Scientific Research Publishing

Open Journal of Psychiatry, 2026, 16(2), 131-138
https://www.scirp.org/journal/ojpsych
ISSN Online: 2161-7333
ISSN Print: 2161-7325

# Uncontrolled Hypothyroidism with Antiphospholipid Syndrome Resulting in Myxedema Psychosis

**Shahzaib Khan[1*], Heather Issa[2]**

[1]Department of Psychiatry, Advocate South Suburban Hospital, Hazel Crest, IL, USA
[2]College of Osteopathic Medicine, Des Moines University, Des Moines, IA, USA
Email: *shahkhando@gmail.com

**How to cite this paper:** Khan, S. and Issa, H. (2026) Uncontrolled Hypothyroidism with Antiphospholipid Syndrome Resulting in Myxedema Psychosis. *Open Journal of Psychiatry*, **16**, 131-138.
https://doi.org/10.4236/ojpsych.2026.162010

**Received:** January 11, 2026
**Accepted:** March 9, 2026
**Published:** March 12, 2026

Copyright © 2026 by author(s) and Scientific Research Publishing Inc.
This work is licensed under the Creative Commons Attribution International License (CC BY 4.0).
http://creativecommons.org/licenses/by/4.0/

Open Access

## Abstract

We describe a female patient with a history of antiphospholipid syndrome, hypothyroidism, and bipolar disorder, who presented with worsening mood and psychotic symptoms following discontinuation of medications. Laboratory evaluations revealed markedly elevated thyroid-stimulating hormone (TSH) of 190 mU/mL. She also had a remote history of intracranial hemorrhage and required long-term anticoagulation with warfarin. We posit that the psychosis and mood presentation were attributable to the interplay between hypothyroidism-induced neuropsychiatric symptoms, decompensation of bipolar disorder, and history of antiphospholipid-related ischemic cerebral injury. Myxedema psychosis was further supported as a diagnosis given her extremely elevated TSH, sudden symptom onset following discontinuation of levothyroxine and other medications, limited improvement with risperidone, and significant clinical improvement after restarting levothyroxine. The etiology of her hypothyroidism was considered to be autoimmune in nature, given its relationship with antiphospholipid syndrome. We emphasize the importance of recognizing autoimmune and endocrine causes of neuropsychiatric symptoms, particularly hypothyroidism, which has a prevalence as high as 18% depending on the population. Optimizing psychiatric medication doses may not be sufficient in these populations, and an accurate prognosis requires accounting for the impact of the untreated hypothyroidism and comorbid autoimmune condition. Our patient was unable to obtain maximum resolution of symptoms until we also treated her hypothyroidism.

## Keywords

Case Report, Myxedema Psychosis, Antiphospholipid Syndrome, Hypothyroidism-Induced Psychosis, Autoimmune Hypothyroidism

## 1. Introduction

Hypothyroidism is a common endocrine condition that can have varying physiologic presentations depending on severity. Common manifestations of insufficient thyroid hormone can include weight gain, fatigue, cold intolerance, hair loss, menstrual irregularities, myxedema, and psychiatric symptoms, including depression and psychosis [1] [2]. Hypothyroidism has a prevalence as high as 18%, depending on the population, with autoimmune thyroid disease being a subsect affecting up to 5% [3] [4]. Myxedema psychosis is a rare neuropsychiatric manifestation of hypothyroidism that presents with hallucinations, delusions, paranoia, and behavioral changes, even in the absence of classical hypothyroid symptoms [3] [5]. Although rare, 5 to 15% of patients with hypothyroidism may develop psychosis [3]. These prevalence rates highlight the necessity in recognizing and distinguishing psychosis due to hypothyroidism.

## 2. Case Presentation

A 48-year-old female was admitted to the inpatient mental health unit for worsening mood and psychosis. The patient had a history of seizure disorder, antiphospholipid syndrome (APS), hypothyroidism, asthma, pulmonary sarcoidosis, chronically elevated human chorionic gonadotropin (hCG), bipolar disorder, and posttraumatic stress disorder (PTSD). She also had a remote history of sinus venous thrombosis, multiple spontaneous abortions, and intracranial hemorrhage requiring hemicraniectomy with residual right hemiparesis, all of which were attributed to APS-induced hypercoagulability.

