

Sub-Acute Thyroiditis presenting as pyrexia of unknown origin: A rare case with literature review

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Abstract

Pyrexia of unknown origin (PUO) is a challenging entity in medical practice from a diagnostic point of view. Sub-Acute Thyroiditis (SAT), that is an inflammatory condition of thyroid, self-limiting and easily treatable, is a very rare cause for PUO with a few published cases and unfortunately not considered in routine for the differential diagnosis (DD) of PUO. Usually, it presents with mild thyrotoxicosis signs and symptoms, painful goiter, and rarely with cervical Lymph adenopathy. Thyroid antibodies might be negative, but inflammatory markers are usually raised. Anti-inflammatory drugs (NSAID) and steroids are a simple but very effective treatment. We present our experience for diagnosing and treating a female patient presenting with PUO. She was diagnosed as a case of sub-acute Thyroiditis on nuclear thyroid scan, High resolution ultrasound (HR-USG) of Thyroid and radioimmunoassay (RIA) for thyroid hormones and thyroid antibodies. The Patient was successfully treated with NSAIDs and steroids. The consent of the patient was taken to publish her case.

Keywords: Sub Acute Thyroiditis, Nuclear scan, Pyrexia of unknown origin, Thyroid antibodies.

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Introduction

If temperature $>101^{\circ}\text{F}$ ($>38.3^{\circ}\text{C}$) is recorded on several occasions, persists for more than 3 weeks, and remains undiagnosed after 1 week inpatient investigations, it is defined as Pyrexia of unknown origin (PUO).¹ PUO is one of the challenging diagnostic problems in medicine.² Its common causes include infection, autoimmune diseases, and malignancies.³

Sub-Acute Thyroiditis (SAT) is one of the very rare causes of PUO, with only few case reports in literature.² That's why SAT is not considered in Differential Diagnosis (DD) of PUO in routine. SAT is an uncommon disease on its own; with a high female to male ratio.⁴ SAT constitutes 5% of thyroid diseases.⁵ Its most likely cause is a viral infection of the thyroid gland and it is more common in middle aged females. However, it may affect all ages.⁶

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Mostly, patients have a painful goiter with or without classical symptoms of thyrotoxicosis, including palpitation, tremors, and weight loss, but PUO without neck pain is very rare. SAT is diagnosed on history, clinical examination, laboratory picture of thyrotoxicosis, nuclear scan showing decreased tracer uptake,⁴ high resolution ultrasound (HR-USG) showing heterogeneous texture, and increased blood flow on the Doppler study.² Non-steroidal anti-inflammatory drugs (NSAIDs) and steroid is the treatment of choice as shown by some studies.⁷ Some patients may develop hypothyroidism after the resolution of hyperthyroid phase that might be treated with levo thyroxin.⁸ We share our experience of diagnosis and treatment of a such patient.

Case Report

A 50 years old female patient presented at nuclear department of MINAR cancer hospital, Multan in June 2019 with PUO over the course of the last weeks. Fever was intermittent, and was associated with weight loss, generalized muscular weakness, and aches, concentrated more in the upper back. There was no history of cough, urinary or gastrointestinal complaint or history of contact with a tuberculosis patient. She underwent investigations in the medicine department to exclude Malaria, Typhoid fever, and tuberculosis. All were negative.

Her Complete Blood Examination (CBC), Complete Urine Examination (CUE), chest x-ray, abdominal USG, and CT scan of the brain were normal. She was being treated with multiregime antibiotics on hit and trial basis. Later on, she developed pain on the right side of her neck. On examination, no mass or cervical lymph node was palpable. Ear Nose & Throat (ENT) examination and indirect laryngoscope (IDL) could not reveal any pathology. She was losing hope.

Unluckily, her treating physician never thought of SAT, but luckily, she randomly came to know about thyroid scan by one of her family friends who had been a thyroid patient. She was presented to the Thyroid clinic of MINAR cancer hospital. No baseline thyroid function tests were available.

