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## Case Report

# Subacute thyroiditis–an unusual endocrine cause of pyrexia of unknown origin: Case report with review of literature

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## Abstract

We report a case of a 58-year-old male who presented with high grade fever of 45 days duration. He had presented with a dry cough and right ear pain. His initial clinical evaluation and diagnostic tests were unremarkable. During the hospital stay, he developed palpitation for which tests for thyroid functions were done which revealed subacute thyroiditis. He recovered fully with the treatment. Subacute thyroiditis is one of the rarely mentioned causes of Pyrexia of Unknown origin. A high index of suspicion and appropriate imaging is required for early diagnosis and management.

## Introduction

Infection-related causes of Pyrexia of Unknown origin are approximately 16%, whereas non-infectious inflammatory conditions contribute up to 22% of cases [1]. Endocrine causes of fever of unknown origin include subacute thyroiditis, thyrotoxicosis, adrenal insufficiency, and pheochromocytoma. Subacute thyroiditis is a clinical condition presumed to be caused by a viral infection or a post-viral inflammatory process. It is a well-known cause of pyrexia of unknown origin but it manifests with classical signs and symptoms [2]. It is usually characterized by neck pain or discomfort and a tender diffuse goiter. Fever and constitutional symptoms are common associations with this disease but persistent fever without neck pain or thyroid tenderness is uncommon. The course that it follows is hyperthyroidism initially followed by euthyroidism, hypothyroidism and later the normal thyroid function may or may not be restored. It is one of those endocrine disorders that must be considered in the workup for pyrexia of unknown origin.

## Case report

A 58-year-old male, with no known comorbidities, presented to our center with complaints of high-grade intermittent fever for 45 days, initially associated with dry cough and later on right earache.

On examination, he was febrile and had tachycardia. Other vitals were stable. Eye examination and thyroid examination were normal. There was no peripheral lymphadenopathy. Other general and systemic examination was unremarkable. ENT opinion was taken which revealed nothing significant.

Routine investigations were done to evaluate the cause of pyrexia of unknown origin.

On evaluation, his laboratory investigations showed mild leukocytosis (12,630/ $\mu$ L), Hemoglobin 11.9 gm %, and platelets 4.5 /mCL. Inflammatory markers were raised. (C reactive protein- 193 mg/L, Erythrocyte sedimentation rate- 150

mm) with normal liver and renal function tests. Serology for Malaria, Dengue, Scrub typhus, and *Leptospira* were negative. Procalcitonin was 0.24 ng/ml. Blood and urine cultures showed no growth. IgM for Measles and Mumps was negative. Serological tests for other viruses could not be done because of the kit's non-availability. COVID antigen testing/Anti cyclic citrullinated peptide/Anti-Nuclear antibody was negative. Computed Tomography chest and abdomen did not reveal any abnormality. 2D Echo showed no evidence of infective endocarditis. On further evaluation, his Thyroid function tests revealed hyperthyroidism Thyroid stimulating hormone < 0.01  $\mu$ IU/mL (0.3-4), fT3 – 6.4(2-7 picomoles /liter, fT4 – 3.7ng/dl (0.9-2.3).

Initially, the patient was started on empirical antibiotics (Ceftazidime and Doxycycline) along with antipyretics, non-steroidal anti-inflammatory drugs, and other supportive measures.

During admission, the patient developed episodes of palpitations and was started on beta blockers (propranolol). Based on these symptoms, further evaluation was done.

Ultrasound Neck: Bulky thyroid gland with raised internal vascularity – possible thyroiditis.

Positron Emission Tomography (Figures 1,2) showed diffuse increased uptake in both lobes of the thyroid gland.

Pertheneate thyroid scan (Figure 3) was suggestive of thyroiditis.

Based on the above findings, a diagnosis of subacute thyroiditis was made. The patient was started on tablet Prednisolone 40 mg once a day. The patient had gradual remission of symptoms and was discharged after 72 hours of defervescence. During the last follow-up in the outpatient

department, the patient was asymptomatic on a tapering dose of steroids at a dose of 10 mg of prednisolone once a day.

