International Journal of Progressive Sciences and Technologies (IJPSAT)
ISSN: 2509-0119.
© 2024 Scholar AI LLC.
Vol. 45 No. 2 July 2024, pp. 545-548

Unmasking Subacute Thyroiditis in a Young Male with PUO: A Case Report

Ramkumar Sundaraperumal MD[1], Rahul Yedpallikar Rajesh[2]

[1]Specialist Internal Medicine, Thumbay hospital, Gulf medical university, Ajman, UAE

[2]Tbilisi State Medical University, Tbilisi, Georgia

(cc) BY

Abstract – Pyrexia of unknown origin (PUO) poses a diagnostic challenge, defined as persistent fever exceeding 38.3°C (100°F) without an identified cause after extensive investigation. Subacute thyroiditis (SAT), an uncommon inflammatory condition of the thyroid gland, typically presents with neck pain, thyrotoxic symptoms, and elevated inflammatory markers. However, it rarely manifests as PUO without typical symptoms. We report a case of a 32-year-old Indian male presenting with a 20-day history of persistent fever without localized symptoms, initially treated empirically with antibiotics without improvement. Clinical examination revealed a firm, non-tender goiter, and laboratory investigations showed elevated erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). Subsequent thyroid function tests indicated elevated free T4 levels with low TSH, suggestive of thyroiditis, after negative thyroid autoantibodies ruling out Graves' disease. Further investigations including imaging and tests for PUO were negative, prompting an empirical trial of steroid therapy which resulted in rapid clinical improvement. Subsequent thyroid function tests revealed transient hypothyroidism, resolving without intervention. Retrospectively, a diagnosis of subacute thyroiditis was established, highlighting its atypical presentation as PUO. Our case sheds light on the importance of considering uncommon thyroid pathologies in the differential diagnosis of PUO, especially when typical symptoms are absent.

Keywords – Pyrexia of unknown origin (PUO), Subacute thyroiditis, Steroid therapy, Inflammatory markers, Goiter.

I. INTRODUCTION

The concept of pyrexia of unknown origin (PUO) describes a persistent fever exceeding 38.3°C (100°F) that remains undiagnosed for at least three weeks, including one week of hospital investigation [1]. PUO presents a significant diagnostic challenge for physicians. Subacute thyroiditis, though rarely associated with PUO, is an infrequent and self-limiting inflammatory condition likely of viral origin, often with a genetic predisposition. It typically manifests as painful neck swelling and mild thyrotoxic symptoms, accompanied by elevated inflammatory markers, but can occasionally present with atypical features such as lymphadenopathy. Thyroid antibodies are usually negative in these cases. Treatment generally involves nonsteroidal anti-inflammatory drugs (NSAIDs) or steroids [2].

The etiologies of fever of unknown origin (PUO) can be categorized into four main groups: non-infectious inflammatory disorders, infections, malignancies, and miscellaneous causes. Subacute thyroiditis (SAT) falls into the miscellaneous category as a rare cause of PUO, often triggered by a preceding viral infection. Due to its rarity and the potential absence of typical symptoms, it is frequently overlooked in differential diagnoses [3]. Here, we present a case of PUO caused by SAT, notable for its lack of typical hyperthyroidism symptoms and significant neck pain.

Corresponding Author: Rahul Yedpallikar Rajesh

Case:
A 32-year-old Indian male presented to the hospital with a fever persisting for 20 days. He reported no other localizing symptoms and had no history of neck pain or thyrotoxic symptoms. Upon clinical examination, the only significant finding was a firm, non-tender goiter. He had been evaluated and empirically treated with ceftriaxone for five days at another facility without improvement. Initial investigations, including a complete blood count, urinalysis, chest X-ray, malarial parasite smear, Widal test, and blood and urine culture sensitivity tests, were all negative. However, both his ESR (140) and CRP (80) were elevated (*Table 1*).

