Acute mania after levothyroxine replacement for hypothyroid-induced heart block

Marc Gregory Yu MD[1], Karen Marie Flores MD[2] , Iris Thiele Isip-Tan MD[1]

[1]Section of Endocrinology, Diabetes, and Metabolism, Department of Medicine
[2]Department of Medicine
University of the Philippines-Philippine General Hospital
Manila, Philippines

Background

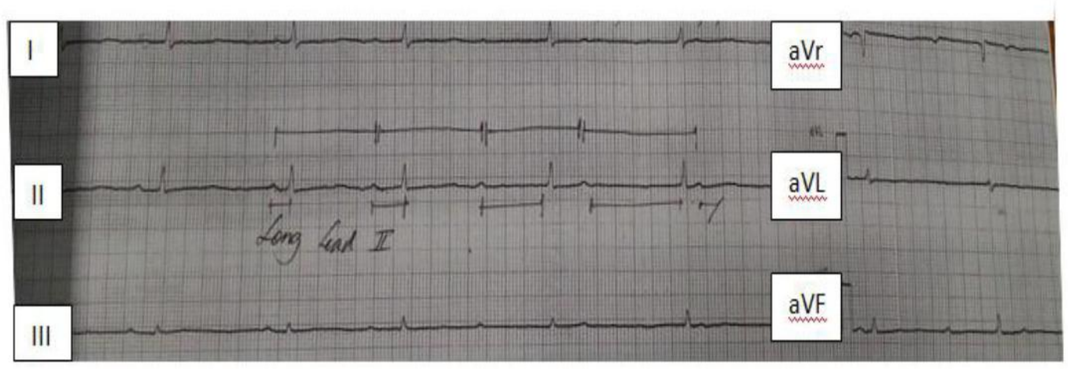
While psychiatric disturbances are well-documented manifestations of hypothyroidism, initiation of levothyroxine (LT4) replacement can also present in a similar manner.

Objectives

1. To present a case of acute mania after LT4 replacement in a hypothyroid patient with cardiac complications
2. To emphasize the importance of an extensive workup to rule out other etiologies in similar cases.

Case Presentation

A 34-year-old Filipino male presented with a two-month history of an anterior neck mass plus symptoms of cold intolerance, constipation, insomnia, and motor slowing. Free thyroxine was low at 5.15 pmol/L (normal 9.01-19.05 pmol/L) while thyroid-stimulating hormone was high at >100 uIU/mL (normal 0.35-494 uIU/mL). The diagnosis of Hashimoto's thyroiditis was established with elevated thyroid peroxidase antibodies at 3771 U/mL (normal <100 U/mL) and thyroglobulin antibodies at 9449 IU/mL (normal <50 IU/mL). An electrocardiogram revealed high grade atrioventricular block (Figure 1). Twenty-four hours after a full replacement dose of LT4 (1.6 mcg/kg), he developed manic symptoms which were addressed with sedatives and neuroleptics with gradual restoration of euthymia the following day. The mania was investigated by doing serum electrolytes, complete blood count, toxicology panel, and cranial magnetic resonance imaging (MRI), which were all normal. A cerebrospinal fluid examination to rule out central nervous system infection revealed only mild protein elevation at 90 mg/dL (normal 15-45 mg/dL) and IgG at 13.7 mg/dL (normal 0.48-5.86 mg/dL). For the heart block, cardiac creatine kinase and troponin I were both normal. 2D echocardiogram with Doppler showed concentric left ventricular hypertrophy with good wall motion and contractility and preserved overall systolic function (ejection fraction by Teicholz 56%, Simpson's 55%) with Doppler evidence of diastolic dysfunction. He remained stable throughout his admission with no relapse of psychiatric symptoms. We ultimately attributed the mania to LT4, and the heart block to hypothyroidism.



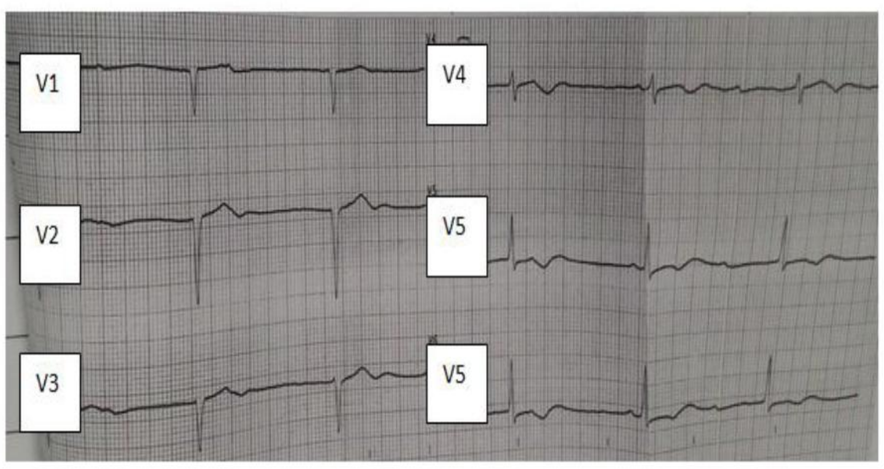


Figure 1. Initial ECG at the emergency room showing high grade AV block.

