An Interesting Endocrine Cause of Pyrexia of Unknown Origin: A Case Report and Review of Literature

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ABSTRACT

Pyrexia of unknown origin (PUO) is one of the most challenging medical problems. Endocrine causes of PUO are rare. Fever is common in a few endocrine disorders (e.g., thyroid storm, adrenal crisis and pheochromocytoma). However, PUO as the sole presenting feature is very rare with only a few reported cases in the literature. We present the case of a middle-aged male who came to us with PUO, weight loss and loss of appetite. The unusual symptomatology like loss of appetite, altered bowel habits made diagnosis difficult. This case highlights the importance of considering thyroid disorder in the differential diagnosis of PUO. Abnormal thyroid function may be an early clue for diagnosis.

Keywords: Pyrexia of unknown origin, hyperthyroidism, endocrine disorders

Pyrexia of unknown origin (PUO) is one of the most challenging medical problems. Most common causes include infections, malignancy and autoimmune disorders. Endocrine causes of PUO are rare. Fever is common in a few endocrine disorders (e.g., thyroid storm, adrenal crisis and pheochromocytoma). However, PUO as the sole presenting feature is very rare with only a few reported cases in the literature.^{1,2} We present a case of hyperthyroidism presenting with PUO. The patient did not exhibit any classic thyroid symptoms at the time of presentation. Therefore, a thyroid disorder was not suspected initially. This unusual presentation of a common medical problem highlights the importance of considering a thyroid disorder in the differential diagnosis of PUO.

CASE DETAILS

A 52-year-old male patient, who was a known case of diabetes mellitus for 10 years on oral hypoglycemic agents, presented with complaints of loss of appetite and

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Greams Road, Chennai - 600 006, Tamil Nadu, India E-mail: neetumariam@gmail.com loss of weight for 2 months. He had lost ~12 kg in 2 months. He also had on and off low-grade fever with associated night sweats for 6 weeks along with altered bowel and bladder habits and increased frequency of urine.

On physical examination, he was moderately built and poorly nourished with height of 178 cm, weight of 69 kg, body mass index (BMI) of 21.78 kg/m² and body surface area (BSA): 1.85 m². He was afebrile and his pulse rate was 120/min with regular rhythm, normal volume, no radial radial delay, with normal vessel wall, and all peripheral pulses well felt. His blood pressure was 100/70 mmHg. Systemic examination was unremarkable. Baseline investigations revealed hemoglobin (Hb) - 11.3 g/dL, total leukocyte count (TLC) - 9.4, differential leukocyte count (DLC) - (N₇₄L₁₅E₀M₁₁), platelet - 2,26,000 cells/mm³. His erythrocyte sedimentation rate (ESR) was 80 mm in the first hour. Peripheral blood smear showed normochromic normocytic cells with moderate rouleaux formation. The blood biochemistry was as follows: blood glucose (random) - 144, urea - 31, creatinine - 0.7, HbA1c - 7.7%, total bilirubin - 0.6 mg/dL (0.3/0.3), total protein - 9.1, albumin - 4, globulin - 5.1, A:G = 0.78, aspartate transaminase/alanine transaminase (AST/ALT) - 84/132, gammaglutamyl transpeptidase (GGTP)-69, alkaline phosphatase (ALP) - 99. Urine routine examination showed glucosuria (3+), ketonuria (1+) with no RBCs or pus cells.

Two sets of blood cultures and urine culture were sterile. In two-dimensional echocardiogram, the valves and the endocardium were free of vegetations. Human

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immunodeficiency virus (HIV) ELISA (enzyme-linked immunosorbent assay) test was negative. 640-slice CT chest and abdomen were done; both were noncontributory. Bone marrow biopsy was done. Aspiration cytology showed hypercellular marrow with trilineage hematopoiesis and erythroid hyperplasia. Histopathological examination confirmed variably cellular marrow with trilineage hematopoiesis and was negative for focal lesions. Xpert MTB test for tuberculosis was negative and culture was sterile.

¹⁸F-fluorodeoxyglucose (FDG)-avid ill-defined hypodense nodule in the lower pole of left lobe of thyroid was found on positron emission tomography-computed tomography (PET-CT) whole body with no other significant metabolically active disease. Thyroid-stimulating hormone (TSH) was <0.01 and free thyroxine (T4) was 2.5. Antithyroid peroxidase (2.83) was negative and anti-triglyceride (9.1) was positive as per thyroid antibody profile. He was started on carbimazole 5 mg twice daily and was reviewed after 3 months. His fever settled, appetite improved and there was 5 kg increase in weight since commencement of treatment.

DISCUSSION

Hormones play an important role in thermoregulation. Various endocrine disorders like thyroiditis, hyperthyroidism, Addison's disease, pheochromocytoma, primary hyperparathyroidism and hypoglycemia can produce fever.^{3,4} Fever is one of the common symptoms in patients with subacute thyroiditis (SAT)^{5,6} and thyroid crisis,^{7,8} but the manifestation of thyroid disease as fever alone is very rare. Prolonged fever as the only manifestation of SAT has been reported previously. SAT follows a triphasic course of thyrotoxicosis, hypothyroidism and subsequent restoration of euthyroidism in most of the patient. Rarely, hyperthyroidism can manifest with persistent fever for many months without clinical symptoms or signs to lead to suspicion of thyroid disease, which may become evident only after exhaustive investigation.9 While we generally see normal appetite in patients with hyperthyroidism, our patient has significant loss of appetite which we generally see in hypothyroidism, which made diagnosis challenging.

The pathogenesis of fever in thyrotoxicosis is not completely understood yet. Although, thyroid hormone is known to be calorigenic, the precise mechanism for this thermogenesis is still debated, and is widely believed to be due to stimulation of the membranebound sodium-potassium ATPase (sodium pump).¹⁰ Heat intolerance and an increased basal metabolic rate are common in hyperthyroidism. The true incidence and grade of fever in uncomplicated hyperthyroidism has not been determined and, if present, is usually of low-grade in most patients. A study by Pala et al revealed that, out of 25 patients, 20 (80%) had SAT and 5 (20%) had hyperthyroidism. Patients with hyperthyroidism received thionamides and β -blockers. Fifty percent patients with SAT received analgesics, 25% received steroids only and 25% received a combination of analgesics and steroids. Early-onset transient hypothyroidism occurred in 40% patients with SAT; permanent hypothyroidism was less common and only 15% of patients were receiving levothyroxine therapy after 1 year of follow-up.¹¹ Our patient was started on antithyroid medications (carbimazole) following which his fever settled and he regained his appetite and gained weight significantly.

CONCLUSION

Endocrine disorders could be one of the rare causes of PUO. Hyperthyroidism should be considered in the differential diagnosis even if clinical symptoms of thyrotoxicosis are not present. Abnormal thyroid function may be an early clue for diagnosis.

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