SUBACUTE THYROIDITIS AND HIV INFECTION: CASE REPORT AND LITERATURE REVIEW.

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SUMMARY:
This case report is on Subacute thyroiditis (SAT) with thyrotoxicosis in a 22year-old housewife . She had been married for 2years to a long-distance driver. She presented with a fever and neurological features which were followed by features of SAT such as pain and difficulty in swallowing, swelling of the anterior aspect of the neck, palpitations, shaking of the body, tenderness over the neck, coarse tremors of the hands and worsening of fever. She appeared depressed and was restless. The fever with the neurological features (lower motor neurone lesion of the facial nerve) suggested a form of viraemia, which could have been from any virus. HIV infection was confirmed in this patient but there was no weight loss, no diarrhoea nor lymphadenopathy. This suggests a probable viraemia of seroconversion of HIV infection. There were also no features of other infections or other diseases. This case report may suggest an aetiological association between HIV and subacute thyroiditis. However, HIV has not been reported before as an aetiology of subacute thyroiditis.

INTRODUCTION

Thyroiditis is classified into acute and chronic types, with acute type being subdivided into acute suppurative and acute non-suppurative varieties. Acute suppurative thyroiditis occurs in an already existing goitre: there is a bacterial infection of the goitre with suppuration, hence it is a surgical condition. Acute non-suppurative thyroiditis is also known as subacute thyroiditis (SAT), granulomatous thyroiditis, de Quervain's thyroiditis, giant cell thyroiditis painful thyroiditis, or painless /postpartum thyroiditis when it occurs within six months of childbirth[1] SAT is an acute inflammatory disease of the thyroid gland whose aetiology is unknown but thought to be due to a viral inflammation although, the cause is rarely established[2]. It has been found to be associated with mumps virus infection as the mumps virus has been cultured from the thyroid gland in some cases of SAT. SAT has also been reported in other viral conditions including measles, influenza, adenovirus infection, infectious mononucleosis, coxsackie virus infection and the common cold virus infection, but it has been difficult to culture these other viruses from patients with SAT[1,2]

The human immunodeficiency virus (HIV) affects almost every tissue in the body. This is due to its effect on the cells of the immune system and on cells that bear the CD^{4+} molecules found on many cells and tissues. Infection with HIV therefore affects many cells including CD^{4+} T-lymphocytes (which are the cells mostly affected), monocytes, macrophages and other antigen-presenting cells like dendritic cells in the blood, langerhan's cells of the skin and follicular dendritic cells of the lymph nodes where much of the early infection and replication of HIV takes place[3,4,5.] HIV infection, therefore, is a multi systemic disorder, and during the seroconversion stage, there could be many manifestations including a flu-like syndrome as well as non-specific symptoms like neurological and endocrine features. Many cases of facial nerve palsies have been reported during this stage[5]. have been reported in literature. Although many viruses

have been implicated in the causation of subacute thyroiditis, the human immunodeficiency virus has not been reported to be implicated. However Cases of acute suppurative thyroiditis in HIV infection[6] as at this phase many tissues are generally affected.

Other conditions associated with SAT include; cat scratch fever, myocarditis, Q fever, sarcoidosis, malaria, emotional crisis or dental works. It has also been associated with manipulations of the immune system by therapy with cytokines such as interleukin-2, tumour necrosis factor alpha and interferon alpha. Radioiodine therapy, Amiodarone therapy, bone marrow transplantation and febrile neutrophilic dermatoses have also been reported to be associated with SAT[2].

SAT is generally associated with the presence of the human leukocyte antigens (HLA) Bw35 and B67. The people with HLA Bw35 seem to have a six times higher incidence of SAT. HLA B67 is more frequent in Japanese patients although Japanese with HLA Bw35 may also be seen. HLA B67 is associated with seasonal occurrences of SAT and a higher tendency to the development of the hypothyroid phase [2].

