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Acute Thyrotoxic Myopathy Combined with Neck Pain: A Case Report

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Abstract

INTRODUCTION: Acute thyrotoxic myopathy (ATM) is a rare and potentially lethal complication of thyrotoxicosis. The typical clinical symptoms of ATM are characterized by bulbar paralysis. Reports of the successful treatment of ATM are sporadic due to its low incidence. However, no English literature has reported Chinese patients with ATM and neck pain. Here, we report for the first time a Chinese patient with ATM and neck pain who recovered through large doses of systemic glucocorticoids and one intrathyroidal steroid injection.

CASE REPORT: A 23-year-old woman visited our hospital with a two-year history of progressive weakness of her bulbar muscles, hoarseness, cough when swallowing, dysphagia, and a one-month history of recurrent painful swelling of the thyroid gland. She was diagnosed with ATM, chronic thyrotoxic myopathy (CTM), and Graves' ophthalmopathy (GO) due to Graves' disease (GD). After she was treated with a combination of low-dose glucocorticoids, antithyroid drugs (ATDs), propranolol, and ultrasound-guided percutaneous intrathyroidal injection of glucocorticoids, her bulbar paralysis, proximal myopathy, and neck pain simultaneously improved without recurrence during follow-up. To our knowledge, this is the first case report of a patient with ATM, CTM, GD, GO and neck pain treated by administering a combination of low-dose glucocorticoids, one intrathyroidal steroid injection and antithyroid agents.

CONCLUSIONS: Clinicians should consider ATM and intervene with aggressive glucocorticoid therapy, and this is the key to reversing the progression of ATM when a patient has bulbar paralysis and thyrotoxic symptoms. Our case report references the clinical diagnosis and treatment of such cases.

CASE REPORT

Abbreviations:

ATM	- acute thyrotoxic myopathy (ATM)
CTM	- chronic thyrotoxic myopathy
TPP	- thyrotoxic periodic paralysis
MG	- myasthenia gravis
GD	- Graves' disease
SAT	- subacute thyroiditis
NSAIDs	- nonsteroidal anti-inflammatory drugs
ATDs	- antithyroid drugs
FT3	- free triiodothyronine
FT4	- free-thyroxine
TSH	- thyroid-stimulating hormone
TRAb	- TSH receptor
TPOAb	- thyroid anti-peroxidase antibody
Tg	- thyroglobulin
AChR	- acetylcholine receptor antibody
GO	- Graves' ophthalmopathy
ESR	- erythrocyte sedimentation rate
MMI	- methimazole (MMI)
PTU	- propylthiouracil

INTRODUCTION

Hyperthyroidism-associated myopathies are an uncommon muscular complication of thyrotoxicosis. They include acute thyrotoxic myopathy (ATM), chronic thyrotoxic myopathy (CTM), thyrotoxic periodic paralysis (TPP), myasthenia gravis (MG), and exophthalmic ophthalmoplegia (Cui & Zhang 2022). These complications can result in myasthenia of variable muscle groups and have adverse effects on quality of life (Cui & Zhang 2022; Kung 2007). ATM is a rare but life-threatening disease with a clinical presentation ranging from hoarseness, dysphagia, dysphonia, and dysarthria (without sensory dysfunction) to dyspnea and death, as first reported in 1944 (Laurent 1944). The most common causes of mortality are respiratory muscle paralysis and aspiration pneumonia (Kung 2007). However, since ATM was recognized nearly 80 years ago, effective treatments and definite laboratory results have rarely been reported, and the exact mechanism has remained unknown (Cui & Zhang 2022; Zhou *et al.* 2012).

To date, no study in English has reported Chinese patients with ATM and neck pain. We report an unusual case of neck pain following ATM. This complicated condition was successfully improved by aggressive medical therapy based on antithyroid drugs (ATDs) and large doses of systemic glucocorticoids and one intrathyroidal steroid injection. We present the following article in accordance with the CARE reporting checklist.

