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Case report

A rare connection between autoimmune thyroiditis and *Yersinia enterocolitica* infection affecting male reproductive health: A clinical case report

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ABSTRACT

Autoimmune thyroiditis (AIT) is the most common autoimmune endocrine disorder, and recognizing infectious triggers like *Yersinia enterocolitica* is crucial for clinicians to improve diagnosis and management. A 53-year-old man presented with fatigue, irritability, sweating, and palpitations. Laboratory tests showed suppressed TSH, elevated FT3, normal FT4, and anti-TPO >1000 IU/mL. Western blot confirmed *Yersinia enterocolitica* infection through IgA and IgG detection, highlighting the importance of specific serological methods for accurate diagnosis. Mild lymphocytosis with relative neutropenia suggested immune activation. The diagnosis was autoimmune thyroiditis (AIT) with transient thyrotoxicosis triggered by *Yersinia enterocolitica*. Treatment with thiamazole and doxycycline resulted in complete resolution of symptoms and normalization of thyroid hormone levels. This case supports the hypothesis that *Yersinia enterocolitica* may trigger autoimmune thyroiditis through molecular mimicry and immune dysregulation, which can also affect male reproductive health, underscoring the importance of a comprehensive assessment. Screening for infectious cofactors, such as *Yersinia enterocolitica*, in men with thyroid autoimmunity is vital for accurate diagnosis and effective management, thereby encouraging clinicians to adopt proactive testing strategies.

KEYWORDS

autoimmune thyroiditis, *Yersinia enterocolitica*, molecular mimicry, thyroid autoimmunity, male fertility

INTRODUCTION

Autoimmune thyroiditis (AIT), or Hashimoto's thyroiditis, is the most common organ-specific autoimmune endocrine disorder, affecting 5%–10% of the global population [1]. The disease is characterized by lymphocytic infiltration of the thyroid gland, progressive follicular destruction, and elevated thyroid autoantibodies, particularly anti-thyroid peroxidase (anti-TPO) and anti-thyroglobulin (anti-Tg). Although women are most often affected, recent data indicate a rising prevalence among men, with significant systemic effects, including metabolic disturbances, ongoing inflammation, and reproductive problems [2,3].

An increasing number of studies suggest that infectious pathogens can act as environmental triggers that initiate or worsen thyroid autoimmunity. *Yersinia enterocolitica* is among the most strongly linked pathogens because of the notable structural similarity between its outer membrane proteins (YOPs) and epitopes of the human TSH receptor (TSHR). This similarity promotes molecular mimicry, where immune responses targeting microbial antigens cross-react with host endocrine tissues, leading to chronic autoimmune inflammation [4,5,6,7].

Furthermore, *Yersinia* antigens activate dendritic cells and promote polarization toward Th1 and Th17 immune responses, leading to increased secretion of interleukin-6 (IL-6), interleukin-17 (IL-17), interferon-γ (IFN-γ), and tumor necrosis factor-α (TNF-α) [8,9]. These cytokines are crucial in disrupting thyroid immune tolerance and advancing autoimmune thyroid disease. Continued exposure to *Yersinia* antigens can cause a persistent inflammatory state, resulting in episodes of transient thyrotoxicosis or fluctuating thyroid function, especially in patients with preexisting conditions, such as AIT [4,10].

Another important aspect is the increasing awareness of the link between AIT and male reproductive issues. Thyroid hormones help regulate gonadotropin release, Leydig cell testosterone production, Sertoli cell metabolism, and spermatogenesis. Even mild thyroid dysfunction can decrease testosterone levels, impair sperm motility and morphology, and increase oxidative stress [11,12]. Autoimmune processes worsen this by disrupting testicular immune privilege, causing germ-cell apoptosis, and increasing sperm DNA fragmentation [13,14].

Infectious triggers like *Yersinia enterocolitica* may contribute to both thyroid issues and male reproductive problems through complex immune and hormonal interactions. This case emphasizes the importance of testing for infectious causes in men with autoimmune thyroid disease and systemic or reproductive symptoms [8,15].

CASE REPORT

A 53-year-old man (initials Sh.K.) presented with worsening fatigue, irritability, sweating, and palpitations over three months, prompting testing for infectious causes given his history of autoimmune thyroiditis and prior antibiotic treatments.