SAT has a reported incidence of 1 in 10,000 population in the USA. It is said to account for between 20% and 25% of all cases of thyrotoxicosis, from liberation of stored thyroid hormones during the inflammatory destruction of the gland, and, accounts for 10% of patients with hypothyroidism from extensive thyroid fibrosis. Generally, it occurs predominantly, in temperate climates and more often in summer, but with viral infections, there can be clusters of cases of SAT. It affects all races equally, and females are more affected, with a female to male ratio of 3-5:1. It has been reported among all ages but commoner between the third and fifth decades of life[3].

SAT often starts some weeks after a viral illness and has four stages-the inflammatory, the destructive, the hypothyroid and the recovery stages. The inflammatory stage is associated with an acutely painful, tender, firm, symmetrical goitre which may be associated with dysphagia and constitutional symptoms such as fever, malaise and sweating. The destructive phase is associated with features of thyrotoxicosis, which are usually transient. The destroyed cells may be replaced by fibrous tissue leading to the hypothyroid phase which also is usually transient. However, the hypothyroidism may progress if the gland is markedly destroyed with most of its tissues replaced by fibrous tissue, but usually, there is full recovery with gradual normalization of thyroid hormone levels in the circulation.

SAT can recur in about 20% of cases, and about 50% of cases have concurrent thyrotoxicosis which is transient, and, with fewer symptoms. Dermatopathy and orbitopathy (features of Grave's disease) are not seen, although thyrotoxic features could be severe at times[3] In SAT, T_3 and T_4 are usually mildly elevated with a T_3 to T_4 ratio less than between 15 and 20. TSH is undetectable in 22% of cases using 3rd generation assay methods. Serum thyroglobulin levels are high. There is anaemia, hyperglobulinaemia and leukocytosis. Erythrocyte sedimentation rate is elevated and diagnostic. Radioactive iodine uptake is reduced and ultrasound scan will show hypoechoic areas which are either diffuse or focal[1,2].

This case report is to make clinicians to be aware of the fact that a case of subacute thyroiditis may actually be associated with HIV infection. This also serves to make clinicians to develop a higher index of suspicion of a causal relationship between HIV and subacute thyroiditis so as to investigate readily for early diagnosis and management.

CASE REPORT

This is the case of a 22year old housewife, who reported to the emergency medical unit of the Jos University Teaching hospital with a one-week history of low-grade fever and malaise. At presentation, she had noticed a deviation of her mouth to the right side with inability to close the left eye in the morning of the incident. There was no history of blood transfusion, no history of multiple sexual partners, but her husband, who was a long distance driver, spent several months away from the house during the course of his work. She had lower abdominal pain with associated vaginal discharge six months before presentation. There was no history of weight loss or diarrhoea prior to presentation.

On examination, she was acutely ill-looking, and febrile (axillary temp. =37.9^{oc}). She was pale, anicteric and had no lymphadenopathy. Her body mass index was 18.1kg/m^2. She had no goitre but had a lower motor neurone lesion of the left facial nerve. Examination of the ear, nose and throat revealed no abnormalities. Her pulse rate was 76/min, small volume and regular. Her blood

pressure was 100/60 mmHg supine. The rest of the physical examination revealed no abnormality. Laboratory investigations carried out were as in table 1.

On the eighth day of admission, while awaiting other results, she developed difficulty and pain on swallowing. She became depressed and restless, tremulous and had profuse sweating including sweating of the palms. She was always under the fan. The axillary temperature had risen to 39.7^{oc}. The pulse rate was 96/min, small volume but were essentially as at admission. Examination, at this time, revealed a very tender grade 2 goitre (a visible goitre). There was no oral thrush but she had hyperaemia of the posterior pharyngeal wall. HIV screening was positive by double ELISA (Enzyme-linked immunosorbent assay) technique and she was confirmed to have HIV I by Western blot by the presence of antibodies to the core protein P24 and envelope protein gp 120 in her serum. The thyroid hormones were assayed and results were as summarized in table 2.

A chest X-ray done was normal. Liver funtion test was unremarkable except for an elevation of the alkaline phosphatase level. Hepatitis B surface antigen was non-reactive.

A diagnosis of Subacute thyroiditis with thyrotoxicosis in HIV infection was made. The patient was placed on 10% dextrose infusion for 48 hours because of the profuse sweating with the difficulty and pain on swallowing making her not to eat. Aspirin was administered for the pain in the anterior aspect of the neck. She was also placed on propranolol for the features of thyrotoxicosis. The pain and difficulty on swallowing subsided immediately, by the next day, while the fever and body weakness gradually subsided. Relatives took her home prematurely against medical advice, for traditional medication.

