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# Hyperthyroidism caused by acquired immune deficiency syndrome

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**Abstract. – BACKGROUND: Acquired immune deficiency syndrome (AIDS) is an immune deficiency disease. The etiology of hyperthyroidism, which can also be immune-related, is usually divided into six classical categories, including hypophyseal, hypothalamic, thyroid, neoplastic, autoimmune and inflammatory hyperthyroidism. Hyperthyroidism is a rare complication of highly active antimicrobial therapy (HAART) for human immunodeficiency virus (HIV). Hyperthyroidism caused directly by AIDS has not been previously reported.**

**PATIENT FINDINGS: A 29-year-old man who complained of dyspnea and asthenia for 1 month, recurrent fever for more than 20 days, and breathlessness for 1 week was admitted to our hospital. The thyroid function test showed that the level of free thyroxine (FT4) was higher than normal and that the level of thyroid-stimulating hormone (TSH) was below normal. He was diagnosed with hyperthyroidism. Additional investigations revealed a low serum albumin level and chest infection, along with diffuse lung fibrosis. Within 1 month, he experienced significant weight loss, no hand tremors, intolerance of heat, and perspiration proneness. We recommended an HIV examination; subsequently, AIDS was diagnosed based on the laboratory parameters.**

**SUMMARY: This is the first reported case of hyperthyroidism caused by AIDS.**

**CONCLUSIONS: AIDS may cause hyperthyroidism by immunization regulation with complex, atypical, and easily ignored symptoms. Although hyperthyroidism is rare in patients with AIDS, clinicians should be aware of this potential interaction and should carefully monitor thyroid function in HIV-positive patients.**

*Key Words:*
Hyperthyroidism, AIDS, Deficiency disease, Highly active antiretroviral therapy, Thyroid function.

## Introduction

The epidemiology of human immunodeficiency virus (HIV) infection in the United States has changed significantly over the last 30 years. HIV or AIDS, which is currently a disease of greater demographic diversity, affects individuals of all ages, genders, and races and involves multiple transmission risk behaviors. Approximately 50,000 new HIV infections will continue to be added each year; however, one fifth of the persons with new infections may not know they are infected[1], and the types of AIDS may vary. Additionally, AIDS may directly or indirectly affect multiple organ systems. Increasing experience with this syndrome has led us to recognize a variety of endocrine disorders, including several thyroid and adrenal disorders, which suggests that HIV infection might play a role in the endocrine system[2].

Hyperthyroidism is a common endocrine disorder that occurs as a result of excessive thyroid hormone secretion. Common clinical manifestations include symptoms due to hypermetabolism, thyroid enlargement and ophthalmopathy. The etiology is usually divided into six classical categories, including hypophyseal, hypothalamic, thyroid, neoplastic, autoimmune inflammatory hyperthyroidism, and others. AIDS is an immune deficiency disease, and the etiology of hyperthyroidism can also be immune-related. However, hyperthyroidism caused by AIDS is exceptionally uncommon. The majority of the published research has emphasized thyroid function abnormalities during the treatment of AIDS with HAART (High Active Anti-Retroviral Therapy) or other immune treatment[3-5]. We believe that the two diseases may share a correlation. In this article, we present a rare case of hyperthyroidism directly caused by AIDS, which, to the best of our knowledge, is the first case reported in the medical literature.

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### Patient

A 29-year-old man who complained of dyspnea and asthenia for 1 month, recurrent fever for more than 20 days, and severe breathlessness for 1 week was admitted to our hospital. One month previously, the patient experienced dyspnea and asthenia without a known precipitating factor; he visited a doctor at a hospital. The thyroid function test results were as follows: free triiodothyronine (FT3), 4.13 pmol/L (normal, 2.62-6.94 pmol/L); free thyroxine (FT4), 26.57 pmol/L (normal, 9.01-19.04 pmol/L); and thyroid-stimulating hormone (TSH), 0.01 mIμ/L (normal, 0.35-4.94 mIμ/L). He did not report heat sensitivity, excessive sweating, anxiety, irritability, tremor, nausea, or vomiting. He was diagnosed with hyperthyroidism and treated with methimazole (10 mg twice daily). Ten days later, he presented to the hospital with symptoms of recurrent fever (temperatures fluctuating between 37°C and 39°C), cough with slight phlegm, dyspnea, night sweats, and hemoptysis. He was diagnosed with pneumonia, and antibiotic therapy was administered. Subsequently, his condition improved slightly, and he was discharged from the hospital. Over the next month, he lost 10 kg of his body weight. One week before being seen in our hospital, the patient presented with repeated dyspnea, which became progressively worse and eventually affected his daily life. He was admitted to our Endocrinology Department for the management of hyperthyroidism. The patient had enjoyed excellent health until suffering from left submaxillary adenitis 2 years previously. The patient's physical examination revealed the following: temperature, 37.5°C; pulse rate, 110 beats/minute; respiratory rate, 26 breaths/minute; and blood pressure, 100/60 mm Hg. The patient was conscious, although he presented with rapid and shallow breathing. His general physical examination showed neither yellowish discoloration nor bleeding spots on his skin and mucous membranes and no superficial lymph node enlargement; however, the conjunctiva was slightly pale. An oral examination revealed an intact oral mucosa, a slightly hyperemic posterior pharyngeal wall but no tonsillar enlargement. His breathing was shallow; upon auscultation of the chest, we heard several scattered wet and dry rales. His heart rate was 110 beats/minute, regular, with no murmur. His abdomen was soft and non-tender; the liver and spleen were not palpable below the ribs. No abscess was found in the perianal region.