The patient had a documented history of Lyme disease, diagnosed in March 2025, before the current presentation. The diagnosis was based on clinical features and serological testing, and the patient was treated with standard antibiotic therapy (doxycycline 100 mg twice daily for 21 days). According to the patient, treatment led to clinical resolution of acute manifestations, and no chronic or relapsing Lyme-related symptoms were noted in the subsequent years. No long-term antibiotic therapy was administered, and there was no clinical suspicion of ongoing active *Borrelia burgdorferi* infection at the time of the present evaluation.

The patient demonstrated a positive rheumatoid factor level of 18.51 IU/mL, marginally exceeding the reference threshold of ≤ 18 IU/mL. Furthermore, IgM antibodies to *Borrelia burgdorferi*, assessed via enzyme-linked immunosorbent assay (ELISA), were positive, with an index of 1.44, surpassing the normal limit of ≤ 0.81. The slight elevation in rheumatoid factor was considered a nonspecific marker of immune activation, given the absence of clinical evidence of inflammatory

joint disease. Western blot analysis of serum IgM antibodies against *Borrelia burgdorferi* indicated reactivity with specific *Borrelia* antigens: p31 (OspA, *Borrelia afzelii*) showed borderline (equivocal) IgM reactivity at an intensity of 22. At the same time, p25 (OspC), a surface protein of *Borrelia afzelii*, showed a positive IgM response with an intensity of 32.

The patient has a long-standing diagnosis of autoimmune thyroiditis (since 2012), with very high anti-TPO titers (>1000 IU/mL), no goiter, and no ophthalmopathy, findings typical of Hashimoto autoimmune thyroiditis. The current episode represents transient thyrotoxicosis (Hashitoxicosis) rather than classic Graves disease. Although TRAb was mildly positive, such findings have been reported in Hashitoxicosis and do not rule out destructive thyroiditis.

Physical examination

The patient seemed anxious but was alert.

- Heart rate: 92 bpm
- Blood pressure: 128/78 mmHg
- Temperature: 36.6°C
- BMI: 25.1 kg/m²
- Skin: warm, slightly moist
- Thyroid gland: normal size, non-tender, no nodularity
- No ophthalmopathy or tremor observed

Table I. Laboratory evaluation

Parameter	Result	Reference
TSH	0.29 μIU/mL	0.4-4.0
FT3	4.98 pg/mL	2.0-4.4
FT4	16.99 pmol/L	12-22
Anti-TPO	>1000 IU/mL	<35
Anti-Tg	mildly elevated	<50
TRAb	2.6 IU/L	<1.75
Thyroglobulin	145.85 ng/mL	<77
HLA-B27	negative	–

The pattern suggests T3-predominant thyrotoxicosis, commonly associated with destructive thyroiditis or immune activation.

Infectious and immunological testing

Western blot for *Yersinia enterocolitica*: IgA: p46, p38 positive; IgG: p46, p44, p38, p36 YopD positive

These findings suggest a recent or active *Yersinia enterocolitica* infection, as indicated by the presence of multiple immunogenic bands.

CBC revealed: Leukocytes: 6.1 × 10^9/L, Lymphocytes: 39%, Neutrophils: 46%

Consistent with infection-induced immune activation. Liver and renal profiles are normal.

We performed a differential diagnosis among the following diseases:

1. Hashitoxicosis (destructive thyroiditis).
2. Infection-triggered autoimmune thyroiditis.
3. Early or subclinical Graves' disease (unlikely without goiter or ophthalmopathy).
4. Drug-induced thyroid dysfunction.
5. Non-thyroidal causes of thyrotoxicosis.

The clinical presentation indicated an AIT flare caused by a *Yersinia* infection.

The patient was given thiamazole 10 mg daily to control thyroid hormone excess caused by the autoimmune flare temporarily. Because a Western blot confirmed active *Yersinia enterocolitica* infection, doxycycline 100 mg twice daily for 14 days was prescribed to eliminate the infectious trigger and decrease immune activation. Clinical symptoms and thyroid parameters returned to normal within six weeks, confirming a successful treatment response.

Thiamazole was used only for the short term, not as definitive Graves therapy, but solely to control symptomatic thyrotoxicosis during the inflammatory flare.