The Thyroid showed no radiotracer uptake on the nuclear thyroid scan done with Technetium 99 per technitate which is one of classical findings of SAT (Figure-1). On high

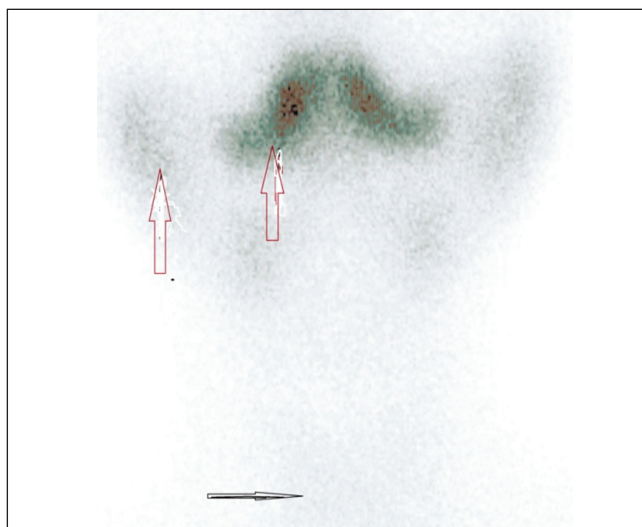


Figure-1: Thyroid scans showing reduced tracer uptake in thyroid with normal uptake in salivary glands and nasal mucosa.

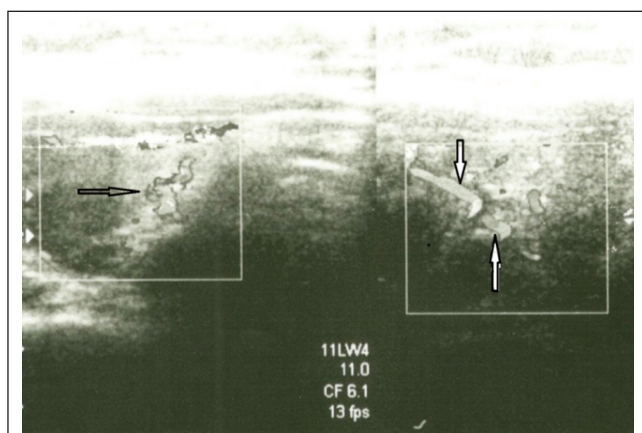


Figure-2: Doppler scan of thyroid gland showing increased vascularity.

resolution ultrasound HR-USG, the thyroid was of heterogeneous texture with increased vascularity on Doppler study (Figure-2 colored image was not possible due to lack of facility). Her Thyroid functions were deranged with TSH=0.01 uIU/ml (N=0.27-4.0), T3=3.3 nmol/L (N=1.30-3.10) and T4 was 209 nmol/L (N=66-180). Thyroglobulin (TG) and Antiperoxidase antibodies (ATPO Abs) levels were raised, measuring 241 ng/ml and 46.4 IU/ml respectively. Normal Tg levels are 1.40 – 29.2 ng/mL (μ g/L) for men, 1.50–38.5 ng/mL for women⁹ while normal ATPO level is below 16 IU/mL.¹⁰ All these investigations led to the diagnosis of SAT.

The patient was treated with anti-inflammatory drugs and steroids. She was given NSAID ibuprofen and prednisone in doses of 400mg and 40 mg a day respectively for one week. The patient was afebrile and euthyroid on follow up after one month with TSH, T4, TG and ATPO Abs within

normal limits measuring 4.0 uIU/ml, 94 nmol/L, 12.2 IU/ml and 23.6 IU/ml respectively. She remained on follow up for one year without any symptoms and normal thyroid parameters.

Discussion

Petersdorf and Beeson described PUO as the most challenging diagnostic problem for medical practitioners. PUO has been defined as a fever that persists for more than 3 weeks with a temperature more than 101°F recorded several times and remains undiagnosed in spite of investigations for one week.² Common causes making the bulk of PUO include malignancies, infections, and autoimmune diseases. Many patients remain undiagnosed even after extensive investigations, resulting in morbidity and psychological trauma to the patient and their family.³ Endocrine disorders are a rare cause of PUO.¹ Our case was one of these rare endocrine causes of PUO.

Thyroiditis is defined as the inflammation of the thyroid gland that may lead to increased or decreased production of thyroid hormones. Different types of Thyroiditis are Hashimoto's Thyroiditis, an autoimmune disease, Silent or painless Thyroiditis, another autoimmune disease, Post-partum Thyroiditis, associated with history of delivery, Radiation induced Thyroiditis, caused by external radiation or by radioactive Iodine given to treat hyperthyroidism and Sub Acute Thyroiditis (SAT) or de Quervain's Thyroiditis a painful condition that is probably of viral etiology.

