

Thyroid

THYROID DISORDERS CASE REPORT

Sub-Acute Thyroiditis Presenting as Pyrexia of Unknown Origin

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Introduction: Pyrexia of unknown origin (PUO) is often a diagnostic challenge. Common causes currently reported include non-infectious inflammatory disorders (NIID) (30.6%), infections (23.1%), malignancy (10.7%) and miscellaneous (12.4%). However, 23.1% remain undiagnosed despite extensive investigations. Fever is a component of subacute thyroiditis (SAT) in 28-83% of subjects reported in the literature. But its presentation as a PUO is reported only in a handful of subjects.

Case Presentation: A 71-year-old Asian male presented with evening fevers of 2-3 weeks duration. He had no accompanying sweats, cough, breathlessness, or weight loss. He had a past history of TB, polio, hydatid cyst and hypertension for which he was on treatment. He was a teetotaler. Several family members living in his native land had active TB and he visited them often. Clinical examination at initial presentation was unremarkable. He interrupted investigations to go back to Asia, and became unwell for over 6 weeks with evening fevers and sweating, a weight loss of over 7 kg, and a poor appetite. At this point he had no neck pain, palpitations or bowel abnormalities. Clinical examination continued to be normal upon his return to the UK and in the Endocrine Clinic. **Investigations:** Investigations were done to exclude (a) *infections* - There was no growth of pathogenic organisms in repeated blood, urine and sputum cultures. Screening tests for TB, hepatitis, and glandular fever were negative. Blood screens for malarial parasites, amoebic and Brucella serology, and stools examination and culture were also negative. Echocardiography was normal. (b) *Malignancy* - Urine Bence Jones proteins and serum protein electrophoresis were normal. Bone marrow examination was suggestive of Leishmaniasis but a PCR test excluded this diagnosis. Humoral markers of malignancy were negative. CT scans of the thorax, abdomen and pelvis were normal and did not show any evidence of visceral abnormalities (c) *NIID* - CRP 120, ESR 130, with blood tests consistent with iron deficiency. Autoimmune screening for dsDNA, ANA, ANCA were negative. Upon return to the UK a PET/CT scan showed the diffuse tracer uptake in both thyroid lobes and changes consistent with a large left lobe. Free thyroxine was 28pmol/l (reference range 9-19.1), and TSH was undetectable (<0.004 mU/l). Thyrotrophin receptor antibodies were negative. **Management and conclusion** He was given carbimazole initially but this was stopped as he became severely hypothyroid. This hypothyroidism persisted for several months even after stopping carbimazole but reversed spontaneously. He therefore had a biphasic pattern of thyroiditis typical of SAT. There are only 9 previous cases

reported of SAT presenting as PUO. Although SAT is a rare cause of PUO, early thyroid testing and if necessary, functional thyroid imaging should be considered in subjects with PUO to confirm it.

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Subacute Thyroiditis After mRNA Vaccine for Covid-19

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Introduction: Subacute thyroiditis is a well-documented clinical condition which typically presents 1-2 weeks after an acute viral illness. Presenting symptoms are classically those of thyrotoxicosis but with associated tenderness in the thyroid. Treatment of acute symptoms is possible and the thyroid function will generally normalize with time. Subacute thyroiditis has rarely been reported after administration of viral vaccinations such as the seasonal flu vaccine. We present a case of subacute thyroiditis which presented after administration of the mRNA COVID-19 vaccine.

Case: Patient is a 42yo female with no past medical history. She received the first dose of the Pfizer/BioNTech mRNA vaccine for COVID-19 on 12/22/20. Five days later, the patient complained of sore throat and palpitations. These symptoms progressed and she was evaluated in an urgent care on 12/31/20 where she was found to have tachycardia. Infectious work-up, including PCR for COVID-19, was negative and she was sent home. She took ibuprofen with some improvement of her symptoms. The following day she went to the ED; she was found to have a heart rate in the 130s with sinus tachycardia on EKG. Thyroid function testing was done which revealed TSH <0.01, fT4 4.58, fT3 11.8. Her TPO antibody was <28 and inflammatory markers were elevated including sed rate of 62. The patient was prescribed prednisone 40mg daily and propranolol 20mg as needed for symptoms. She reports rapid improvement of symptoms with prednisone. On 1/21/20, thyroid function showed TSH <0.01, fT4 down to 3.2, tT3 normal at 135. Thyroglobulin was elevated at 140.8 with negative thyroglobulin antibody, TRAb and TSI. Her inflammatory markers had decreased with sed rate of 26 and normal C-reactive protein. She had improved symptoms.

Discussion: Cases of subacute thyroiditis are most commonly associated with upper respiratory viruses but cases have been reported with traditional inactivated viral vaccines or live-attenuated vaccines such as those for annual influenza. We present the case of a 42-year-old female who has presented with a classic case of subacute thyroiditis which occurred in the time frame after receiving the Pfizer mRNA vaccine for COVID-19. Research has been ongoing for decades regarding development of mRNA vaccines but the mRNA vaccines for the SARS-CoV-2 virus have been the first to be widely distributed to the general population. Thyroiditis has not been reported as a common side effect but the cross recognition between the coronavirus spike protein targeted with the mRNA vaccine and healthy thyroid cell antigens exists as evidenced by this case.