Collateral information was obtained from the patient's family, who reported that her symptoms began worsening over the previous three months after abruptly discontinuing her medications. Her reported symptoms included erratic behavior, disorganized speech, aggressive outbursts, verbalizing suicidal thoughts, and speaking to herself. A urine drug screen was negative for all substances.

The patient complained of having stress-induced seizure-like episodes for the past several weeks. She denied any recent travel, fever, cough, chest pain, dyspnea, vomiting, diarrhea, or abdominal pain. There were no recent falls or head injuries. She had documented allergies to clarithromycin, heparin, olanzapine, ciprofloxacin, and topiramate. She had episodic bradycardia with heart rate in the 50s. She displayed dysarthria, right-sided facial droop, and right-sided hemiparesis. She was noted to be edentulous with thinning hair. Her speech was slow and largely incoherent, which was below baseline per her family. Cranial nerves 2 through 12 were otherwise bilaterally intact. Proprioception, light touch, pinprick, and vibratory senses were intact bilaterally. Strength was intact on the left but relatively reduced on the right. She displayed asymmetrically-reduced deep tendon reflexes without other signs of neuropathy. She had a hemiplegic gait with foot drop and circumduction of the right lower extremity. She was noted to be irritable, withdrawn, guarded, and dysphoric. Her thought process was circumstantial and illogical with intermittent periods of lucidity. She typically avoided eye contact and

appeared to be responding to internal stimuli. She reported an extensive history of trauma. She also expressed delusional beliefs and distrust towards her family members. She overall displayed poor insight into her symptoms and was unable to explain why she discontinued her medications. She was lethargic and somnolent during her first few days of admission with complaints of poor sleep and reduced appetite.

She received an EEG which displayed no interictal epileptiform waveforms or seizure activity. There was concern for an acute cerebrovascular accident (CVA) given her history of APS and prior stroke. She received a brain MRI which did not show any acute intracranial abnormality, but did demonstrate chronic findings of prior left-sided cranioplasty with encephalomalacia and gliosis in the left frontal, parietal, and temporal lobes.

Laboratory studies revealed elevated hCG at 10 mU/mL (milliunits per milliliter), with normal for non-pregnant individuals being less than 5 mU/mL. This was consistent with past results and she had a documented history of chronically elevated hCG. A transabdominal pelvic ultrasound was still ordered to assess for possible pregnancy but was unremarkable without any evident mass. Thyroid-stimulating hormone (TSH) was elevated at 190.218 μU/mL (microunits per milliliter), with normal typically being 0.35 to 5.0 μU/mL. Free T4 was low at 0.4 ng/dL (nanograms per deciliter), with normal typically being 0.8 to 1.9 ng/dL. Her lab values were consistent with hypothyroidism. She refused both oral or intravenous levothyroxine for treatment of hypothyroidism. She was previously on oral levothyroxine 100 mcg but discontinued it prior to symptom onset. She was unable to provide a reason for medication refusal and displayed poor insight into the importance of medication compliance. The remainder of her lab results were unremarkable or within normal limits.

Despite her refusal of levothyroxine, she was willing to resume certain home medications, including levetiracetam 1500 mg twice daily, lacosamide 50 mg twice daily, venlafaxine 150 mg daily, and ropinirole 0.25 mg three times daily. Ropinirole was discontinued to reduce possible contributory effects on psychotic symptoms. Warfarin for APS was resumed and dosed per international normalized ratio (INR).

She was agreeable with starting risperidone 1 mg nightly for psychosis, insomnia, and mood stabilization on day 1 of hospitalization. Risperidone was gradually titrated over four days to 1 mg daily and 2 mg nightly. There was observable improvement in thought organization, but she continued to express paranoid delusions and passive death wishes. She ultimately agreed to restart prior dose of levothyroxine 100 mcg daily on day 5 of hospitalization. Within two days of starting levothyroxine, there was notable improvement in energy level, affect, and engagement. There were no other medication changes during this time. Delusional thoughts diminished substantially without further antipsychotic dose escalation. She displayed clearer speech and her family felt she returned to premorbid baseline by day 7 of hospitalization.