The patient presented mainly with dyspnea rather than hypermetabolic symptoms, which are usually characteristic of hyperthyroidism. Additional laboratory analyses revealed a low serum albumin level (24 g/L) and chest infection, along with diffuse lung fibrosis. In view of these findings, the patient's short medical history (barely 1 month) and marked weight loss, we recommended an HIV examination. The result was positive for HIV. After further queries regarding his medical history, the patient admitted that he was a homosexual. We diagnosed the patient with AIDS and transferred him for additional therapy. The thyroid function test results and key biochemical indicators are described in Table I. Figure 1 presents the patient's chest CT scan, diffuse lesions, and lung inflammation.

The patient received azithromycin and cefperazone-sulbactam for anti-inflammatory treatment and stavudine, lamivadin, and efavirenz for HAART treatment.

## Discussion

The number of patients affected by AIDS is increasing[3]. According to the epidemiology data and analyses collected by the Joint United Nations Programme on HIV/AIDS (UNAIDS) at the end of 2011, the number of HIV-infected and HIV patients totaled 34.0 million. In 2011, the number of people newly infected with HIV was 2.5 million, and there were 1.7 million deaths. Many patients are often misdiagnosed in general hospitals because these patients intentionally conceal their medical history and hide aspects of their condition, which exhibits a diversity of clinical manifestations.

Hyperthyroidism directly induced by AIDS is a rare event. Most research has focused on thyroid function abnormalities during the treatment of AIDS with HAART or other immune treatment rather than hyperthyroidism directly caused by AIDS[3,4]. In the era of HAART, a more complex situation has developed: many patients are experiencing insulin resistance, diabetes mellitus, sex hormone abnormalities and osteoporosis, but no unifying mechanism has been established for these conditions[5].

Whether AIDS is associated with hyperthyroidism has not been established. Madge et al[6] investigated the prevalence of overt and subclinical thyroid disease in HIV-positive patients to de-

**Table I.** Laboratory tests. The hyperthyroidism index recorded virtually no abnormality, except for liver damage. The AIDS indicators revealed no abnormalities.

| Project | Detection value | Normal |
|---|---|---|
| ALT (μ/L) | 206 ↑ | < 58 |
| AST (μ/L) | 142 ↑ | < 40 |
| ALB (g/L) | 24 ↓ | 35-55 |
| γ-GT (μ/L) | 173 ↑ | < 73 |
| AKP (μ/L) | 254 ↑ | 40-130 |
| Cr (nmol/L) | 60 | 59-104 |
| BUN (mmol/L) | 2.8 | 1.8-7.1 |
| TC (mmol/L) | 3.14 | 2.82-5.2 |
| TG (mmol/L) | 0.84 | 0.56-1.7 |
| HDL (mmol/L) | 0.48 | 0.9-1.68 |
| LDL (nmol/L) | 1.87 | 0.1-3.35 |
| TT4 (nmol/L) | 122 | 54-174 |
| TT3 (nmol/L) | 1.2 | 1.2-3.4 |
| FT3 (pmol/L) | 4.8 | 3.5-6.5 |
| FT4 (pmol/L) | 25 | 10.2-31 |
| TSH (mμ/L) | 0.1 | 0.35-5.5 |
| γ-T3 (ng/ml) | 1.03 | 0.16-0.95 |
| TPO Ab (IU/mL) | 34 | < 40 |
| TG Ab (IU/mL) | 90 | < 110 |
| TM Ab (IU/mL) | 5.5 | 0.16-10 |
| HIV Ab | Strongly positive | Negative |
| CD8 percentage (%) | 65%↑ | 20%-30% |
| CD8 absolute value (Cell/μl) | 344 | |
| CD4 percentage (%) | 2%↓ | 35%-55% |
| CD4 absolute value (Cell/μl) | 13 | |

