REVISTA MEXICANA DE ENDOCRINOLOGÍA, METABOLISMO & NUTRICIÓN CASO CLÍNICO

Subacute thyroiditis following influenza vaccine

Santiago Guzmán-García[1]*, Rogelio Domínguez-Moreno[1], Israel Rojas-De Ita[1], Claudia Guzmán-Morales[1], Álvaro Valladares-Pasquel[1], Fabiana Samaniego-Burneo[2] and Lidia Moreno-Castañeda[3]

[1]Internal Medicine Unit, Medica Sur Clinic & Foundation, Ciudad de México, México; [2]Biochemistry and Pharmacy, Universidad Técnica Particular de Loja, Loja, Ecuador; [3]Internal Medicine Unit and Metabolism Clinic, Medica Sur Clinic & Foundation, Ciudad de México, México

ABSTRACT

Subacute thyroiditis is a granulomatous acute inflammation characterized by thyroid pain and goiter that may be associated with fever and elevated erythrocyte sedimentation rate. Most of the time it is preceded by a self-limited viral infection. However, subacute thyroiditis following influenza vaccination has rarely been reported. We report a case following the administration of an influenza vaccine. (REV MEX ENDOCRINOL METAB NUTR. 2016;3:34-8)

Corresponding author: Santiago Guzmán-García, saggrecho@hotmail.com

Key words: Subacute thyroiditis. Influenza vaccine. Erythrocyte sedimentation rate.

RESUMEN

La tiroiditis subaguda (SAT) es una inflamación aguda granulomatosa caracterizada por dolor tiroideo y bocio, que puede estar asociado a fiebre o elevación de la velocidad de sedimentación eritrocitaria (ESR). La mayor parte del tiempo es precedida por una infección viral autolimitada. De cualquier forma, la tiroiditis subaguda posterior a la vacunación con influenza ha sido rara vez reportada. Reportamos un caso posterior a la aplicación de vacuna contra influenza.

Palabras clave: Tiroiditis subaguda. Vacuna contra influenza. Velocidad de sedimentación eritrocitaria

Dirección para correspondencia:
*Santiago Guzmán-García
Internal Medicine Unit
Medica Sur Clinic & Foundation
Puente de Piedra, 150
Col. Toriello Guerra, Del. Tlalpan
C.P. 14050 Ciudad de México, México
E-mail: saggrecho@hotmail.com

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CLINICAL CASE

A 33-year-old Asian male, with no family history of thyroid disease, with a smoking history of 2.8 pack-years (suspended seven years before his current illness). He has sporadic consumption of alcoholic beverages. No history of other diseases. He had influenza virus vaccination two weeks prior the onset of symptoms. He was admitted to the hospital with complaints of daily malaise and insomnia of two weeks. He also complained of fatigue, weakness, nocturnal sweating, intermittent pulsatile moderate-intensity frontal headache (without red flags), palpitations, sore throat, and pain in the left-anterior part of his neck. The pain radiated to the ipsilateral maxillary area. He also had loose stools, 2-3 bowel movements a day without blood or mucus, and unintentional weight loss of 6 kg in the last month. On physical examination he had an increased thyroid gland, at the expense of the left lobe, indurated, with irregular borders, without nodules, painful at palpation, mobile to swallowing, without associated lymph nodes. His heart rate was 101 beats per minute. His extremities showed discrete distal upper limb resting tremor. The laboratory tests revealed normochromic normocytic anemia, elevated erythrocyte sedimentation rate (ESR), and biochemical pattern suggestive of primary hyperthyroidism (Table 1). These biochemical findings were complemented with a thyroid ultrasound that showed increase in thyroid size (goiter), with hypo-echogenic areas, pseudo-nodular images, and decreased vascularity, with some cervical lymphadenopathies of inflammatory characteristics (Fig. 1). A thyroid iodine uptake and scan showed poor ^{131}I uptake of 1% (Fig. 2). Subacute thyroiditis (SAT) was diagnosed based on the Japan Thyroid Association Criteria (Table 2)[1]. He was intentionally questioned about signs or symptoms related to airway, gastrointestinal, or any other infection, which he completely denied. Because of the intensity of the symptoms, management with acetaminophen 750 mg twice daily and prednisone 40 mg once daily with weekly descending doses was selected. Propranolol 20 mg twice daily was used to control signs and symptoms of hyperthyroidism and alprazolam 5 mg once daily at bedtime to promote sleep onset. Our patient had an adequate response to treatment. Follow-up tests every four weeks after the patient was discharge were performed, which revealed a euthyroid profile and a decrease in ESR (Table 1). The patient was completely asymptomatic at four weeks. The unique event related to the development of thyroiditis was the application of influenza vaccine two weeks prior to the onset of symptoms (which was at the same time when the symptoms first appeared).