## 3. Discussion

Hypothyroidism is implicated in various neuropsychiatric symptoms involving mood and cognition, which is hypothesized to be due to disruptions in serotonin and norepinephrine pathways and impaired neurotransmitter synthesis [1] [2] [6]. In addition to regulating energy metabolism and protein synthesis, thyroid hormones are crucial in regulating energy metabolism, protein synthesis neurodevelopment, including neuronal function, synaptic transmission, and plasticity [7]. Patients with prior psychiatric history may be at risk for psychosis from severe hypothyroidism [8]. Although there are no specific tests to diagnose myxedema psychosis, it is diagnosed by way of thyroid panel monitoring in the setting of clinical signs, and should be considered in psychotic patients [9]. Findings in a patient presenting with myxedema may include nonpitting edema, thinning hair, hypothermia, delayed deep tendon reflexes, bradycardia and hypotension [7]. Bradycardia, thinning hair, and reduced deep tendon reflexes were present in our patient.

APS is an autoimmune condition that can contribute to thrombosis and frequent miscarriages for women of child bearing years [10] [11]. Patients typically present with recurrent thromboses or history of stroke [10] [11]. Diagnosis requires a confirmatory laboratory detection of aPL antibodies, lupus anticoagulant, anticardiolipin antibodies, or anti-$\beta$glycoprotein 1 antibodies [10] [11]. There are various non-criterial findings in APS, including libman-sacks endocarditis, dermatological patterns like livedo reticularis, and neuropsychiatric symptoms including cognitive dysfunction, seizures, and psychosis [10]. The proposed pathophysiology of neuropsychiatric symptoms in APS is of a hypercoagulable and inflammatory state resulting in microvascular ischemic brain injury disrupting particular regions and neurotransmitter systems [11]. Management for APS includes long term anticoagulation and steroid treatment [11]. Hypothyroid patients with APS may have an autoimmune form of thyroid disease, as both can contribute to recurrent pregnancy loss [4] [12]. Additionally, the prevalence of APS is increased in patients with autoimmune thyroid disease, which has a prevalence of about 5% [4] [12]. Furthermore, APS can present with psychiatric symptoms and there is an association between APS and psychosis [13]. There is also an association of 15 to 42% between cognitive dysfunction and aPL antibodies [13].

These findings were consistent with our patient's MRI results, history of CVA, sinus venous thrombosis, multiple miscarriages, and were strongly suspected to be contributing to her presentation. Her diagnosis of APS had previously been established based on both clinical and laboratory criteria. Laboratory evaluation performed in prior admissions demonstrated persistently positive aPL antibodies, including lupus anticoagulant and elevated anticardiolipin IgG antibodies on two occasions. These findings fulfilled the revised Sydney classification criteria for APS, which require at least one clinical thrombotic or obstetric event in combination with persistent laboratory positivity for aPL antibodies [14].

Due to the patient's limited response to previously effective antipsychotic med-

ication, symptom onset coinciding with discontinuation of levothyroxine, history of autoimmune disease and CVA, and a known association between thyroid disease and APS and psychiatric symptoms, a primary psychiatric diagnosis was deemed insufficient. Alternative contributors to her psychosis and altered behavior were carefully considered. Acute CVA was considered given her APS history, but brain MRI demonstrated only chronic findings. Seizure-related psychosis was considered; however, EEG revealed no epileptiform activity and there was no postictal pattern temporally associated with her behavioral changes. Substance-induced psychosis was unlikely given a negative urine drug screen and collateral confirmation of medication nonadherence rather than substance use. Medication-induced psychosis was also considered, particularly from dopaminergic agents such as ropinirole; however, symptoms predated its discontinuation and persisted despite its cessation. Primary bipolar mania with psychotic features was possible given her psychiatric history, but her limited response to appropriately titrated risperidone and the temporal association with severe biochemical hypothyroidism supported an organic contributor. Collectively, these findings made severe hypothyroidism a more plausible proximate driver of her acute decompensation.