SAT is a relatively uncommon thyroid problem, making up 5% of the total thyroid disorders, and has an incidence of 0.005 cases per 100 per year.^{5,6} It usually follows an upper respiratory tract viral infection and often regresses spontaneously by itself.¹¹ Corona virus, the causative agent of COVID-19, the most concerning current health issue that might lead to SAT, as few cases have been reported in literature.¹²

SAT usually affects middle aged women, but may rarely affect any sex at any age.^{4,6} The patient usually presents with severe pain and tenderness in the anterior part of the neck with a small, diffuse goiter that may be associated with mild thyrotoxicosis symptoms including fatigue, palpitation, and weight loss.¹³ Presentation of SAT with fever in absence of classical symptoms is very rare with only few cases reported yet in literature, causing diagnostic challenges, and may allow the patient to remain undiagnosed for many weeks.² Our patient presented with fever, fatigue, and weight loss, but with no complaint of pain, tenderness, or palpable thyroid in the neck.

Diagnosis is based on history clinical examination which is confirmed on increased levels of thyroid hormones.⁴

Table: Differential diagnosis of SAT with Grave's disease.

Element	Graves Disease	SAT
Neck Pain	Yes	No
Recent H/O upper respiratory tract infection	Yes	No
Symptoms of fever	Yes	No
Tenderness	yes	No
Thyroid symptoms i.e palpitation, tremors, weight loss etc.	Yes	Yes
*ESR	Elevated	Normal
**CRP	Elevated	Normal
***TSH	Initially ↓ Later on ↑	↓
Thymoglobulin	Elevated	Elevated
Nuclear Scan	Low tracer uptake/ Not visible	Diffusely increased tracer uptake
****USG Echo-genicity	Heterogeneous	Might be diffusely Hypo-echoic
Vascularity on Doppler study	Increased	Normal

*Erythrocyte sedimentation Rate, **C- Reactive Protein, *** Thyroid stimulating hormone, **** ultrasonography.

Differential diagnosis of SAT with Grave's disease is shown in Table. TG or ATPO Abs may or may not be raised, as per literature review, it might be raised in 5-20 % only.¹³ Nuclear scan shows reduced tracer uptake, while on HR USG the neck shows a heterogeneous texture of the thyroid with increased blood flow on the Doppler study.^{4,14}

The clinical presentation of our patient was not classical as mentioned in literature, but later on she developed pain on swallowing. Ear, Nose and Throat (ENT) and Indirect laryngoscope (IDL) examination were normal. Investigations revealed the classical picture of SAT. There was reduced tracer uptake on the nuclear scan which raised the suspicion for SAT, so further evaluation was done revealing raised thyroid hormones, TG and ATPO Abs levels with heterogeneous texture and increased blood flow on HR USG.

There is no guideline available for the treatment of SAT.¹ Literature review shows that some patients may require no treatment while others can be treated with NSAIDs, anti-inflammatory drugs, and steroids.⁷ There is no recommendation for the dose of steroids, but many studies show a low dose usage of steroids.^{6,15} Our patient was treated with NSAIDs and Prednisone in doses of 400 and 40 mg per day respectively with satisfactory results. The patient became afebrile and euthyroid with normal TG and ATPO Abs levels within one month.

Different studies show the occurrence of subclinical or overt hypothyroidism during follow-ups within three months.^{8,13} Our patient remained on follow up for one year without developing hypothyroidism.

Conclusion

SAT is a rare cause of PUO and may cause challenges in diagnosis for physicians. The presented case was diagnosed late as SAT was not considered as a probable cause in the early period of the illness. This could be due to the absence of any localized thyroid symptoms. If diagnosed in time, the treatment for SAT is simple with excellent results. SAT should thus be considered in the DD of PUO even in the absence of a tender goiter or symptoms of hyperthyroidism. A timely diagnosis will prevent morbidity, unnecessary investigations and an early recovery.

Ethical approval: Approval was obtained from the ethical committee of the institute for publishing the case.

Disclaimer: None.

Competing interests: None.

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