CASE REPORT

Two years before admission, the initial assessment of a Chinese female was unremarkable other than revealing that she had difficulty standing up from squatting. Eight months before admission, her lower muscles became weaker. Apart from the above symptoms, she had accompanying palpitations, hand tremors, heat intolerance, excessive sweating, fatigue, diarrhea, tightness in the chest, and dyspnea. Seven months before admission, the patient experienced extraocular muscle involvement. One month before admission, she experienced recurrent high-grade fever and painful neck swelling radiating to her ears. Subsequently, the doctor gave the patient a prescription for 0.1 g ibuprofen every day after excluding SARS-CoV-2 infection, and her painful neck slightly improved. In March 2021, due to her symptoms of hoarseness, cough while swallowing water, dysphagia, weakness in all limbs and recurrent painful swelling in the front of her neck, she was admitted to the endocrine department. She denied taking excess iodides, ATDs, or therapeutic corticosteroids, as well as any family history of thyroid disease.

The examination at admission revealed a conscious woman with a hoarse, hypophonic voice. Her vital signs were as follows: temperature, 36.4°C; blood pressure, 130/59 mmHg; pulse rate, 96 beats/min; and respiratory rate, 20 breaths/min. Clinical examination revealed a diffuse grade 3 goiter with thyroid tremor, tenderness and bruit, a mild degree of left exophthalmos with soreness, and swelling of the left upper eyelid. A pistol-shot sound with each pulse was heard over the bilateral femoral artery. Neurological findings showed that the pharyngeal reflex was absent. Motor examination showed proximal muscle atrophy and muscle strength power of grade 4/5 in her upper limbs and 3/5 in her lower limbs. The remaining systematic investigations were unremarkable.

The patient's serum concentrations of thyroid hormones, which evaluate the patient's thyroid function, demonstrated overt hyperthyroidism with a free triiodothyronine (FT3) concentration of 27.50 pmol/L (normal range: 3.60-6.00 pmol/L), a free-thyroxine (FT4) concentration of 67.38 pmol/L (normal range: 7.86-14.41 pmol/L), and a thyroid-stimulating hormone (TSH) concentration of 0.01 mIU/ml (normal range: 0.34-5.65 mIU/ml). The level of antibody against the TSH receptor (TRAb) was 27.78 IU/L (normal range: 0–1.50 IU/L), the level of anti-thyroglobulin antibody (TGAb) was 6.78% (normal value: <30.00%), and that of thyroid anti-peroxidase antibody (TPOAb) was 226.00 IU/ml (normal range: 0–30.00 IU/ml). The concentration of thyroglobulin (Tg) was 381.76 ng/ml (normal range: 0-35.00 ng/ml). The erythrocyte sedimentation rate (ESR) was 20.00 mm (normal range: 0-20 mm). Electrocardiogram confirmed sinus tachycardia. Ultrasonography of the thyroid showed a diffuse lesion. Blood cultures and lung CT were used to rule out common infectious diseases. Thyroid uptake of I revealed that the total radioiodine uptake was increased and that the peak uptake time was shifted forward. Acetylcholine receptor antibody (AChR) and neostigmine tests were negative. The remainder of the laboratory findings were normal and were as follows: complete blood cell count, blood biochemistry, urinalysis, chest X-ray, electronic laryngoscopy, and magnetic resonance

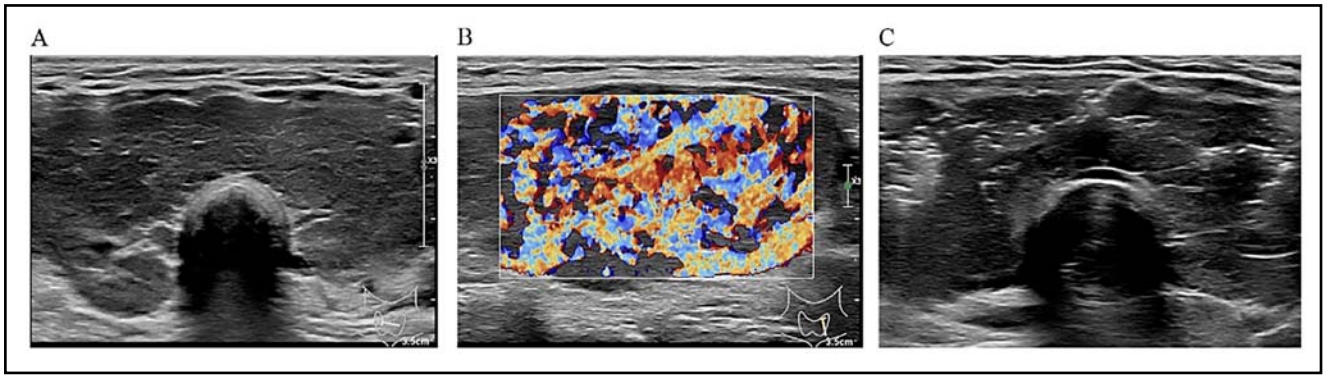

Fig. 1. Ultrasonography of the thyroid. (A) A grayscale image showed a diffuse and symmetrical goiter with inhomogeneous and hypoechoic areas before treatment, and no nodules, cysts, or abscesses were detected; (B) Color Doppler sonography revealed a hypervascular pattern referred to as thyroid inferno; (C) A grayscale image shows glucocorticoids with short intrathyroidal linear and hyperechogenicity after injection.