Confirmed by the Department of Infectious Diseases. ↑: elevated value for the laboratory; ↓: low value for the laboratory; ALT: alanine aminotransferase; AST: aspartate aminotransferase; ALB: albumin; GGT: γ-glutamyltransferase; AKP: alkaline phosphatase; Cr: creatinine; BUN: blood urea nitrogen; TC: total cholesterol; TG: triglyceride; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; TT4: serum total thyroxine; TT3: serum total triiodothyronine; FT4: free thyroxine; FT3: free triiodothyronine; TSH: thyroid-stimulating hormone; γ-T3: γ-tocotrienols; TPO Ab: thyroid peroxidase antibodies; TG Ab: thyroglobulin antibodies; TM Ab: thyroid microsome antibodies; HIV Ab: human immunodeficiency virus antibodies.

termine risk factors associated with the development of thyroid dysfunction. Overall, 3,584 samples were analyzed. Thirty-nine (2.5%) patients were found to have overt hypothyroidism, and eight (< 1%) patients had overt hyperthyroidism. Sixty-one (4%) patients had subclinical hypothyroidism, five (< 1%) patients had subclinical hyperthyroidism and 263 (17%) patients had a nonthyroidal illness. A multivariate analysis suggested that no independent variables were significantly associated with overt hypothyroidism. The researchers can not determine that there was any association between the HIV disease and its treatment and thyroid function. There was no evidence of a uniform pattern of association between thyroid dysfunction and HIV infection before therapeutic management with HAART[7-9].

AIDS is an immune deficiency disease. Hyperthyroidism is also considered to be immune-related. Whether AIDS is associated with hyperthyroidism and the mechanism between AIDS and hyperthyroidism have not been established. Recent reports have focused on abnormal thyroid function when patients with AIDS received HAART or other immune treatment. Jubault et al[10] found that patients with AIDS would suffer hyperthyroidism or thyroid peroxidase (TPO) antibody elevation during the treatment with HAART, which suggests that the thyroid function may be related to the increase of CD4+ cells resulting from the treatment or the production of TRAb (TSH receptor antibodies) stimulated by Th cells. However, in our case, the patient was a homosexual male with a clear diagnosis of AIDS. His hyperthyroidism characteristics were as follows: his status was not typically hypermetabolic, his thyroid hormone level was mildly elevated, the associated antibodies were negative, and his thyroid function was normalized after a short-term treatment with drugs. Additionally, there