At the six-week follow-up, the patient had complete resolution of palpitations, sweating, fatigue, and irritability. Thyroid function tests showed normalization of TSH (0.29 μIU/mL) and FT3 (4.98 pg/mL), with FT4 remaining stable within the reference range (16.99 pmol/L). No adverse effects from thiamazole or doxycycline were reported, and liver function remained normal throughout treatment. These clinical and biochemical improvements support the conclusion that the effective elimination of *Yersinia enterocolitica* resolved the autoimmune flare.

The patient had been evaluated by a urologist for several years due to male infertility, as he has been living with his wife for 15 years without having children. His wife is completely healthy, with no gynecological disorders identified, and her fertility has been preserved. Urological examination

did not reveal any urinary tract infections; however, semen analysis demonstrated the presence of immotile spermatozoa. Despite multiple attempts to achieve pregnancy, all attempts were unsuccessful.

In patients with autoimmune thyroiditis and concomitant *Yersinia enterocolitica* infection, immune dysregulation is more likely to affect endocrine and reproductive functions. Autoimmune thyroiditis has been linked to alterations in male reproductive hormone profiles and semen parameters, suggesting that thyroid autoimmunity may contribute to impaired male fertility [5,16]. Infectious agents, including *Yersinia enterocolitica*, are considered potential environmental factors that may initiate or modulate autoimmune thyroid disease through immune-mediated mechanisms such as molecular mimicry [5,17]. In this context, infection-related immune activation, combined with thyroid autoimmunity, may indirectly affect male reproductive function by disrupting endocrine regulation and spermatogenesis [18,19,20].

DISCUSSION

The current case illustrates a complex interaction between infectious and autoimmune mechanisms in a patient with autoimmune thyroiditis (AIT), complicated by transient thyrotoxicosis and immune activation caused by *Yersinia enterocolitica*. This case adds to the growing body of literature suggesting that infectious agents may play a key role not only in triggering autoimmune thyroid disease but also in influencing its clinical progression and systemic effects, including impacts on male reproductive health.

Infectious triggers and molecular mimicry in autoimmune thyroid disease

Yersinia enterocolitica has long been considered a potential infectious trigger of AIT, but recent advances in molecular immunology have strengthened this association. Several *Yersinia* outer membrane proteins (YOPs), especially p46, p38, p44, and p36, share structural and antigenic similarities with the human TSH receptor (TSHR). This similarity enables molecular mimicry, in which the immune system produces antibodies against bacterial antigens that unintentionally cross-react with thyroid tissue.

In the patient described, Western blot positivity for multiple YOP immunogenic bands (IgA and IgG) indicates recent or ongoing exposure to *Yersinia* antigens. The presence of high anti-TPO titers (>1000 IU/mL) further suggests an elevated autoimmune state that may be intensified or maintained by this infection. This pattern aligns with previous research showing that patients with AIT often have increased seroreactivity to *Yersinia* antigens compared to healthy controls [5,6]. Immune cross-reactivity between these antigens and TSHR may accelerate follicular destruction, cause transient thyrotoxicosis, or lead to fluctuations in thyroid function.

Notably, the patient exhibited a pattern of transient thyrotoxicosis with elevated FT3 and suppressed TSH but normal FT4 – a biochemical profile linked to acute inflammatory activation or antigen exposure in the context of underlying AIT.

Role of Th1/Th17 responses and cytokine activation

Another important aspect of immunopathogenesis is the activation of Th1 and Th17 pathways. *Yersinia enterocolitica* is known to stimulate the production of IL-6, IL-17, TNF-α, and IFN-γ. These cytokines are crucial in the development of thyroid autoimmunity and can worsen glandular infiltration, oxidative stress, and the breakdown of immune self-tolerance.

Persistent Th17 activation has been associated with more severe structural damage to the thyroid and fluctuating thyroid hormone levels. The patient's mild lymphocytosis and relative neutropenia are consistent with an activated cellular immune response, which may indicate chronic antigenic stimulation.

Additionally, *Yersinia*-induced dendritic cell activation may boost antigen presentation, further promoting the production of anti-thyroid autoantibodies. These mechanisms highlight why chronic infections – especially in the gastrointestinal system – can have lasting effects on autoimmunity even after the initial infection has cleared.

