, MD; and Stephen M. Soltys, MD

This case report reviews the consequences of nonadherence to a hypothyroidism medication schedule and examines the complexity of hypothyroidism treatment. Both biologic and psychosocial aspects are discussed. The physician-patient relationship is a key to improving adherence, and medication alone is not sufficient to improve outcomes. It is essential for the physician to address and successfully manage the psychosocial factors involved as well.

Prim Care Companion J Clin Psychiatry 2010;12(3):e1–e3

Submitted: *July 20, 2009; accepted October 1, 2009.*
Published online: *May 13, 2010 (doi:10.4088/PCC.09m00863gre).*
Corresponding author: *Stephen M. Soltys, MD, Department of Psychiatry, Southern Illinois University School of Medicine, PO Box 19642, Springfield, IL 62794-9642 (ssoltys@siumed.edu).*

Nonadherence to medication schedules by patients with chronic illnesses has long been recognized as a problem. It is estimated that approximately 50% of patients follow treatment recommendations.[1] The consequences of untreated hypothyroidism can vary from physical symptoms to psychiatric illnesses like depression, psychosis, delirium, and dementia.[2,3] Hypothyroidism can damage the central nervous system resulting in irreversible neurocognitive and behavioral changes in severe cases[4,5] that, in turn, can affect a patient's activities of daily living and occupational functioning.

Fortunately, the usual treatment for hypothyroidism is simply a tablet of levothyroxine once a day. Most studies suggest that more complicated treatment regimens, such as combination treatment with thyroxine and liothyronine, do not improve well-being, quality of life, or cognitive function when compared with thyroxine alone.[6–8] Thyroid replacement therapy is easily monitored via simple blood tests.[9] Yet, in spite of the simplicity of treatment and monitoring, noncompliance rates are the same for hypothyroidism when compared with other chronic illnesses (ie, hypertension, diabetes mellitus, hypercholesterolemia, or osteoporosis) that require more complex treatment regimens and monitoring.[1]

This case report focuses on medication noncompliance in a patient with hypothyroidism that had disastrous consequences and reflects on interventions that might have aided in avoiding this outcome.

CASE REPORT

Mr A, a 23-year-old white male, was brought to the hospital by his cousin after he appeared confused to his coworkers. He was easily distracted, paranoid, delirious, and unable to provide a history. Collateral information was obtained from the cousin who noted that a few days previously Mr A appeared to move slowly, with complaints of cold intolerance, fatigue, constipation, confusion, and prominent mental slowing. Mr A's affect was flat. He talked slowly with markedly delayed responses even to simple "yes" or "no" questions.

Mr A had a prophylactic thyroidectomy at the age of 5 years for multiple endocrine neoplasia type IIb (MEN IIb) syndrome. His mother died of MEN IIb-metastatic medullary cancer when he was 17 years old. Mr A was estranged from his father and started living with his friends and a cousin after his mother's death. After completing high school, he entered junior college but subsequently dropped out and became a janitor. His cousin was his primary support and visited Mr A about every 2 days.

The patient continued to take medication on and off after his mother's death and was under the care of an endocrinologist. A review of medical records showed that he had missed 2 recent appointments and had not filled his thyroid prescription for about 3 months. Mr A had experienced similar symptoms 2 years previously when he stopped taking levothyroxine. At that time, he was treated in the hospital for hypothyroidism and psychosis and was discharged to a local nursing home for 3 months. He started living independently thereafter.

On physical examination at the emergency department, Mr A's vital signs were temperature: 97.5°F, pulse: 74 beats/min, blood pressure: 115/74 mm Hg, and respiration: 16 breaths/min. Findings of his physical examination were remarkable for thick tongue and lips with multiple papillary lesions consistent with mucosal neuromas, dry skin, coarse hair, and a well-healed thyroidectomy scar. His neurologic examination was notable for decreased muscle mass and tone in all

extremities with significant delay in the relaxation phase of deep tendon reflexes. Gait and general movements were very slow. On mental status examination, he had psychomotor retardation, poor eye contact, slow and low volume speech with delayed responses, and flat affect. He denied suicidal or homicidal ideation. He had ideas of persecution and auditory hallucinations. He could not cooperate with the Mini-Mental State Examination[10] and had poor insight into his illness.

On admission, Mr A's laboratory values revealed a thyroid-stimulating hormone level of greater than 200 mIU/mL, a total T_4 level of 4.9 μg/dL, and a free T_3 level of 1.08 ng/dL. A comprehensive metabolic panel and complete blood count were within normal range. A magnetic resonance image of the brain showed an enlarged pituitary gland unchanged from previous scans. Other blood work, an electrocardiogram, and an electroencephalogram were unremarkable. Mr A was started on intravenous levothyroxine, quetiapine, and citalopram. While his psychosis cleared and mood improved, Mr A had persistent memory and executive functioning deficits that resulted in discharge to a nursing home, where he has lived for the past 2 years because he is unable to care for himself.