DISCUSSION

The diagnosis of subacute thyroiditis was made based on a one week history of fever and malaise prior to presentation, followed by pain and difficulty on swallowing eight days of admission, severe tenderness over the anterior aspect of the neck which was swollen. This was supported by the elevated erythrocyte sedimentation rate which is said to be a diagnostic feature of subacute thyroiditis [5.] The tenderness in the neck suggests that there is an acute inflammation, affecting the surrounding skin, resulting in increase of temperature. A diagnosis of subacute thyroiditis with thyrotoxicosis was also entertained because of the features she developed while on admission. These include palpitations, profuse sweating, shaking of the whole body, i.e. coarse tremors, sweating of the palms, restlessness and she became intolerant of heat. This suggests that the thyroiditis was in the destructive phase with release of stored thyroid hormones from the destroyed thyroid follicles. This was supported by the mild elevation in serum thyroxine. The serum T_4 was higher than normal and although T_3 (the active thyroid hormone) was within normal limits, the pre event level might have been lower than the estimated level during the illness. This is probably why she had symptoms suggestive of thyrotoxicosis with a normal T_3 level. In AIDS patients, the hormone levels are usually lower because of the effect of non thyroidal illness on thyroid function - the so called euthyroid sick syndrome. It was not a suppurative inflammation of the thyroid gland as the full blood count did not support a bacterial infection. The full blood count was within normal range.

Subacute thyroiditis is said to be caused by viruses. Mumps virus has been cultured from cases of subacute thyroiditis, but other viruses have only been associated and not cultured from the gland during a course of subacute thyroiditis. However, subacute thyroiditis has not been reported with HIV infection although the thyroid gland of immunosuppressed persons has been known to be involved in cytomegalovirus (CMV) infections and some fungal infections, particularly cryptococcal infection (which are opportunistic infections). These occur when the immune system has depreciated particularly during progression of the HIV infection to the acquired immunodeficiency syndrome stage [5,6]. Early phase of HIV infection in this patient is supported by a week history of fever, followed by the appearance of a lower motor neurone lesion of the seventh cranial nerve at presentation. The flu like illness in this patient also supports the diagnosis of a viraemia, probably at HIV seroconversion. It has been reported that seroconversion may take place with or without a metabolic derangement while some patients may have fever and a flu like illness and others may have fever with neurological features [4,5] as in this patient. The fact that there was no history of weight loss or diarrhoea also supports the fact that this was an early stage of HIV infection. The fact that there were no lymphadenopathy may support the suggestion that the infection was probably in the early stage.

The laboratory findings of a low PCV may suggest the suppressing effect of fever on haematopoiesis. The WBC differential count was consistent with the normal findings in the African [10] i.e higher percentage of lymphocytes than neutrophils. The ESR was markedly elevated which is consistent with the findings in viral thyroiditis [5]. The elevation in alkaline phosphatase is also consistent with what has been reported about viral thyroiditis [9].

In conclusion, patients with HIV infection could have associated subacute thyroiditis as HIV affects all cells with CD^{4+} molecules and these cells are numerous in the body.

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Table 1: Laboratory results during admission

Tests	Results
PCV	31%
Total WBC	$6500/mm^3$
Differential WBC	
Neutrophils	43%
Lymphocytes	55%
Monocytes	1%
Eosinophils	1%
Erythrocyte Sedimentation rate (ESR)	130mm/hr
Malaria Parasites	None seen
Stool Microscopy	No ova or cysts were seen
Urine Microspy, culture and sensitivity	No abnormality seen

Table 2: Thyroid hormone concentration

Results	Reference range	Tests
Thyroxine(T_4)	16.0 ng/100ml	4 - 12 ng/100ml
Tri-iodothyronine(T_3)	1.9 ng/ml	0.5 - 2.1ng/ml
Thyrotropin (TSH)	0.9m.i.u/ml	0. 5 - 5m.i.u/ml