Clinical significance of antibiotic treatment in infection-associated AIT

Several reports suggest that targeted antibiotic therapy can reduce autoimmune activity in patients with infection-related thyroid autoimmunity [5,6,8]. In this case, treatment with doxycycline – a standard therapy for *Yersinia* infections – led to normalization of TSH and FT3 within six weeks and complete symptom relief. Although thiamazole temporarily controlled hyperthyroid symptoms, the return of normal thyroid function strongly indicates that removing the infectious trigger was crucial in reversing the immune and hormonal disturbances.

This supports the hypothesis that, in selected patients, particularly those with serological evidence of *Yersinia* infection, antimicrobial therapy may be beneficial in addition to standard endocrine treatment. Although this approach is not universally recommended, emerging research underscores the importance of individualized assessment of infectious triggers in patients who exhibit atypical thyroid fluctuations, systemic inflammatory signs, or resistance to conventional therapy.

Relationship between autoimmune thyroiditis and male reproductive dysfunction

AIT is increasingly recognized as a condition with systemic effects that go beyond the endocrine system. Thyroid hormones directly affect spermatogenesis, Leydig cell testosterone production, Sertoli cell metabolism, and epididymal sperm maturation. Changes in TSH or thyroid hormone levels, whether hyperthyroid or hypothyroid, can significantly harm male reproductive health.

Three mechanisms appear to be particularly important:

Hormonal dysregulation of the HPG axis

Thyroid hormones affect GnRH secretion, which then regulates the release of LH and FSH. Transient thyrotoxicosis, as seen in this patient, can reduce LH pulsatility and testosterone production. Even slight elevations in FT3 levels have been associated with decreased sperm concentration and motility.

Autoimmune-driven testicular inflammation

Autoimmunity is increasingly associated with male infertility. Elevated systemic cytokines (IL-6, IL-17, TNF-α) can weaken the blood–testis barrier, allowing immune cells to infiltrate and cause apoptotic damage to germ cells. Cross-reactive antibodies, arising from molecular mimicry, may target testicular antigens, potentially leading to autoimmune orchitis – a condition that may go unnoticed clinically.

Oxidative stress and DNA fragmentation

Both thyroid dysfunction and cytokines from infection increase oxidative stress, impairing mitochondrial function in sperm and raising DNA fragmentation – a key factor in male subfertility. Studies show that men with AIT have notably higher sperm DNA damage indices compared to healthy controls [8,9,20]. In the context of *Yersinia* infection, additional mucosal immune activation may further enhance these pathways, worsening the adverse effects on male reproductive health.

The diagnostic value of screening for infectious triggers in AIT

This case highlights the importance of laboratory screening for infectious agents in patients with AIT who exhibit:

- sudden or unexplained fluctuations in thyroid hormone levels
- persistent lymphocytosis or elevated inflammatory markers
- systemic symptoms such as fatigue, sweating, or irritability
- a history of other autoimmune or infectious conditions
- reproductive concerns

Testing for *Yersinia enterocolitica* (IgA/IgG, Western blot), *Borrelia burgdorferi*, *Chlamydia*, and other immune-modulating pathogens can reveal clinically significant interactions that directly affect thyroid function and systemic immunity.

Comparison with published cases

Published literature includes several observations linking *Yersinia* infection to thyroid dysfunction, but reports documenting simultaneous reproductive implications in men are rare. This case offers a new perspective by highlighting the dual endocrine–immune–gonadal interaction and emphasizing the need for interdisciplinary evaluation. While most cases of AIT follow a chronic, slowly progressive course, infection-triggered episodes may present acutely, fluctuate unpredictably, and respond more favorably to antimicrobial treatment than classic Hashimoto's disease.

Clinical implications

1. *Yersinia* should be included in the differential diagnosis of atypical or transient thyrotoxicosis.
2. Screening for infectious triggers might alter diagnostic and treatment strategies in AIT.
3. In men with thyroid autoimmunity, assessing reproductive function should be a routine part of evaluation.
4. Treating underlying infections can help stabilize thyroid function and enhance endocrine and reproductive outcomes.

CONCLUSIONS

Yersinia enterocolitica infection may initiate or exacerbate autoimmune thyroiditis through molecular mimicry and inflammatory responses. The resulting endocrine–immune disturbances may negatively affect male reproductive health. Screening for infectious triggers may improve the management of men with thyroid autoimmunity.

Conflict of interest

The authors declare no conflict of interest.

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Use of AI tools statement

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Authors' contribution

Study design – R. Zhurayev

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