DISCUSSION

This case is an example of how hypothyroidism can manifest initially with nonspecific symptoms such as weakness, fatigue, and loss of interest and can progress to neurocognitive changes such as inattentiveness, inability to concentrate, slowing of thought processes, inability to understand complex tasks, and memory impairment.[11]

When Mr A's mother died, he lost his sole source of adult support and guidance. There is no record of any inquiry as to the adequacy of his social supports, living situation, or income after his mother's death. No referrals to the child protective agency were noted. Mr A was turned loose to fend for himself.

Providing appropriate social services at that time might have prevented Mr A's subsequent first hospitalization and improved his quality of life. Even after the first hospitalization, no steps were taken to assure continuity of care even though the patient needed 3 months in a nursing home to recover functioning. The fact that Mr A developed serious psychiatric symptoms secondary to medication noncompliance resulting in the first hospitalization should have served as a "red flag" that special aftercare arrangements might be needed on a long-term basis.

However, in this patient, careful case management might not have been enough. An exploration of what his illness meant to him in terms of his future (it had killed his mother) might have highlighted fears or misconceptions that could have been addressed by the primary care physician or a counselor, resulting in improved compliance. Mr A eventually slipped into another pattern of noncompliance that resulted in the second hospitalization and the development of cognitive symptoms that were apparent on admission. If Mr A had not been brought in to receive treatment, he may have progressed into myxedema coma. Even after thyroid replacement therapy, Mr A continued to have residual neurocognitive impairment that led to what may be a permanent placement in a nursing home.

Medication noncompliance is common in adolescents. It can stem from many sources including a desire to not be different from peers, a belief of personal invulnerability, or a rebellion against authority figures who are seen as being overcontrolling.[12] Since the discontinuation of treatment in hypothyroidism can lead to a return of symptoms in a short period of time,[13] assuring close follow-up for adolescents should be the central feature of any management plan.

Providing the patient with education about medication is not enough. In a randomized controlled trial of thyroxine adherence, distributing booklets about thyroxine medication did not improve adherence between the study group and the control group.[14] The doctor-patient relationship plays a key role in adherence to medication regimens. Physicians who use understandable language and encourage open doctor-patient exchanges in friendly, caring environments are more likely to foster participation by patients in their own medical care, increasing the likelihood of adherence. Asking simple questions regarding any difficulties in taking medication and the presence of side effects while addressing forgetfulness in a nonjudgmental manner will enhance the therapeutic relationship.[15,16]

Crowley, in his 14-year study on psychosis in myxedema,[17] emphasized that only some patients responded to treatment. He recognized that some reasons for not responding to thyroid treatment might include not only noncompliance secondary to emotional and personality characteristics but also might even be due to the presence of neurocognitive damage that has not been fully realized by the clinician.

There are case reports that suggest that weekly direct observed thyroxine therapy can be effective in preventing relapse in noncompliant patients; however, more research is needed to confirm the efficacy of this approach in postsurgical thyroidectomy patients. The case reports suggest that a weekly total dose of levothyroxine (intramuscularly, intravenously, or orally) can work as effectively as daily doses and help to avoid noncompliance.[18,19] All of these routes administered under direct observation either at a physician's office or by a home health nurse showed benefit in moderate to severe cases of hypothyroidism in noncompliant patients.[20] The rationale behind this treatment strategy

is the long half-life of levothyroxine, which is in the range of 5.3 to 9.5 days.[21–23] There may have been a better chance for compliance in this case if the patient had participated in a weekly dosing regimen.

In general medicine, the concept of disease management programs for chronic illnesses is becoming increasingly more common. Many of these programs have outreach to patients in the community, just as in the field of mental health, assertive treatment teams[24] regularly go into the community to help patients deal with social, financial, and personal issues that impact compliance. Perhaps this proactive approach will become a standard of care for chronic medical illnesses as it is for chronic psychiatric illnesses.

CONCLUSION

Hypothyroidism is a chronic illness with simple treatment, yet noncompliance is common. Noncompliance with medication can result in neurocognitive changes that are potentially irreversible and may further complicate the management of the patient.

Physicians should spend more time assessing patients with hypothyroidism for psychosocial factors that may impact compliance. By verbalizing that remembering to take a medication even once a day can sometimes be difficult and reporting missed doses will not result in a lecture, the physician can create an environment wherein open discussion of nonadherence to medication can occur. While laboratory tests can be helpful to detect noncompliance, they are not sufficient. Missed appointments by patients with hypothyroidism should result in efforts to contact the patient, calls to family if proper releases have been obtained, or sending out a home health nurse or case manager to check on the patient. Special vigilance in developing long-term case management plans and counseling should be used if the noncompliance has resulted in psychiatric symptoms. By using assertive community treatment principles, the primary care physician can reduce the possibility that patients with a relatively easily treated illness like hypothyroidism do not have serious adverse outcomes.

Drug names: citalopram (Celexa and others), levothyroxine (Synthroid, Levoxyl, and others), liothyronine (Cytomel, Triostat, and others), quetiapine (Seroquel).

