THYROID DYSFUNCTION IN AN AIDS PATIENT

M. Gafencu^{1,2}, T.O. Bizerea^{1,2,*}, R.F. Stroescu^{1,2}, R. Costa², O. Marginean^{1,2}, G. Doros^{1,2}¹“Victor Babeș” University of Medicine and Pharmacy, Dept. of Pediatrics, ²“Louis Turcanu” Children’s Clinical and Emergency Hospital, Dept. of Pediatrics, Timișoara, Romania**Abstract**

Objective. Highly active antiretroviral therapy (HAART) is involved in the potential pathogenic mechanisms linking thyroid autoimmunity with immune restoration.

The objective is to emphasize the emergence of autoimmune thyroid disease in a HIV patient long period after restoration of immune competence, unlinked to the immune reconstitution inflammatory syndrome (IRIS) occurring shortly after HAART initiation.

We report a case of acute autoimmune thyroiditis with thyrotoxicosis in a patient with stage C3 HIV infection, who had been under HAART for more than 7 years.

From the beginning there was a good immune response to the regimen, due to a good adherence and compliance (over 90%). Nine months after HAART initiation the viral load was undetectable (under 34 copies/ μ L) and the CD4 count reached 645 cells/ mm^3 (within normal range) after one year of treatment. Eight years after HAART initiation, based on clinical and laboratory findings, autoimmune thyroiditis was diagnosed. At this time immune competence with a normal CD4 count and a CD4/CD8 ratio over 1 was achieved. The chronic inflammation status of an HIV infection is the reason that autoimmunity appears outside the IRIS period. Treatment was initiated with antithyroid drugs.

Thyroid function should be monitored periodically in HIV patients undergoing HAART. Future observations must be made for HIV related thyroid disorders using new classifications and studies with a larger number of patients.

Key words: HIV, autoimmune thyroiditis, HAART.

INTRODUCTION

We report a case of acute autoimmune thyroiditis with thyrotoxicosis in a female patient with stage C3 human immunodeficiency virus (HIV) infection, who had been under highly active antiretroviral therapy (HAART) for more than 7 years.

HAART is suspected to be involved in the

potential pathogenic mechanisms linking thyroid autoimmunity with immune restoration. The immune reconstitution inflammatory syndrome (IRIS) can occur as a complication, shortly after HAART initiation and has been linked to autoimmune thyroid disease (1). In our case, the patient developed autoimmune thyroiditis seven years after the restoration of immune competence following HAART, thus emphasizing the possible association of autoimmune thyroiditis in HIV-infected patients even after successful immune restoration and good adherence to HAART. The chronic inflammation status of an HIV infection is the reason that autoimmunity appears outside the IRIS period.

CASE REPORT

A 26 year old Caucasian female has been monitored in our clinic for HIV infection since November 2004, when she was 14 years old. She was diagnosed with autoimmune thyroiditis at the age of 22 years, in August 2012, when she was admitted for anxiety, hyperactivity and palpitations. The past medical history of the patient revealed that she was horizontally infected in the first year of life. She was diagnosed with stage C3 HIV infection, only at the age of 14 years, because of recurrent pneumonia and leucopenia. At that time she had a very low CD4 count (28cells/ mm^3) and a very high viral load (HIV-RNA 2.442.326 copies/ μ L = 6.4log₁₀). HAART was started immediately with 2NRTI+1PI (d4T+3TC+kal). IRIS, presenting as cerebral toxoplasmosis, occurred three weeks after HAART initiation. Following treatment the cerebral toxoplasmosis had a good outcome. From the beginning the patient showed a good immune response to the regimen, due to a good adherence and compliance (over 90%). Nine months after HAART initiation the viral load was undetectable (under 34 copies/ μ L) and the CD4 count reached 645 cells/ mm^3 (within normal range) after one year of treatment,

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Figure 1. CD4 count - monitoring between 0 and 132 months (starting November 2004).

Figure 2. Viral load dynamics - monitoring between 0 and 132 months (starting November 2004).

Figure 3. Progression of thyroid hormones from diagnosis until present reevaluation (starting August 2012).

(Figs 1 and 2). After four years of treatment, taking into account the side effects due to HAART, lipodystrophy with hypertriglyceridemia and hypercholesterolemia, it was decided to switch Stavudine (d4T) to Zidovudine (AZT) (AZT/3TC+Kal) and start the patient on statins (initially Pravastatin and subsequently Atorvastatin).

At admission the patient had a weight of

Figure 4. Thyroid ultrasound after 4 years of disease progression: a) heterogeneous texture; b) hypervascularity; c) thyroid nodule.

55.5kg, height of 1.7m and a BMI of 19.2 kg/m², body temperature within normal range, an elevated heart rate of 120 beats/minute and high blood pressure of 134/71 mmHg. Palpation of the thyroid revealed an enlarged, firm, and rubbery goiter without any tenderness or bruit. Admission blood tests demonstrated abnormal thyroid function with TSH - 0,023μIU/ml (normal

Figure 5. CD4/CD8 ratio dynamic - monitoring between 0 and 132 months (starting November 2004).

range 0.27-4.20 μ IU/mL) and free thyroxin (T4) - 73.38 pmol/L (normal range 10.6-22.7pmol/L), with elevated levels of antithyroidperoxidase antibodies (TPOAb) of 334.4IU/mL (normal under 5.6IU/mL), normal levels of long acting thyroid stimulator (LATS) - 0.60IU/L (normal under 1.75IU/L) and antithyroglobulin antibodies (TGAb) - 33.4IU/mL (normal under 40IU/mL). Thyroid ultrasound revealed a diffusely enlarged thyroid gland (thyroid volume 31.86 mL) with a heterogeneous texture, isthmus (0.8cm), hypervascularity and a prominent reactive tracheal lymphadenopathy, with a 0.4 cm diameter, with normal morphologic features.