Treatment for myxedema psychosis involves appropriate and timely use of thyroid hormone replacement [2]. Levothyroxine weight-based dosing of 1.61 - 1.8 mcg/kg/day is considered optimal replacement treatment [3] [8]. Interestingly, older adult patients may respond better to thyroid hormone treatment than younger patients with psychosis [8]. We were initially uncertain if oral levothyroxine would be sufficient, but a literature review supported oral levothyroxine as an appropriate alternative to intravenous replacement [15]. Psychosis in myxedematous patients typically resolves in about one week with thyroid supplementation, but can reoccur with medication discontinuation [3]. Full resolution may take up to months, but if left untreated, myxedema psychosis may progress to myxedema coma which has a significant mortality rate [8]. Myxedema coma, a life-threatening form of hypothyroidism, defined by bradycardia, hypotension, hypothermia, hypoventilation, depressed mental status, and shock, was considered unlikely in our patient as her symptoms had not progressed to the level of being life-threatening [16]. Although her markedly elevated TSH suggested profound biochemical hypothyroidism, we elected to restart her prior outpatient dose of 100 mcg daily as it was historically sufficient, rather than immediately initiate full weight-based replacement. This decision was made due to her psychiatric instability and uncertainty with adherence, intermittent bradycardia, and complex medical comorbidities. A cautious reinitiation strategy was chosen to reduce the theoretical risk of precipitating arrhythmia, agitation, or rapid metabolic shifts while monitoring clinical response.

Hypothyroidism should be treated in all patients with neuropsychiatric symptoms given that 5 to 15% of patients with hypothyroidism may develop psychosis and 50% of patients with treatment-resistant depression may have subclinical hypothyroidism [3]. 20% of patients with depressive symptoms can have detectable

titers of antithyroid antibodies [3]. Additionally, APS may be associated with thyroid autoimmunity, both APS and thyroid autoantibodies can result in miscarriages, and both APS and thyroid autoantibodies can involve ischemic disease of the central nervous system [4]. Thyroid autoantibodies were not obtained during this admission. Although autoimmune thyroiditis is the most common cause of primary hypothyroidism and is epidemiologically associated with APS, we cannot definitively attribute her hypothyroidism to autoimmune thyroid disease in the absence of antibody testing. This represents a limitation in etiologic certainty. Additionally, repeat thyroid function testing was not obtained prior to discharge, limiting our ability to directly correlate biochemical normalization with clinical recovery. Although the temporal association between levothyroxine reinitiation and symptom improvement is compelling, absence of short-interval laboratory confirmation limits causal inference.

## 4. Conclusion

Taking everything into consideration, decompensation of bipolar disorder due to medication discontinuation, untreated hypothyroidism-induced neuropsychiatric symptoms, and chronic APS-related ischemic cerebral injury likely caused our patient's symptoms, which is why treatment with only risperidone was inadequate. It is important for clinicians to distinguish between primary psychosis and other medical causes, as the treatment regimen can vary tremendously. Had our patient been solely treated with antipsychotic medications, she may not have responded to treatment and symptoms could have worsened. A thorough neurological and physical exam, in addition to proper laboratory and radiographic studies, is warranted in patients with medical conditions that could contribute to neuropsychiatric symptoms. Clinicians should be familiar with the various presentations of hypothyroidism and proper treatment interventions. Autoimmune thyroid disease should be considered in patients where symptoms are present and there is evidence of another autoimmune condition. A multidisciplinary approach is essential in medically complex patients with neuropsychiatric symptoms, even in cases of highly prevalent conditions, such as hypothyroidism.

## Highlights

- Myxedema should be considered in psychotic patients with a history of hypothyroidism.
- Myxedema psychosis requires treatment with levothyroxine.
- Myxedema psychosis can progress to myxedema coma if untreated.
- Antiphospholipid syndrome can cause neuropsychiatric symptoms.
- There is an association between antiphospholipid syndrome and autoimmune thyroid disease.

## Data Availability

The data used to support the findings of this study are included within the article.

## Consent

Patient consent and consent form were obtained during this case report.

## Authors' Contributions

(I) Conception and design: All authors; (II) Manuscript writing: All authors; (III) Editing and review: All authors; (IV) Final approval of manuscript: All authors.

## Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this article.