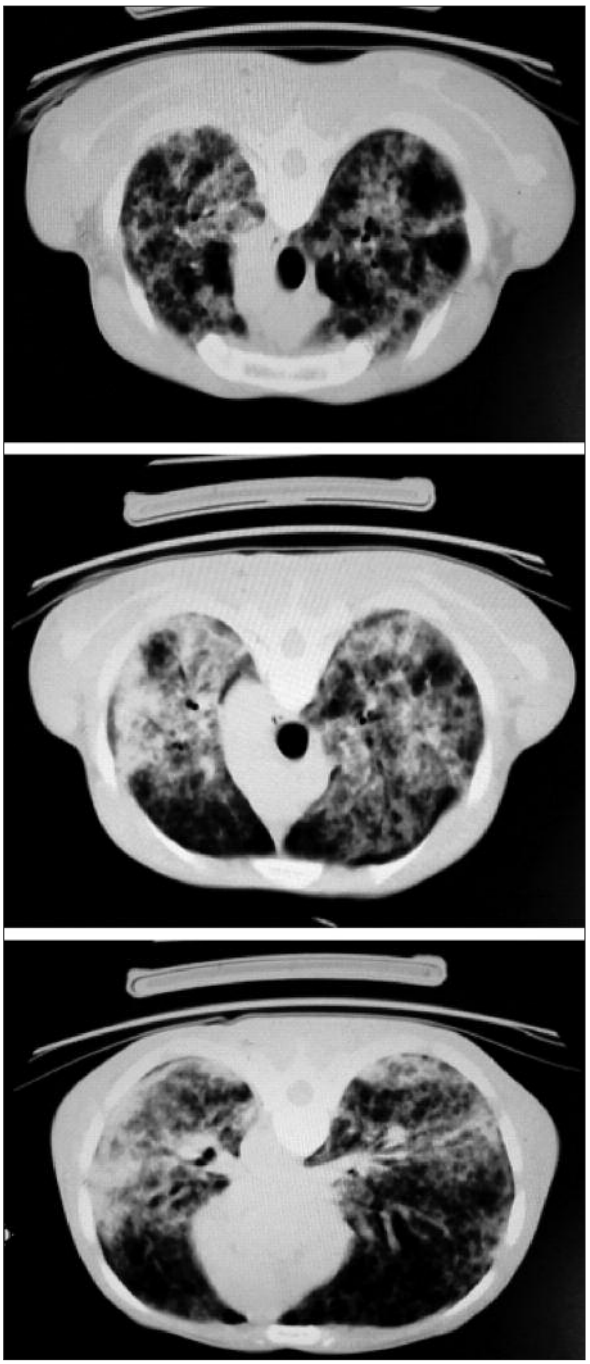

**Figure 1.** CT scans of patients with Lung fibrosis. More fiber-cable between the two lungs and a large quantity of wool seeps through the shadows of real variable, bronchi fill with air, thickening both of interstitial lung.

was a drop in the CD4 cells and an increase in CD8 cells; these findings were in line with the symptoms of AIDS. We cannot explain the mechanism linking hyperthyroidism and AIDS and the elevation of CD8+ cells or the production of thyrotropin receptor antibody (TRAb) stimulated by Th cells. Because we cannot interpret the immune modulation mechanisms in the medical literature, additional research is warranted to explore these mechanisms.

The mechanism underlying hyperthyroidism caused by HAART also includes inflammatory imbalances. According to Autran et al[11] and Komanduri et al[12], hyperthyroidism caused by AIDS may be due to an immune reconstitution inflammatory syndrome (IRIS) that acts against infectious or self-antigens during HIV treatment. HAART has a dramatic effect on plasma HIV ribonucleic acid (RNA) load, induces a marked increase in memory and naive CD4+ cells[13], and results from local or systemic inflammatory imbalances. IRIS with autoimmune manifestations may occur even years after the initiation of an effective antiretroviral therapy[14]. Hyperthyroidism may be a late manifestation of immune reconstitution in HIV-positive patients who receive HAART, and immune deregulation may be an important factor[15]. Patients with an advanced form of the HIV disease suffer from opportunistic infections and neoplasms that may affect the thyroid gland, thereby causing transient thyroiditis, hyperthyroidism or hypothyroidism[16]. We hypothesize that hyperthyroidism in our case may be the consequence of a kind of thyroiditis, which is directly caused by the immune-related disorders of AIDS.

In our case, we conclude that AIDS may be the direct cause of hyperthyroidism. A 29-year-old male with a five-year history of homosexual behavior was found to be negative for HIV two years ago. The onset of this case can be summarized by the following characteristics: (1) abrupt outbreak; (2) thyroid disease; (3) lung disease; (4) liver damage; and (5) malnutrition.

Pulmonary fibrosis, another important feature of our patient, is also an immune-related disease. The patient had been treated in a nearby hospital half a month previously, and the chest radiograph showed no abnormalities at that time. He was diagnosed with pneumonia, and antibiotic therapy was administered. Although his health improved slightly over the following month, he presented with repeated dyspnea soon. On admission to our hospital, he underwent a pulmonary CT scan; we observed extensive fibrosis, which demonstrated the rapid progression of the disease.

AIDS as a cause of hyperthyroidism has been rarely reported in the literature. This case report aims to remind clinicians that AIDS may cause hyperthyroidism by immunization regulation or an

unknown mechanism and may present with complex, atypical, and easily ignored symptoms. Weight loss, which may be the only feature, in a patient with otherwise stable HIV disease should prompt an examination for the diagnosis or exclusion of hyperthyroidism. Awareness of the increasing nonconventional complications in patients with HIV and AIDS is essential for timely diagnosis and management of this serious condition[17]. It is advisable to monitor thyroid function changes when administering immunotherapy to patients with AIDS to avoid misdiagnosis. In treating patients with hyperthyroidism, particularly patients with atypical clinical symptoms, physicians should consider the causes of AIDS to avoid misdiagnosis.

## Conclusions

We report the first case of hyperthyroidism caused by AIDS. The mechanism, characteristics and treatment of hyperthyroidism directly caused by AIDS have not been established. We recommend that additional investigations must be conducted.

### Conflict of Interest

The Authors declare that there are no conflicts of interest.

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