imaging of the central nervous system. A diagnosis of GD, ATM, CTM, and Graves' ophthalmopathy (GO) was made based on these results. The patient was promptly started on treatment by oral administration of 10 mg methimazole (MMI) every 8 hours, 10 mg propranolol every 8 hours, and intravenous infusions of 100 mg hydrocortisone daily. The corticosteroid dose was adjusted appropriately based on the clinical manifestation and side effects.

Over the next few days of observation, the patient showed significant clinical improvement, especially regarding liquid ingestion, dysphagia, and voice quality. However, her painful neck was not resolved. After excluding neck pain caused by suppurative infection, cancer and bleeding in the thyroid, we considered the possibility of subacute thyroiditis (SAT), which could not be confirmed. After sufficient communication and signing of the consent form with the patient, she was treated with an ultrasound-guided percutaneous intrathyroidal injection of glucocorticoids because oral glucocorticoids yielded slow symptom relief. Both thyroid gland lobes of the patient were visualized with intraoperative ultrasonography, and then a mixture of 40 mg dexamethasone (1 ml), 5 mg triamcinolone acetonide (1 ml) and 0.1 g lidocaine (5 mL) was prepared for injection in a 1:1 ratio into each lobe. Of note, complete relief of neck pain was achieved after 1 hour.

As the clinical symptoms of ATM and neck pain improved, the patient was discharged on the 12th day of hospitalization with advice for treatment with hydrocortisone acetate 40 mg twice a day, and this dose was tapered off. In addition, MMI every 8 hours and 10 mg propranolol every 6 hours were given to control hyperthyroidism.

After hospital discharge, the patient returned to her daily life and regular follow-up. Sixty days later, she presented in good health. Repeat physical examinations and evaluations of ATM symptoms were performed. The pharyngeal reflex remained absent, but the remainder of the bulbar muscles had returned to normal. The patient gradually regained muscle strength in her proximal muscles following the remission of her hypermetabolic symptoms. Her exophthalmos and eyelid swelling partially improved, and her pain from GO disappeared. The neck pain has not recurred to date. A thyroid function test taken after 60 days of glucocorticoid and ATD therapy showed a serum TSH concentration of 16.01 mIU/L, FT_3 concentration of 4.54 pmol/L, FT_4 concentration of 5.22 pmol/L, TPOAb concentration of 119 IU/ml, and TRAb concentration of 15.44 IU/L. Re-examination of ESR decreased but was within the normal range. The doctor concluded that she was hypothyroid because of treatment with excessive ATDs. Following the advice of her doctor, the dose of the MMI was reduced to 5 mg every day; she was gradually tapered off glucocorticoids, including methylprednisolone, which was given at a dose of 4 mg every day over the next 30 days, and the patient was arranged to have a follow-up one month later. She was satisfied with the treatments she received because she could see recovery from ATM in a short period. Written informed consent was obtained from the patient for publication of this case report.

DISCUSSION

Excessive thyroid hormones can lead to increased protein catabolism, resulting in muscle atrophy (Wood-Allum & Shaw 2014). Although hyperthyroidism with muscle weakness and atrophy are usually present in thyrotoxic myopathy, the bulbar muscle is rarely involved (Cui & Zhang 2022). ATM has long been reported but is seldom described because of its low incidence (Cui & Zhang 2022). The etiology of ATM and CTM has not been elucidated to date (Zhou *et al.* 2012). Perhaps a combination of increased energy use with increased catabolism and deficiency of muscle carnitine leads to muscle dysfunction (Sinclair *et al.* 2005). Catecholamine action or thyroid hormone receptor distribution in different brain areas may explain the effect on bulbar muscles (Boddu *et al.* 2013; Kuang *et*