## References

[1] Bauer, M., Goetz, T., Glenn, T. and Whybrow, P.C. (2008) The Thyroid-Brain Interaction in Thyroid Disorders and Mood Disorders. *Journal of Neuroendocrinology*, **20**, 1101-1114. https://doi.org/10.1111/j.1365-2826.2008.01774.x

[2] Chaker, L., Bianco, A.C., Jonklaas, J. and Peeters, R.P. (2017) Hypothyroidism. *The Lancet*, **390**, 1550-1562. https://doi.org/10.1016/s0140-6736(17)30703-1

[3] Heinrich, T.W. and Grahm, G. (2003) Hypothyroidism Presenting as Psychosis: Myxedema Madness Revisited. *The Primary Care Companion for CNS Disorders*, **5**, 260-266. https://doi.org/10.4088/pcc.v05n0603

[4] Versini, M. (2017) Thyroid Autoimmunity and Antiphospholipid Syndrome: Not Such a Trivial Association. *Frontiers in Endocrinology*, **8**, Article No. 175. https://doi.org/10.3389/fendo.2017.00175

[5] Sardar, S., Habib, M., Sukik, A., Tanous, B., Mohamed, S., Tahtouh, R., *et al.* (2020) Myxedema Psychosis: Neuropsychiatric Manifestations and Rhabdomyolysis Unmasking Hypothyroidism. *Case Reports in Psychiatry*, **2020**, Article ID: 7801953. https://doi.org/10.1155/2020/7801953

[6] Hage, M.P. and Azar, S.T. (2012) The Link between Thyroid Function and Depression. *Journal of Thyroid Research*, **2012**, Article ID: 590648. https://doi.org/10.1155/2012/590648

[7] Bernal, J. (2025) Thyroid Hormones in Brain Development and Function. https://www.ncbi.nlm.nih.gov/books/NBK285549/

[8] Moeller, K.E., Goswami, R. and Larsen, L.M. (2009) Myxedema Madness Rapidly Reversed with Levothyroxine. *The Journal of Clinical Psychiatry*, **70**, 1607-1608. https://doi.org/10.4088/jcp.08l04958yel

[9] Krüger, J., Kraschewski, A. and Jockers-Scherübl, M.C. (2021) Myxedema Madness—Systematic Literature Review of Published Case Reports. *General Hospital Psychiatry*, **72**, 102-116. https://doi.org/10.1016/j.genhosppsych.2021.08.005

[10] Miyakis, S., Lockshin, M.D., Atsumi, T., Branch, D.W., Brey, R.L., Cervera, R., *et al.* (2006) International Consensus Statement on an Update of the Classification Criteria for Definite Antiphospholipid Syndrome (APS). *Journal of Thrombosis and Haemostasis*, **4**, 295-306. https://doi.org/10.1111/j.1538-7836.2006.01753.x

[11] Ruiz-Irastorza, G., Crowther, M., Branch, W. and Khamashta, M.A. (2010) Antiphospholipid Syndrome. *The Lancet*, **376**, 1498-1509. https://doi.org/10.1016/s0140-6736(10)60709-x

[12] Lu, D., Song, Z., Gao, Y., Zhang, J. and Guo, X. (2022) Patients with Autoimmune

Thyroid Diseases Have Higher Prevalence of Positive Antiphospholipid Antibodies: A Systematic Review and Meta-Analysis. *International Journal of Endocrinology*, **2022**, Article ID: 8271951. https://doi.org/10.1155/2022/8271951

[13] Man, Y.L. and Sanna, G. (2022) Neuropsychiatric Manifestations of Antiphospholipid Syndrome—A Narrative Review. *Brain Sciences*, **12**, Article No. 91. https://doi.org/10.3390/brainsci12010091

[14] Chaturvedi, S. and McCrae, K.R. (2017) Diagnosis and Management of the Antiphospholipid Syndrome. *Blood Reviews*, **31**, 406-417. https://doi.org/10.1016/j.blre.2017.07.006

[15] Gadaen, R. and Tummers-de Lind van Wijngaarden, R. (2021) Hypothyroid Crisis: Oral or Intravenous Treatment? A Report of Two Cases. *European Journal of Case Reports in Internal Medicine*, **8**. https://doi.org/10.12890/2021_002752

[16] Wall, C.R. (2000) Myxedema Coma: Diagnosis and Treatment. *American Family Physician*, **62**, 2485-2490. https://www.aafp.org/pubs/afp/issues/2000/1201/p2485.html