Table 1. Laboratory findings

Parameters	On admission	1 month later	2 months later
Hemoglobin (14-18 g/dl)	13.3 g/dl		
Average globular volume (83-98)	38.6 fl		
Mean corpuscular hemoglobin (27-32)	29.1 pg		
Leucocytes (4.5-11)	9.5×10^3/µl		
Absolute neutrophils (1.8-7.7)	6.3×10^3/µl		
Absolute lymphocytes (1.0-4.8)	1.8×10^3/µl		
Erythrocyte sedimentation rate (< 10 mm/h)	80 mm/h	16 mm/h	27 mm/h
Thyroglobulin AB: (0-4)	5.4 IU/ml		
Thyroid peroxidase AB (0-8.9)	2.4 IU/ml		
Thyroid stimulating hormone (0.55- 5.46)	0.03 µUI/ml	0.02 µUI/ml	0.40 µUI/ml
Total triiodothyronine (0.73-1.62)	3.01 ng/ml	1.15	1.10
Total thyroxine (5.67-10.35)	29.27 µg/dl	10.1 µg/dl	10.3 µg/dl
Free thyroxine (0.49-1.14)	5.06 ng/dl	1.16 ng/dl	1.18 ng/dl

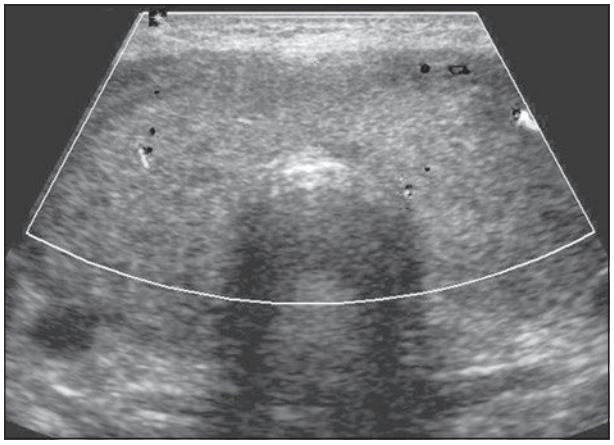

Figure 1. Thyroid gland US Doppler: in the left lobe is observed 52 × 25 × 26 mm, 10 mm isthmus, right lobe 51 × 30 × 29 mm, heterogeneous parenchyma by diffuse hypo- and hyper-echoic areas, without calcifications or fluid collections.

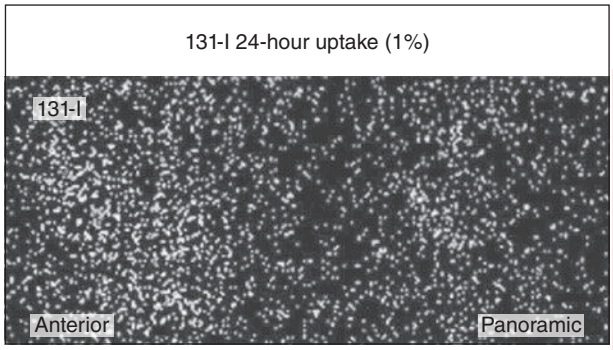

Figure 2. Thyroid scintigraphy with 131-I, in which poor uptake of 131-I is observed with irregular distribution with decreased uptake at 24 hours, 1% normal parameters are from 15 to 35%.