al. 2020). Generally, there are no definite biochemical features found in patients with ATM and CTM (Kung 2007). Therefore, the diagnosis of ATM and CTM is primarily clinically based on a patient's clinical manifestations and physical examination results (Zhou *et al.* 2012). Before obtaining a diagnosis of ATM, it is essential to rule out other causes, as the treatment differs significantly. The first differential diagnosis that should be considered is MG, which is one of the hyperthyroidism-associated myopathies, especially in patients with bulbar or respiratory muscle symptoms (Zhou *et al.* 2012). MG is an autoimmune neuromuscular disorder that results from a primary abnormality in the number of acetylcholine receptors affected by antibodies at neuromuscular junctions, causing muscle weakness and abnormal fatigability (Virameteekul *et al.* 2019). However, the low AChR concentrations in this patient and the negative neostigmine test were not consistent with MG. These test results went against this diagnosis. Other differential diagnoses (including TPP, rhabdomyolysis; Guillain–Barré syndrome; voice paralysis; bleeding; or injury to the cranial nerve nuclei) were excluded by our laboratory tests and imaging examinations. To date, there are no clear guidelines for alleviating ATM (Zhou *et al.* 2012). In this case, we attempted to use corticosteroids to eliminate the inflammatory state that may contribute to bulbar muscle derangement (Cui & Zhang 2022). In addition, corticosteroids are used to reduce the conversion of T_4 to T_3 and promote vasomotor stability (Ross *et al.* 2016). This patient recovered without progression or complications by our treatments, such as respiratory muscle paralysis and aspiration pneumonia. It seems to confirm that a low-dose steroid pulse is a potentially advantageous intervention in the inflammatory and stress state (Zhou *et al.* 2012). After clinical improvement of ATM, glucocorticoids can be tapered and discontinued (Cui & Zhang 2022). Currently, ATDs, including MMI and propylthiouracil (PTU), may be preferred in treating hyperthyroidism (Ross *et al.* 2016). We administered low-dose steroids and MMI to the patient every day and monitored the recovery of bulbar muscle function. A combination of hydrocortisone and ATDs promptly controlled the ATM in our case. For patients with fatal complications, such as respiratory muscle paralysis and aspiration pneumonia, artificial mechanical respiratory support should be considered (Zhou *et al.* 2012). Our patient's exophthalmos was resolved during the treatment of ATM. She gradually regained proximal muscle power following biochemical remission of her hyperthyroidism. In instances in which evidence or guidelines are lacking, our case supports the use of low-dose glucocorticoids as a feasible method of improving the outcomes of ATM. However, given the lack of scientific surveys used to assess ATM severity, we could only ascertain the ATM outcomes via daily observations of the symptoms (Zhou *et al.* 2012).

Considering that the patient had anterior neck swelling, pain, and fever, through medical history, laboratory examination, and ultrasound imaging we excluded neck trauma and internal infection, venous thrombosis, lymphadenitis, and common thyroid diseases, such as acute suppurative thyroiditis, thyroid neoplasm, thyroid cyst rupture, and thyroid nodule bleeding. First, we considered that anterior neck pain due to the thyroid capsule can be stretched rapidly, which is caused by GD. However, the patient's front neck was swollen for several months. In addition, pain is not a common symptom in some patients with large simple goiter in the front neck. Second, we considered neck pain due to SAT. First, the patient's thyroid is noticeably tender and hard in texture. Second, local injection therapy may have a good therapeutic effect. However, we cannot confirm the diagnosis of SAT. First, the patient's thyroid is noticeably hard in texture. Second, local injection therapy has a good therapeutic effect. However, there are contradictions in diagnosing SAT. First, there is high thyroid uptake of radioiodine. Second, there is a lack of elevated ESR levels. Third, diffuse and symmetrical glandular thyroid enlargement on ultrasound significantly increased vascularization. Fourth, the patient had no fever at the time of admission, so we cannot exclude infectious (or other) causes, which might have been present before. Fine needle aspiration biopsy (FNAB) should be performed in doubtful cases. This is a limitation of our treatment process.

CONCLUSION

To our knowledge, this is the first case report of a patient with ATM and neck pain overlap treated by glucocorticoid administration and antithyroid agents. For patients presenting with ATM during an acute attack, the management goals are to treat them with a combination of low-dose glucocorticoids, ATDs, and propranolol. With prompt and adequate control, most clinical manifestations of ATM are reversible. CTM symptoms are gradually relieved following hyperthyroidism control. In summary, we provide a reference for the clinical diagnosis and treatment of such cases.

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