Author affiliations: Department of Psychiatry, Southern Illinois University School of Medicine, Springfield, Illinois (Drs Kandukuri, Khan, and Soltys).

Potential conflicts of interest: **Drs Kandukuri**, **Khan**, and **Soltys** report no financial or other affiliations relevant to the subject of this article.

Funding/support: None reported.

REFERENCES

1. Briesacher BA, Andrade SE, Fouayzi H, et al. Comparison of drug adherence rates among patients with seven different medical conditions. *Pharmacotherapy*. 2008;28(4):437–443.
2. The Clinical Society of London. Report of a Committee to Investigate the Subject of Myxoedema. *Trans Clin Soc London*. 1888;21(suppl):1–215.
3. Heinrich TW, Grahm G. Hypothyroidism presenting as psychosis: myxedema madness revisited. *Prim Care Companion J Clin Psychiatry*. 2003;5(6):260–266.
4. Clarnette RM, Patterson CJ. Hypothyroidism: does treatment cure dementia? *J Geriatr Psychiatry Neurol.* 1994;7(1):23–27.
5. Dugbartey AT. Neurocognitive aspects of hypothyroidism. *Arch Intern Med*. 1998;158(13):1413–1418.
6. Clyde PW, Harari AE, Getka EJ, et al. Combined levothyroxine plus liothyronine compared with levothyroxine alone in primary hypothyroidism: a randomized controlled trial. *JAMA*. 2003;290(22):2952–2958.
7. Joffe RT, Brimacombe M, Levitt AJ, et al. Treatment of clinical hypothyroidism with thyroxine and triiodothyronine: a literature review and metaanalysis. *Psychosomatics*. 2007;48(5):379–384.
8. Grozinsky-Glasberg S, Fraser A, Nahshoni E, et al. Thyroxine-triiodothyronine combination therapy versus thyroxine monotherapy for clinical hypothyroidism: meta-analysis of randomized controlled trials. *J Clin Endocrinol Metab*. 2006;91(7):2592–2599.
9. England ML, Hershman JM. Serum TSH concentration as an aid to monitoring compliance with thyroid hormone therapy in hypothyroidism. *Am J Med Sci*. 1986;292(5):264–266.
10. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res.* 1975;12(3):189–198.
11. Miller KJ, Parsons TD, Whybrow PC, et al. Verbal memory retrieval deficits associated with untreated hypothyroidism. *J Neuropsychiatry Clin Neurosci*. 2007;19(2):132–136.
12. Turkel SB, Jacobson JR, Pao M. Children's reaction to illness and hospitalization. In: Saddock BJ, Saddock VA, Ruiz P, eds. *Comprehensive Textbook of Psychiatry*. 9th ed. Philadelphia, PA: Lippincott, Williams & Wilkins; 2009:805–3814.
13. Libow LS, Durell J. Clinical studies on relationship between psychosis and regulation of thyroid gland activity. *Psychosom Med*. 1965;27:369–376.
14. Crilly MA. *Thyroxine Adherence Study: A Randomized Controlled Clinical Trial in Primary Care* [MD thesis]. Manchester, UK; University of Manchester: 2003.
15. Schifferdecker E, Balz F, Jungmann E, et al. Compliance problems in therapy with levothyroxine. *Med Klin*. 1990;85(8):477–480.
16. Beck JS. A cognitive therapy approach to medication compliance. In: Kay J, ed. *Integrated Treatment of Psychiatric Disorders*. Washington, DC: American Psychiatric Publishing; 2001:113–141.
17. Crowley RM. Psychosis with myxedema. *Am J Psychiatry*.1940;96:1105–1116.
18. Rangan S, Tahrani AA, Macleod AF, et al. Once weekly thyroxine treatment as a strategy to treat non-compliance. *Postgrad Med J*. 2007;83(984):e3.
19. Grebe SK, Cooke RR, Ford HC, et al. Treatment of hypothyroidism with once weekly thyroxine. *J Clin Endocrinol Metab*. 1997;82(3):870–875 [PMID: 9062499].
20. Pickett P, Iqbal R, Mundinamani D, et al. Directly observed medication supplementation for non-compliance in a patient with hypothyroidism and hypoparathyroidism. *Endocrine Abstracts*. 2009;19:79.
21. Sethi MJ, Parr M, Bhatia V. Management strategies for hypothyroidism in non-compliant patients: a case report and review of literature. *S D Medicine*. 2008; 61(10):368–369.
22. Synthroid [package insert]. North Chicago, IL: Abbott Laboratories; 2010.
23. Tirosint [package insert]. Cranford, NJ: Akrimax Pharmaceuticals, LLC; 2010.
24. Bustillo J, Keith SJ, Lauriello J. Schizophrenia: psychosocial treatment. In: Saddock BJ, Saddock VA, eds. *Comprehensive Textbook of Psychiatry*. 7th ed. Philadelphia, PA: Lippincott, Williams and Wilkins; 2000:1210–1217.