Investigation	Results	Reference Values	Remarks
ESR	Initial: 140; Repeat: 115	< 20 mm/hr	Elevated
CRP	Initial: 80; Repeat: 132	< 10 mg/L	Elevated
Free T3	3.27 pg/mL	2.0 - 4.4 pg/mL	Normal
Free T4	194 pmol/L	9.0 - 23.0 pmol/L	Elevated
TSH	0.007 mIU/L	0.4 - 4.0 mIU/L	Low
Thyroid Ultrasound (USG)	Bilateral multinodular goiter, no thyroiditis	Normal echogenicity	Presence of goiter
Anti-TPO Antibodies	Negative	< 35 IU/mL	Rules out Hashimoto's and painless sporadic thyroiditis
TSH Receptor Antibodies	Negative	< 1.75 IU/L	Rules out Graves' disease
Ferritin	Elevated	20 - 300 ng/mL	Elevated, supports diagnosis of thyroiditis

Table 1: Relevant investigations and their results in a 32-year-old male presenting with fever of unknown origin (PUO) and diagnosed with subacute thyroiditis. ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; Free T3 and Free T4: thyroid function tests; TSH: thyroid-stimulating hormone; USG: ultrasound of the neck; Anti-TPO Antibodies and TSH Receptor Antibodies: thyroid autoantibodies

During his hospital stay, the patient experienced continuous high-grade fever, which responded to paracetamol and ibuprofen but recurred at the end of each dose. Repeat baseline investigations at the hospital were within normal limits, except for elevated ESR (115) and CRP (132). Given the presence of a clinical goiter and pyrexia of unknown origin (PUO), a thyroid function test and an ultrasound (USG) of the neck were performed. The USG revealed bilateral multinodular goiter without features of thyroiditis (*Figure 1*). Thyroid function tests showed normal free T3 (3.27) and elevated T4 (194), with low TSH (0.007) (*Table 1*). An endocrinologist was consulted, who considered the possibilities of PUO with euthyroid sick syndrome, thyroiditis, or Graves' disease, and recommended testing for thyroid autoantibodies. Both anti-TPO and TSH receptor antibodies were negative, ruling out Graves' disease. The thyroid function tests favored thyroiditis, but the patient lacked other typical symptoms and signs of subacute thyroiditis, such as neck pain, tenderness, or a hypoechoic pattern on USG, except for elevated ESR, CRP, and ferritin levels.

Further workup for PUO was conducted, including a CT scan with contrast of the abdomen, echocardiogram, MRI, PET scan of the whole body, ANCA, and ANA global tests, all of which were negative. The next logical step was either a radionuclide scan or an empirical trial of steroid therapy. Given the thyroid function test results suggestive of thyroiditis, despite the atypical clinical presentation, an empirical steroid therapy was chosen. After obtaining informed consent, the patient was started on oral prednisolone 60 mg once daily (1 mg/kg). Despite the high-grade fever, the patient remained clinically well throughout his hospitalization.

The patient was discharged on oral steroids and followed up in the outpatient department. Remarkably, his fever began to improve within a day of starting steroids. Within a week, his ESR decreased to 54, and CRP to 3.9. Four weeks later, his thyroid function tests showed hypothyroidism (Free T4 – 8.73, TSH – 13.75), though he did not develop any symptoms of hypothyroidism and was therefore observed without thyroxine supplementation. The steroids were gradually tapered and discontinued over two weeks. By then, his ESR and CRP had returned to baseline levels. Three months post-treatment, his thyroid function tests were normal. Retrospectively, a diagnosis of subacute or De Quervain's thyroiditis was established.

II. Discussion

Thyroiditis constitutes approximately 10% of all thyroid-related illnesses. It can arise from various causes, including acute bacterial infections, painless sporadic thyroiditis, Hashimoto's thyroiditis, subacute De Quervain's thyroiditis, postpartum thyroiditis, radiation-induced thyroiditis, Riedel's thyroiditis, and drug-induced thyroiditis. Acute bacterial suppurative thyroiditis was ruled out in this case as it typically presents with severe illness, high spiking fevers, and a severely tender thyroid, none of which were observed in our patient. Other potential causes, such as postpartum thyroiditis, drug-induced thyroiditis, and radiation-induced thyroiditis, were excluded based on the patient's medical history. Painless sporadic thyroiditis and Hashimoto's thyroiditis were ruled out due to negative anti-TPO antibody titers. Graves' disease was also excluded due to negative anti-TSH receptor antibodies, making radionuclide imaging unnecessary in this case.

After ruling out these potential causes, subacute thyroiditis emerged as the likely diagnosis. Subacute thyroiditis typically presents with painful thyroid inflammation; however, our patient did not exhibit any thyroid tenderness. This raised the question of whether subacute thyroiditis can present with a prolonged fever of over three weeks. The diagnosis was supported by significantly elevated ESR and ferritin levels, thyroid function tests indicative of thyroiditis, and a positive response to steroid therapy. Subacute or De Quervain's thyroiditis is relatively uncommon, with an incidence of 3.6 cases per 100,000 per year according to a study from Minnesota, USA [4]. It is more prevalent in females, with a female-to-male ratio of 6:1. Most patients with subacute thyroiditis present with fever, thyroid pain, and thyrotoxicosis, and clinical examination typically reveals a tender thyroid.

