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Case Reports

The Vasospastic Thyroid: Bilateral Leg Pain as a Vascular Manifestation of Hypothyroidism

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Abstract

Hypothyroidism is an endocrine disorder that causes widespread systemic effects, but its impact on vascular tone is often under-recognized. We present a case of severe, longstanding hypothyroidism leading to bilateral lower extremity vasospasm and failure to thrive in a complex patient with significant psychiatric and medical comorbidities. A 46-year-old male with a history of type 2 diabetes, chronic DVT, bipolar disorder, and recent untreated hypothyroidism presented with progressive bilateral leg pain, weakness, and inability to ambulate. He had been discharged a week prior with a TSH of 101 mIU/L and newly initiated levothyroxine 50 mcg. On return, symptoms had worsened, and his mother reported cognitive slowing. Workup revealed stable chronic DVT and new arterial duplex findings showing diffuse high-resistance waveforms consistent with vasoconstrictive physiology in both lower extremities, without stenosis. Creatinine was elevated, likely due to vasomotor nephropathy. Neurological and rheumatological causes were previously excluded. Severe hypothyroidism is known to increase systemic vascular resistance and reduce endothelial-mediated vasodilation, potentially contributing to vasospastic phenomena. In this patient, no other etiology for bilateral vasoconstriction was found. With no history of Raynaud's, vasoactive drug use, or active thrombosis, hypothyroidism remained the most plausible cause. Although rare, such vascular manifestations can lead to functional decline, especially in vulnerable patients. This case highlights the importance of considering hypothyroidism in the differential diagnosis of unexplained vasospasm and functional decline. Timely thyroid hormone replacement may reverse vascular dysfunction and prevent further complications.

BACKGROUND

Hypothyroidism is an endocrine disorder that has significant effects on the cardiovascular system. The thyroid gland plays a crucial role in maintaining cardiovascular homeostasis by modulating cardiac output, heart rate, and systemic vascular resistance through thyroid hormones. In the hypothyroid state, cardiac output is decreased, and systemic vascular resistance is markedly increased. This often leads to diastolic hypertension and endothelial dysfunction.[1] Hypertension is estimated to be nearly three times more prevalent in patients with overt hypothyroidism compared to euthyroid individuals.[2] Severe hypothyroidism is known to increase systemic vascular resistance and reduce endothelial-mediated vasodilation, potentially contributing to vasospastic phenomena. We present a case of severe, longstanding hypothyroidism leading to bilateral lower extremity vasospasm and failure to thrive in a complex patient with significant psychiatric and medical comorbidities.

CASE PRESENTATION

A 46-year-old male, with past medical history significant for acid reflux, anxiety, bipolar 2 disorder, depression, type 2 diabetes mellitus, hypertension, post-traumatic stress disorder, seizures, and chronic deep vein thrombosis (DVT), presented to the hospital with complaints of failure to thrive, bilateral leg pain and inability to ambulate for over a year, resulting in multiple hospital and rehabilitation admissions. He stated that he has had pain all over his body, more pronounced in his legs. He has had trouble walking due to pain and weakness. He had been unable to push himself in his own wheelchair. He also noted that his legs have been feeling cold. The patient's mother also noted that the patient's responses have been slow. He denied any lightheadedness, bowel and urinary

incontinence, nausea, vomiting, cold-induced vasospasm. He denied any recent fall or traumatic injury. The patient did not take any vasoconstrictive medications, which could contribute to his presentation. The patient was on apixaban 5 mg daily for bilateral lower extremity DVT. An MRI of the brain and entire spine had been unremarkable on prior admissions, within the last six months. A spinal tap was previously done, and CSF analysis was unremarkable, apart from a slightly elevated CSF protein. The workup during his previous hospitalizations ruled out underlying neurological causes of his symptomatology.