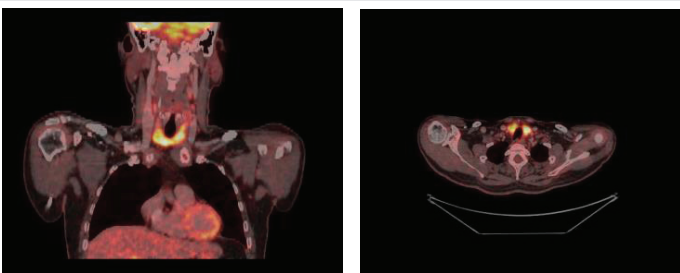
## Discussion

Pyrexia of unknown origin is a diagnostic dilemma and a detailed history taking and extensive evaluation are required often. We rarely encounter endocrine disturbances as the cause of Pyrexia of Unknown origin.

Thyroiditis may be acute, subacute, or chronic. Acute thyroiditis is secondary to bacteria-mediated suppurative infection and is characterized by painful thyromegaly and fever [3]. Chronic thyroiditis is secondary to autoimmune conditions [3]. Literature review suggests that subacute thyroiditis rarely presents as Pyrexia of Unknown origin without anterior neck pain or symptoms of thyrotoxicosis [4]. Subacute thyroiditis has an incidence of 12.1 cases per 100,000/year with a higher incidence in females than in males [5]. It is a self-limiting disease that may last 2 to 7 months [6]. Subacute thyroiditis is presumed to be caused by a viral infection or a postviral inflammatory process. Many viruses have been implicated in the causation such as coxsackie, mumps, measles, and influenza viruses [7]. Some studies have shown an association with HLA B 35 [8]. Clinically it is characterized by neck pain or discomfort, a tender diffuse goiter, and a predictable course of thyroid function evolution. Solivetti, et al. have described juxta jugular and supra-isthmus lymph node enlargement as a sign of occult subacute thyroiditis [9]. Diagnosis is mostly clinical and is supported by deranged thyroid tests, a high ESR, which can be >50 mm/hour, or elevated CRP, and reduced radioiodine uptake in thyroid scan [10]. Histopathologically, the affected follicles show infiltration with mononuclear cells and disruption of epithelium [11]. NSAIDs and steroids are the mainstays of treatment. Beta-blocking agents can be administered for the relief of thyrotoxic symptoms in the initial stage. Antithyroid drugs have no role in the management of established subacute thyroiditis as the excess thyroid hormone levels result from the release of preformed thyroxine and triiodothyronine from inflamed tissue.

Steroids are tapered gradually once RAIU and serum  $T_4$  return to normal [12].

Saeed Ahmed, et al. conducted a study on 26 patients with thyroiditis who attended the endocrine clinic. The mean age of subjects was 41 years. Approximately 70% were females. Major symptoms reported were: sore throat (69.2%), weight loss (38.5%), upper respiratory tract infection, thyroid pain, tremor, sweating, and fever of unknown origin in 26.9% of cases. All the patients had raised ESR. Low (TSH) < 0.4 mIU/L was seen in 88.5% and 57.7% had raised Free  $T_4$  > 1.8 ng/dL. Complete recovery was seen in 88.5% of patients while 11.5% had early hypothyroidism [13]. In another study conducted at a tertiary care center in eastern India, the mean age of presentation was 51 years in the 12 patients who were diagnosed with sub-acute thyroiditis. Fever was found in 83 % of patients and neck pain and tenderness were found in 91% of patients [14]. After the episode of subacute thyroiditis, hypothyroidism can develop in 34% of patients in 6 to 12 months [15]. Recurrence of SAT



**Figures 1,2:** FDG PET Suggestive of diffused increased FDG uptake in both lobes of the thyroid gland likely infective/inflammatory in etiology.



**Figure 3:**  $^{99m}\text{Tc}$  pertheneate thyroid scan-Severely impaired trapping. In the present clinical and biochemical context scan findings are suggestive of thyroiditis.



has been reported in about 1.6% - 4% of all the cases [16]. Male gender, advanced age, absence of thyroid tenderness, and absence of any thyroid illness-specific signs and symptoms make this case a rare entity.

### Limitations

The limitation of this study was the inability to test against certain viruses like coxsackie that are associated with subacute thyroiditis due to the non-availability of kits.

### Conclusion

In the case of PUO, in the absence of any other cause, thyroiditis has to be considered as one of the important differentials if there are no localizing signs or symptoms. Early thyroid testing and Radionuclide thyroid studies should be considered for early detection.

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