Literature review indicates that subacute thyroiditis presenting as PUO is rarely reported. Fever exceeding 38°C is seen in only 28% of patients, usually peaking within 3-4 days and subsiding within a week. Thyrotoxic symptoms are present in 60% of cases [5], and painful thyroid swelling occurs in 80% of cases [6]. Elevated transaminases and alkaline phosphatase levels are common [7], and thyroid ultrasound often shows hypoechogenicity [6]. Our patient exhibited several atypical features: male sex, fever for more than three weeks with high spikes (exceeding 38.3°C), absence of thyrotoxic symptoms, and a painless thyroid. Only one previous case report described subacute thyroiditis with elevated ferritin, PUO, and a painless thyroid [8], and very few cases of painless subacute thyroiditis have been reported [9, 10].

The response to steroid treatment in subacute thyroiditis is nearly universal, with 90% of patients experiencing complete and spontaneous recovery, returning to normal thyroid function. One retrospective study reported permanent hypothyroidism in 5.9% of patients, with bilateral hypoechogenic areas on ultrasound serving as a prognostic marker [11].

III. Conclusion

Subacute thyroiditis is a rare cause of PUO, particularly in males and in the absence of thyroid tenderness. Awareness of such atypical presentations is crucial for early diagnosis and effective management, ensuring better patient outcomes and avoiding unnecessary prolonged investigations.

IV. Ethical Statement

This case report was conducted in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Informed consent was obtained from the patient and his guardians for the inclusion in the case report and for the publication of any potentially identifiable information. All efforts were made to ensure patient confidentiality and anonymity.

V. Conflict of Interest

The authors declare that they have no conflicts of interest related to this case report.

References

[1]. Petersdorf RG. Beeson PB. Fever of unexplained origin: report on 100 cases. Medicine (Baltimore) 1961;40:1–30.

[2]. Dalugama C. Asymptomatic thyroiditis presenting as pyrexia of unknown origin: a case report. J Med Case Rep. 2018;12(1):51. Published 2018 Feb 23. doi:10.1186/s13256-018-1590-6

[3]. Lee SY, Er C. Subacute Thyroiditis Causing Fever of Unknown Origin: A Reminder of the Uncommon Cause. Cureus. 2023;15(10):e47037. Published 2023 Oct 14. doi:10.7759/cureus.47037

[4]. Fatourechi V, Aniszewski JP, Fatourechi GZ, Atkinson EJ, Jacobsen SJ. Clinical features and outcome of subacute thyroiditis in an incidence cohort: Olmsted County, Minnesota, study. J Clin Endocrinol Metab. 2003;88(5):2100-2105. doi:10.1210/jc.2002-021799

[5]. Benbassat, C.A., et al., Subacute Thyroiditis: clinical characteristics and treatment outcome in fifty six consecutive patients diagnosed between 1999-2005. J Endocrinol Invest, 2007.30(8): P.631-35 – Thyrotoxicosis

[6]. Nishihara E, Ohye H, Amino N, et al. Clinical characteristics of 852 patients with subacute thyroiditis before treatment. Intern Med. 2008;47(8):725-729. doi:10.2169/internalmedicine.47.0740

[7]. Matsumoto Y, Amino N, Kubota S, et al. Serial changes in liver function tests in patients with subacute thyroiditis. Thyroid. 2008;18(7):815-816. doi:10.1089/thy.2007.0374

[8]. Cunha, B.A., Chak, A., & Strollo, S.L. (2010). Fever of unknown origin (FUO): de Quervain's subacute thyroiditis with highly elevated ferritin levels mimicking temporal arteritis (TA). Heart & lung : the journal of critical care, 39 1, 73-7 .

[9]. Daniels GH. Atypical subacute thyroiditis: preliminary observations. Thyroid. 2001;11(7):691-695. doi:10.1089/105072501750362772

[10]. Janssen OE. Atypische Präsentation einer Thyreoiditis de Quervain [Atypical presentation of subacute thyroiditis]. Dtsch Med Wochenschr. 2011;136(11):519-522. doi:10.1055/s-0031-1274535

[11]. Nishihara E, Amino N, Ohye H, et al. Extent of hypoechogenic area in the thyroid is related with thyroid dysfunction after subacute thyroiditis. J Endocrinol Invest. 2009;32(1):33-36. doi:10.1007/BF03345675