Vital signs at presentation were temperature 98.2°F, heart rate 90 bpm, respiratory rate 22 breaths/min, blood pressure 162/86 mmHg, and oxygen saturation 99% on room air. BMI was 31.52 kg/m^2. Neurologically, he was able to nod yes or no to questions, follow basic commands, and demonstrated cranial nerves were grossly intact. Notably, he exhibited hyperreflexia in the upper extremities and jaw, with hyporeflexia in the lower extremities. Initial labs on admission revealed a markedly elevated TSH of 102.589 μIU/mL (reference 0.400–4.500), free T4 <1.0 ng/dL (reference 0.8–1.8), and total T3 of 0.75 pg/mL (reference 2.3–4.2). The morning cortisol was 20 μg/dL (reference 7–25). No thyroid antibody testing was performed. These results confirmed severe overt hypothyroidism. Renal parameters demonstrated acute kidney injury (AKI), with BUN 49 mg/dL (reference 6–24) and creatinine 1.80 mg/dL (reference 0.60–1.20) on 6/13/25. Repeat testing two days later showed improvement to BUN 27 mg/dL and creatinine 1.30 mg/dL after treatment with intravenous fluids, suggesting partially reversible vasomotor nephropathy in the setting of hypothyroidism-induced vascular dysfunction and intravascular volume depletion.

In addition to arterial duplex imaging, further studies were performed to exclude alternative structural and vascular causes of the patient's presentation. MRI of the lumbar spine with contrast was unremarkable, showing no foraminal or central stenosis. CT imaging of the head, cervical, and thoracic spine was negative for mass effect, compression, or acute pathology. Lumbar puncture was unrevealing apart from a mildly elevated CSF protein. These findings effectively excluded compressive etiologies or CNS pathology as contributors to the bilateral lower extremity vasospasm. A paraneoplastic panel and HTLV-1 antibody testing for tropical spastic paraparesis were negative. Electromyography showed no evidence of peroneal neuropathy or radiculopathy. Electroencephalography was mildly abnormal due to diffuse background slowing, consistent with encephalopathy, without epileptiform activity.

Autoimmune and vasculitis causes of diffuse arterial dysfunction were carefully considered. The patient's inflammatory markers were not suggestive of systemic vasculitis. Hepatitis B and C serologies were negative, ruling out viral-associated vasculitis such as polyarteritis nodosa or cryoglobulinemic vasculitis. Given the absence of systemic features (e.g., rash, hematuria, pulmonary involvement), unremarkable cerebrospinal fluid, and negative spinal and brain imaging, no further vasculitis serologies were pursued. The overall low pre-test probability, together with normal screening studies, made an autoimmune vasculitis etiology unlikely in this case. The patient was discharged home on levothyroxine 50 mcg and instructed to follow up with his PCP, but he failed to do so. He was rehospitalized one month later with myxedema coma and subsequently died.

DISCUSSION

Vascular involvement in hypothyroidism is multifactorial. Hypothyroidism contributes to arterial stiffening, increased intima-media thickness, and even myxedematous infiltration of the arterial wall, resulting in impaired vascular compliance.[3] In a study comparing 18 sub-clinically hypothyroid patients to 231 euthyroid controls, the prevalence of peripheral arterial disease (PAD) was found to be significantly higher among the hypothyroid group.[4] Additionally, pulse wave Doppler analysis has demonstrated increased arterial stiffness in hypothyroid patients, a finding shown to improve with levothyroxine therapy. A separate study confirmed the reversibility of increased intima-media thickness over a six-month period of hormone replacement.[5]

Gender also appears to be a significant effect modifier in the relationship between hypothyroidism and lower extremity arterial disease, with a positive association observed in men and a negative association in women.[6] Vasospasm has also been reported in the context of hyperthyroidism, particularly Graves' disease, where excess thyroid hormone increases sympathetic activity, amplifies catecholamine sensitivity, and disrupts endothelial nitric oxide balance, leading to vasoconstrictive episodes.[7-12] In contrast, hypothyroidism promotes vasospasm through reduced basal metabolic rate, diminished nitric oxide–mediated vasodilation, increased systemic vascular resistance, and impaired smooth muscle relaxation.[13,14] Beyond thyroid disease, other endocrinopathies such as pheochromocytoma (catecholamine-induced vasospasm) and hyperaldosteronism (via vascular remodeling and impaired endothelial function) can also precipitate vasospastic physiology. Recognizing these mechanisms is critical, as they underscore the broad vascular consequences of endocrine disorders and the potential reversibility with targeted therapy.