Case (Age-Sex)	Aetiology/duration of hypothyroidism	Prior to initiation of thyroid replacement therapy	PFI	Onset of PFI	Duration of PFI
58—F (Ziegler, 1931)	Spontaneous/1 yr	O.P.[1]	O.A.[2] (manic)	a few days	gradually improved
43—F (Karnosh and Stout, 1935)	Spontaneous ?	O.A. (depressed)	O.A. (manic)	4 days	1 month)
58—F (Karnosh and Stout, 1935)	Spontaneous ?	O.D.[3]	O.P.	early	temporary manifestation
58—F (Akelaitis, 1936)	Spontaneous/4 yrs	O.A.*[4] (depressed)	O.D.*	2 days	7 days
41—F (Akelaitis, 1936)	Spontaneous/6 yrs	O.A. (depressed)	O.A.* (manic)	4 days	10 days
66—F (Akelaitis, 1936)	Spontaneous/6 yrs	O.A. (depressed)	O.A.* (manic)	11 days	3 days
10—F (Means, 1948)	Spontaneous/4 yrs	None	O.A.* (manic)	7 days	9 days
53—F (Asher, 1949)	Spontaneous/6 mths	O.D.	O.D.*	at first	2 weeks
64—F (Asher, 1949)	Spontaneous/1 yr	O.D.	O.A. (manic)	3 days	2 weeks
54—F (Asher, 1949)	Spontaneous/1 yr	O.A. (mixed)	O.A. (mixed)	6 days	5 weeks
73—F (Asher, 1949)	Spontaneous ?	Dementia	O.A.	5 days	1 day (death due to myocardial infarction)
48—F (Calvert *et al*, 1954)	Spontaneous ?	Other OBS	O.A.* (manic)	21 days	1 week
55—F (Browning *et al*, 1954)	Spontaneous/1 yr	O.A. (manic)	O.A. (manic)	13 days	gradual diminution
34—F (Easson, 1966)	Spontaneous/2 yr	O.P.	O.D.	4 days	2 weeks
44—M (Easson, 1966)	Post thyroidectomy 2 mths	O.D.*	O.A.* (manic)	4 days	6 days
41—F (Easson, 1966)	Spontaneous/1 yr	O.A.* (depressed)	O.A.* (manic)	6 days	gradually subsided
31—F (Easson, 1966)	Post thyroidectomy 18 mths	O.D.	O.A.* (manic)	5 days	7 days
34—F (Josephson and Mackenzie, 1979)	Post I^{131} ablation	O.A. (mixed)	O.A.* (manic)	3 days	2 weeks

[1]O.P. = Organic Personality Syndrome: A marked change in personality occurs involving one of emotional lability, poor impulse control, apathy, or suspiciousness.
[2]O.A. = Organic Affective Syndrome: The predominant clinical feature is a disturbance in mood, with evidence for at least two associated symptoms of mania or depression.
[3]O.D. = Organic Delusional Syndrome: Delusions are the predominant clinical feature, although hallucinations and language disorder may be present. Delusions occur in a state of wakefulness.
[4]* = Received psychiatric intervention, including medication, restraints, consultation or transfer.

Table 1. Characteristics of patients with LT4-induced mania in a case series. (Source: Josephson, AM and Mackenzie, TB. Thyroid-induced mania in hypothyroid patients. Br J Psychiatry. 1980; 137: 222-8).

Discussion

The temporal relationship between LT4 intake and onset of mania, plus the lack of other findings on workup, suggest that the mania was probably LT4-induced. The pathophysiology is thought to be related to the abrupt augmentation of postsynaptic catecholamine receptor sensitivity, leading to a hyperadrenergic state and the appearance of manic symptoms. In a case series on LT4-induced mania, most patients were female and had either a personal or family history of psychosis, which were absent in our case. The onset of manic symptoms ranged from as short as one day (as in our patient) to as long as three weeks after the first LT4 dose, with cases resolving after one day (as in our patient) to several months, either on their own or after temporary cessation of LT4 therapy (Table 1). While the average initial dose of LT4 was relatively high (180mcg/d), the psychiatric disturbances can also manifest at low doses (25-50 mcg) and with gradual dose titration. For our patient, we gave the full replacement LT4 dose due to his young age, profound hypothyroidism, and the absence of co-morbidities. The presence of high grade heart block was an urgent indication to restore euthyroidism, since it was eventually attributed to the severe hypothyroid state after an unremarkable cardiac workup. Our case is significant in the sense that it is the first report involving a double-edged sword: dealing with psychiatric disturbances from LT4 administration at the same needing to urgently correct severe hypothyroidism with cardiac complications.

Learning Points

- Hypothyroidism can manifest with psychiatric signs and symptoms. At the same time, LT4 treatment can present in a similar manner.
- In hypothyroid patients with psychiatric and cardiac manifestations, an exhaustive workup is needed to rule out other diagnoses.
- In patients presenting with unexplained psychiatric disturbances and heart block, thyroid function testing is also essential.
- The pros and cons of each treatment modality should be carefully considered, and timely referrals should be made.

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