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An Elderly Woman with Pyrexia of Unknown Origin

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ABSTRACT

Pyrexia of unknown origin represents a diagnostic challenge in the daily practice. Clinical features are often subtle or inadequate to recognize the etiology of prolonged fever. Endocrine etiology of pyrexia of unknown origin is not common. Here we present a case of an elderly female seeking medical advice from her general practitioner due to a four-week history of moderate fever, malaise and loss of appetite.

Initial outpatient diagnostic workup was negative. During repeated examination a slight enlargement of thyroid gland was noticed. Thyroid function tests revealed a very low level of thyroid stimulated hormone along with elevated free T4 suggesting subacute thyroiditis. Low dose administration of corticosteroids led to clinical improvement and fever remission.

Physicians involved must be aware about this unusual presentation of thyroiditis and include the condition in the differential diagnosis of prolonged unexplained fever. In the absence of clinical signs and symptoms, an abnormal thyroid function test may prevent from unnecessary investigations and inefficient hospital admission.

Keywords: pyrexia of unknown origin, subacute thyroiditis, fever, diagnosis, hyperthyroidism.

INTRODUCTION

Subacute thyroiditis is an inflammatory process of the thyroid characterized by a progressive appearance of neck tenderness, enlargement of the thyroid gland and elevated erythrocyte sedimentation rate (1, 2). Its onset is usually linked with a preceded viral infection (1, 2). General systemic symptoms such as fever, malaise and weight loss may occur in the acute phase (1, 2). In this paper, we present the case of a patient seeking medical advice from his general practitioner due to a history of prolonged fever. ❑

CASE REPORT

A 78-year-old Caucasian female was admitted to a primary health care setting due to moderate-grade persistent fever for the last four

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weeks. She has also complained of malaise and anorexia. Her past medical history was unremarkable, except for hypertension and dyslipidaemia. She has also reported an upper respiratory tract infection six weeks before, which has remitted spontaneously with symptomatic care (analgesics).

Her vital signs on admission were: temperature 38.5°C; blood pressure 140/95 mm Hg; pulse 105 beats *per* minute; oxygen saturation 97% on ambient air. Physical and systemic (ophthalmological and neurological) examination was normal. Palpation of the temporal artery was negative for pain, thickening and reduced pulsation.

Initial laboratory investigations revealed an erythrocyte sedimentation rate (ESR) 89 mm after one hour (normal ≤ 20 mm/hr); C reactive protein (CRP) 48 mg/dL (normal range 0.3 to 1.0 mg/dL); Routine hemogram, white blood counts 11x 10^9/L (range 4.00-11.0 x 10^9/L), hemoglobin 11.8 g/dL (12-16 g/dL). Blood cultures (X2) urine analysis, renal and liver function tests, electrolytes were within normal limits.

A tuberculin skin test (evaluated at 48 and 72 hours) was also negative. Further laboratory tests included rheumatoid factor, antinuclear antibodies, antibodies for cytomegalovirus, herpes simplex and Epstein-Barr virus and the results were also negative. Electrocardiogram showed sinus tachycardia, while chest x-ray did not disclose any pathological finding. Imaging investigations included thoracic and abdominal computed tomography (CT) which was normal. The patient denied referral to a secondary care centre due to the lack of social support. Routine primary care consultations were suggested on a daily basis.

On repeated clinical examination after three days, a non-tender slight enlargement of the thyroid gland was noticed. Thyroid function tests were: thyroid-stimulating hormone (TSH) 0.05 μU/mL (normal 0.5–5.0); free serum tri-iodothyronine (FT3) 11 pmol/mL (2.5–6.5 pmol/mL), free serum tetra-iodothyronine (FT4) 41 pmol/L (normal 11.6–21.9).

Thyroid scintigraphy with the radio-isotope Iodine-123 was consequently arranged in order to evaluate the etiology of the overactive thyroid gland. A significant low uptake of radioactive tracer recorded at 24 hours suggested the diagnosis of subacute thyroiditis.

Initial therapy consisted of a low dose of oral steroid (prednisone 10 mg daily) for 10 days. A significant clinical improvement was recorded with fever remission within three days. During follow up the patient' course was uneventful and was found in good clinical health. Repeated thyroid function tests after four weeks showed gradual improvement in TSH levels, while ESR and CRP levels became normal. A thyroid ultrasound performed four weeks later disclosed a patchy heterogeneous pattern suggestive for post-inflammatory status. ❑

DISCUSSION

Pyrexia of unknown origin (PUO) refers to fever that is not resolved spontaneously, while its etiology cannot be determined despite extensive diagnostic work up (3). The term of PUO was first introduced by Petersdorf and Beeson in 1961 (4). It was defined as temperature higher than 38.3 °C (> 101 °F) on several occasions, duration of illness of more than three weeks, and failure to establish a certain diagnosis after one week of investigations in the hospital setting (3, 4). Pyrexia of unknown origin is considered a significant diagnostic challenge. In regards to the etiology, infectious diseases account for the majority of cases followed by neoplastic and autoimmune conditions. Well recognized diseases with unusual clinical presentation trigger PUO more often (3).

Initial diagnostic assessment requires a careful history. Information about occupation, recent travels, animal exposure, familial diseases and previous illnesses is necessary (3). Failure to properly evaluate available test results and delays in ordering the appropriate investigations are the main reasons of misdiagnosis (3). Pyrexia of unknown origin requires a demanding work-up in order to narrow the list of potential pathological conditions. A specific algorithm does not exist and is not useful (3). Repeated interview and reexamination of the patient's file may help recognise useful diagnostic clues (3).

Subacute thyroiditis is an unusual, but well documented cause of PUO (3, 5). It is characterized by an inflammatory process of the thyroid gland (1, 2). Viral etiology has been suggested (6). Mumps, adenoviruses and coxsackie virus are reported among the potential agents that trigger thyroid inflammation (6).

A potential role of the cytokine interleukin-6 in thyroid destruction has been reported (7). Severe neck pain in a diffusely enlarged thyroid gland is the main symptom at onset (5, 8). Pain may be located to the lower jaw, ear or occiput (7, 9). However, classical features may be absent at onset and the patients may seek medical care for generalized symptoms such as prolonged fever, anorexia and weight loss (5, 7, 9). Diagnosis is performed on the basis of clinical and laboratory findings of hyperthyroidism, a high ESR (>50 mm/hour), elevated CRP and reduced radioiodine uptake in thyroid scan (5, 7). ESR and CRP may help to monitor therapeutic response (5). Leucocytosis, low hemoglobin levels may also be present along with elevation of hepatic enzymes in the initial hyper-thyroid state (5).

Therapy if required consists of pain and inflammation relief (5, 7, 9). Non-steroidal-anti-inflammatory drugs at the beginning and steroids in case of no improvement are suggested (5, 7). Symptoms of hyperthyroidism if present are controlled with beta blocker administration (5).

Thyroid disorders are rarely implicated in the etiology of PUO. In our patient, typical clinical manifestations of subacute thyroiditis were absent at onset. Initial clinical assessment and negative previous medical history were not suggestive for thyroid disorder. ❑

CONCLUSION

Physicians involved in the management of patients with PUO should include subacute thyroiditis in their differential diagnosis. When classical features of neck pain, tenderness on palpation and diffuse goiter are absent, they have to carefully re-assess patient's history and revisit available clinical clues. Thyroid function tests in the context of PUO may prevent unnecessary, ineffective investigations and hospital admissions. ❑

Conflicts of interest: none declared.

Informed consent: Written informed consent was obtained for the publication of this case report.

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