Clinical examination, blood test results and the ultrasound appearance established the diagnosis of autoimmune thyroiditis. No family history of thyroid or autoimmune disease was recorded. At that time, the patient had a CD4 count of 1560 cells/mm³ and an undetectable viral load (<34 copies/ μ L) and he was on the same HAART regimen for more than 7 years (Fig. 2). Treatment with methimazole was initiated.

After one year of treatment TSH was 2.96 μ UI/mL (0.27-4.20 μ IU/mL), free thyroxin (T4) 10.93pmol/L returned within normal ranges and the patient was euthyroid. The patient was started on Levothyroxine, administered concomitantly with methimazole, for two years. Thereafter, all thyroid medication was stopped for one year.

Four years after establishing the diagnosis of autoimmune thyroiditis, blood tests showed again subclinical hyperthyroidism with low TSH levels of 0.04 μ IU/mL and normal free thyroxin (T4) levels of 13.64pmol/L. The thyroid hormones profile from diagnosis until the current admission is illustrated in Figure 3. Control thyroid ultrasound, shown in Figure 4, revealed the same aspect of a diffuse goiter (thyroid

volume = 17.33cm³) with a heterogeneous texture, Fig. 4a), isthmus 0.5cm, hypervascularity Fig. 4b), with the tendency to form nodules in the right thyroid lobe; at this level, a nodule was observed, measuring 0.87/0.62cm Fig. 4c). The treatment with methimazole was resumed.

DISCUSSION

Thyroid function abnormalities were described in AIDS patients without antiretroviral therapy, usually in the absence of direct thyroid disorders. Frequently there are similar changes as those present in autoimmune thyroiditis, but with euthyroid status (2).

The presence of autoantibodies can be correlated with an increased incidence of autoimmune diseases which are reported in patients with HIV infection. In a study published in 2002 by Zandman-Goddard and Shoenfeld the authors proposed a classification of the autoimmune manifestations related to HIV/AIDS, based on the CD4 cell count and viral load, allowing the identification of the autoimmune disease and the establishment of appropriate therapy. Thus, in stage IV amid immune competence restoration following HAART, there is a predisposition to develop autoimmune diseases. The presence of antithyroid antibodies has been reported in patients with HIV/AIDS and this category included antithyroid peroxidase antibodies (3). According to Chen *et al.* the mean duration of immune restoration is 17 months, during which time there is a predisposition to develop autoimmune thyroid disease (4). In our case, restoration of immune competence following HAART with a normal CD4 count was achieved after 1 year of treatment. CD4/CD8 ratio over 1 was achieved four years prior to the onset of hyperthyroid symptoms and the emerging diagnosis of autoimmune thyroiditis, (Fig. 5).

Silent lymphocytic thyroiditis is a transient autoimmune inflammation of the thyroid and is often associated with anti-thyroid peroxidase antibodies, and other disorders, as sarcoidosis, or chronic urticaria (5, 6). It follows a clinical course with a hyperthyroid phase followed by transient hypothyroidism and recovery and occurs most often in the postpartum period but may also occur sporadically. Viral infections are frequently cited as a major environmental factor implicated in silent lymphocytic thyroiditis and autoimmune thyroid diseases (7). Ciampolillo *et al.* found that retrovirus-like sequences could be associated with thyroid autoimmunity (8). Primary HIV infection was found

References

to be linked with subacute thyroiditis as stated by a study published by Bouillet *et al.* (9). Recurrent silent lymphocytic thyroiditis has been reported manifested as postpartum thyroiditis in subsequent pregnancies (10).

Postpartum thyroiditis (PPT) occurs in 5–9% of women and presents as transient hyperthyroidism (median onset 13 weeks postpartum) followed by transient hypothyroidism with median onset 19 weeks postpartum. During the hyperthyroid phase patients can be asymptomatic. In contrast, at onset of the hypothyroid phase, patients experience persistent symptoms and require levothyroxine treatment (11, 12). The exact mechanisms of postpartum thyroiditis remain unknown, some authors hypothesize that it occurs as an aggravation of underlying autoimmune thyroiditis after resolution of the inflammation during pregnancy (13). A similar mechanism to that occurring in PPT is probably involved in HIV thyroiditis IRIS-related, both having common dysimmune findings and possibly the same mechanism leading to thyroid disturbance. This mechanism was firstly suspected in the presented case but in the absence of IRIS, we reconsidered. In our case, the thyroid recurrent dysfunction was related to persistent inflammation in HIV, predisposing to autoimmune diseases.

In conclusion, the peculiarity of the case is that thyroiditis did not occur during the period in which the patient did not receive antiretroviral therapy, neither during the period when she had manifestations of IRIS, but in a period when immune restoration was considered to be complete. It seems that despite of a normal CD4 count and a CD4/CD8 ratio > 1, there is a persisting immune dysfunction that can cause autoimmune manifestations, autoimmune thyroiditis in our case.

Conflict of interest

The authors declare that they have no conflict of interest concerning this article.

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