Thyroid hormones play a crucial role in regulating cardiovascular and endothelial function. In hypothyroid states, there is a decrease in basal metabolic rate, cardiac output, and nitric oxide-mediated vasodilation, alongside increased systemic vascular resistance and sympathetic tone. These changes contribute to reduced perfusion,

particularly in distal vasculature, and can lead to vasoconstrictive phenomena mimicking peripheral arterial disease or Raynaud's phenomenon. However, unlike Raynaud's, hypothyroidism-related vasospasm is not cold-induced and is more persistent and generalized.[13,14] Gender may also influence the vascular effects of hypothyroidism. Estrogen has protective effects on endothelial function, arterial compliance, and lipid metabolism, which may counteract some of the arterial stiffness and intima-media thickening associated with hypothyroidism.[6]

In this patient, overt hypothyroidism was associated with both diastolic hypertension and vascular dysfunction. His initial presentation of bilateral leg pain, cold extremities, and impaired ambulation resembled peripheral arterial disease, but pulses were palpable, and duplex imaging did not reveal obstructive disease. Rather, his clinical picture was more consistent with diffuse vasospasm in the setting of severe hypothyroidism. Importantly, his renal dysfunction improved after intravenous fluid administration, consistent with vasomotor nephropathy due to systemic vascular resistance and intravascular volume shifts, highlighting the partially reversible nature of this process with supportive care. Despite the initiation of thyroid hormone replacement, the patient's outcome was poor. His failure to follow up, compounded by the severity of his disease, ultimately led to progression to myxedema coma and death within one month of discharge. This underscores the importance of close monitoring and early endocrinology involvement in patients with severe hypothyroidism, particularly when vascular manifestations are present.

While hypothyroidism-induced vasospasm is rare, it has been documented in both animal and human studies. One study demonstrated impaired endothelial-dependent vasodilation and increased peripheral resistance in hypothyroid rats, which normalized after thyroxine replacement.[15] Similarly, human case reports have shown reversal of vasospastic symptoms with thyroid hormone therapy, though resolution typically takes several weeks.[16] Although vascular dysfunction in hypothyroidism has been widely described in terms of arterial stiffness and endothelial dysfunction, only a small number of reports have specifically documented hypothyroidism-induced vasospasm. To date, fewer than five human case reports in the literature have described peripheral vasospasm as a direct manifestation of severe hypothyroidism, most of which demonstrated symptomatic improvement after thyroid hormone replacement.[16]

Conversely, in hyperthyroid states, coronary and even cerebral vasospasm are better documented. At least eight cases of coronary vasospasm associated with Graves' hyperthyroidism have been described in case series,[17] with additional individual reports including right coronary and left main coronary artery spasm relieved by nitroglycerin,[18] a case of a 51-year-old man with Graves'-related coronary spasm,[19] and two reports of myocardial infarction precipitated by thyrotoxicosis-related coronary vasospasm.[20] Cerebral vasospasm, though rare, has also been reported in hyperthyroid patients.[21,22] Taken together, these data suggest that both extremes of thyroid dysfunction can predispose to vascular tone abnormalities—hypothyroidism more often through endothelial dysfunction and arterial stiffness, and hyperthyroidism through enhanced vasoreactivity and coronary or cerebral spasm. Recognition of these patterns is important, as thyroid hormone replacement or suppression can lead to resolution of vasospastic symptoms.

CONCLUSION

This case highlights a rare but clinically significant manifestation of hypothyroidism—peripheral arterial vasospasm mimicking peripheral artery disease. While atherosclerosis remains the most common cause of PAD, this report emphasizes the need to consider hypothyroidism as a potential and reversible contributor, particularly in patients without classic risk factors. Several studies have demonstrated a strong association between hypothyroidism and vascular dysfunction, including increased arterial stiffness and intima-media thickness, yet this connection is often overlooked in clinical practice. Clinicians should maintain a high index of suspicion for thyroid dysfunction in patients presenting with unexplained vascular symptoms. Recognizing hypothyroidism as an underlying cause allows for targeted treatment with thyroid hormone replacement, which can lead to meaningful symptomatic and vascular improvement. Further research is warranted to better understand the pathophysiologic mechanisms and to guide early identification in similar cases.

Disclosures/Conflicts of Interest

The authors have no conflicts of interest to disclose.

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