Sources: 1. Prummel M, Strieder T, Wiersinga WM. The environment and autoimmune thyroid diseases. *Eur J Endocrinol.* 2004;150:605-618. Altay FA, Guz G, Altay M. 2. Subacute thyroiditis following seasonal influenza vaccination. *Hum Vaccin Immunother.* 2016;12(4):1033-1034.

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Subacute Thyroiditis After SARS-CoV-2 Infection Presenting With Pyrexia of Unknown Origin

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Subacute thyroiditis (SAT) is associated with viral (destructive) or post-viral (inflammatory) origin. [1] The most common clinical characteristics of SAT are female sex preponderance, anterior neck pain and fever. [2,3] Heart rhythm disorders and silent cervical forms have been described in SAT associated with SARS-CoV-2 infection, which occurs 16 to 36 days after resolution of COVID-19. [1,3] Symptomatic improvement occurs in a few days after initiation of therapy with steroids or NSAID. [3] Pyrexia of Unknown Origin (PUO) is a very rare presentation of SAT. [2] Hereby, a case of SAT, presenting with painful neck swelling and persistent fever (5 weeks duration), two weeks after resolution of COVID-19, is being discussed. The index patient was a 50-year old obese, normotensive, diabetic (10 years duration, HbA1c-6.6% on SU, metformin, sitagliptin and dapagliflozin) male. TSH was suppressed (0.02 mIU/L), FT4 (3.06 ng/dl, upper limit of normal-1.48 ng/dl) and FT3 (3.9 pg/ml, upper limit of normal-3.71 pg/ml) were elevated. Total T4 and T3 were normal. HS-CRP was markedly elevated. IL-6 and TBG were not estimated. Cervical USG revealed diffuse hypoechoic nature of thyroid gland and thyromegaly. There was reduced uptake in thyroid scan (technetium). The patient became afebrile after 4 days of initiation of 30 mg prednisolone (tapered by 10 mg every 5 days). The initial tachycardia reverted to sinus rhythm with marked reduction of neck tenderness. This case highlights certain considerations for SAT associated with SARS-CoV-2 infection. Firstly, it can present with PUO (first case report). Secondly, it may be associated with normal total T4 and T3 which can happen due to reduced TBG consequent upon increased IL-6. [4] **References:** 1. Caron Philippe: Thyroid disorders and SARS-CoV-2 infection: From pathophysiological mechanism to patient management. *Ann Endocrinol (Paris)*, 2020, Sept. 2. Fever of Unknown Origin as a Sole Presentation of Subacute Thyroiditis in an Elderly Patient. A Case Report with Literature Review. Raj R, Yada S, Jacob A et al: *Hindawi Case Reports in Endocrinology*, 2018, Article ID 5041724 3. Brancatella A, Ricci D, Latrofa F et al: Is subacute thyroiditis an underestimated manifestation of SARS-CoV-2 infection? Insights from a case series. *J Clin Endocrinol Metab*, 2020, Aug 11, dgaa537. 4. Bartaleno L, Brogioni S, Grasso L and Martino E: Increased serum interleukin-6 concentration in patients with subacute thyroiditis: relationship with concomitant changes in serum T4-binding globulin concentration. *Journal of Endocrinological Investigation*, 1993, 16, 213-218.

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Subacute Thyroiditis Associated With Liraglutide

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Objective: Incretins are expressed in thyroid tissue but without clearly-known clinical significance in human. The long-term effect of GLP-1 receptor activation on the thyroid is unknown. In the literature, liraglutide-related thyroiditis has not been reported yet and here we wanted to draw attention to this association. **Case Summary:** A 52-year-old woman with type 2 diabetes mellitus presented with thyroid tenderness, tremor and fever. Her lab results were as follows: undetectable TSH, free T4 (FT4) = 2.4 ng/dl (0.93-1.7), free T3 (FT3) = 4.4 pg/mL (2-4.4). Erythrocyte sedimentation rate (ESR) was 60 mm/hour, C-reactive protein (CRP) was 80 mg/L. Thyroid autoantibodies were negative. USG revealed that thyroid gland was in normal localization and the right lobe was 24x22x46 mm and the left lobe was 20x21x45 mm, isthmus thickness was 5 mm. The parenchyma was heterogeneous, coarsely granular, with bilateral patchy hypoechoic areas. All these findings suggested that the patient had subacute thyroiditis. When we examine the etiological factors of subacute thyroiditis in the patient, there was no history of trauma, no previous viral or bacterial illness, contrast agent exposure. But, she had only been using liraglutide for a week. Firstly liraglutide therapy was ceased and then 20 mg prednisolone and 40 mg beta-blocker therapy was initiated. At the 8 weeks' of cessation, patient had no symptoms. Also thyroid function tests and other laboratory values were all in normal limits. **Conclusions:** It has been proven by previous studies that liraglutide has several effects on the thyroid gland. Liraglutide therapy might be related to subacute thyroiditis, as well.

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Subacute Thyroiditis With Very Elevated Thyroglobulin Level in a Patient on Chronic Adalimumab Therapy

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Background: Viral infections are a well-recognized cause of subacute thyroiditis (SAT), but other etiologies are occasionally seen. Here we present a case of SAT in a patient receiving chronic tumor necrosis factor inhibitor (TNF- α) therapy. Serum thyroglobulin (Tg) levels in healthy individuals have been reported and range 1.40-29.2 ng/mL