DISCUSSION

Subacute thyroiditis, also known as De Quervain thyroiditis, granulomatous, or viral thyroiditis, is an uncommon cause of hyperthyroidism (5% of all thyroid diseases); the peak incidence occurs between the third and fifth decade with a higher incidence in women (ratio 3.0-5:1)[2]. Among its clinical features that stand out are constant neck pain with or without irradiation to the jaw, ear, or the occipital region and often worsened by neck movement or swallowing. Patients may present with variable degree of fever, dysphagia, malaise, and in some cases, if the patient presents in the hyperthyroid phase, with signs and symptoms of hyperthyroidism (anxiety, sweating, distal limb tremor, increased bowel movements, and palpitations). On physical exam a soft, tender, enlarged, irregular, and painful thyroid can be palpated[3]. The natural history of the disease usually starts with a hyperthyroid phase (with biochemical profile of primary hyperthyroidism), which usually lasts 3-6 weeks, followed by a hypothyroid phase of 4-6 months, with a usual return to the euthyroid state after 6-12 months (in 95% of cases). Subacute thyroiditis is usually considered a self-limited disease (in one year). Uncommonly, there is a relapse rate in up to 4% of cases. In the active hyperthyroid phase, an elevated ESR is noted, occasionally more than 80 mm/hour, associated with increased levels of C-reactive protein and thyroglobulin; rarely, anti-thyroid peroxidase antibodies can be found (< 25%). Low radioactive ^{131}I uptake is observed in the initial (destructive) phase. Low levels of thyroglobulin are typically found after high follicular cell destruction (after 1-2 weeks). Thyroid ultrasound usually reveals a hypo-echogenic thyroid gland, heterogeneous echogenicity, with normal to decreased vascularization. In some cases, medical treatment is not needed. When low to moderate pain is present, anti-inflammatory drugs or aspirin are usually sufficient to relieve the pain. In severe cases, after acute suppurative thyroiditis has been ruled out, oral prednisone can help reduce severe pain and swelling within hours. Prednisone 40 mg is the usual dose, but doses as low as 15 mg have been used with good results. Dose is usually tapered within six weeks or so. Non-selective beta-blockers, such as propranolol, are useful for sympathetic effects of thyrotoxicosis. If the hypothyroid phase is prolonged, levothyroxine can be initiated to avoid hypothyroid signs and symptoms[4].

Several etiological associations have been described. The most common is a history of upper airway infection, viral in most cases (varicella, Coxsackie, influenza, and adenovirus)[5,6]. However, there are few cases in the literature associated with influenza vaccination[7-9].

Table 2. Criteria for diagnosis of subacute thyroiditis by The Japan Thyroid Association

Clinical findings (in the thyroid gland)	Laboratory findings	Criteria	Exclusionary conditions	Notes
Swelling	Elevation of C-reactive protein and/or erythrocyte sedimentation rate	A patient shall be said to have subacute thyroiditis if he/she has satisfied all 4 criteria (clinical + 3 lab findings)	A patient may not be said to have subacute thyroiditis if he/she is experiencing acute exacerbation of chronic thyroiditis	Patients often have preceding episodes of upper respiratory inflammation and high fever
Pain	Elevation of free thyroxine and suppression of thyroid stimulating hormone: < 0.1 U/ml	A patient shall be said probably to have subacute thyroiditis if he/she has satisfied clinical criterion, and 2 laboratory criteria	Bleeding into a thyroid cyst	Pain and tenderness often moves gradually (creeps) to the opposite lobe of the thyroid gland
Tenderness	Hypo-echoic lesion at a painful portion of the thyroid gland confirmed by ultrasonography		Acute suppurative thyroiditis	Anti-thyroid autoantibodies are usually negative, but May rarely become weak-Positive transiently during the course
			Thyroid anaplastic carcinoma	

Adapted with permission from The Japan Thyroid Association, Guidelines for the Diagnosis of Subacute Thyroiditis[1].

According to previous research, there might be a link between the influenza vaccination and the development of subacute thyroiditis due to the presence of viral antigens and a probable immune activation of cytotoxic T lymphocytes. Hsia, et al., in their case series report, state that in patients without history of infection and recent exposure to vaccination, influenza vaccine should be suspected as a trigger of the disease; however, there is no accurate method to confirm this cause-effect relationship[9].

In the previous series of cases, recurrence has been documented (in 2 out of 6 cases) with new vaccinations. There is a risk association probably determined by the presence of HLAB35 haplotype. The haplotype has been identified as a risk factor for immunological diseases, as described in other cases[10].

The biochemical findings in this patient are compatible with subacute thyroiditis, since a previous history of recent bacterial or viral infection was not found and the symptoms appeared after administration of the vaccine against influenza. As described before, we suspect the history of vaccination as the probable trigger of the disease. The worldwide use of influenza vaccine and its excellent tolerance, coupled with the absence of reports of direct association to thyroid disorders, makes it difficult to establish a direct cause-effect relationship. However, based on the time sequence of the events described in this and other patients by Hsia, et al., it should prompt physicians to consider influenza vaccine as an etiologic trigger to develop subacute thyroiditis.

So far, this correlation has been reported in less than a dozen cases. Subacute thyroiditis is usually self-limited and without consequences for the patient. Treatment to control pain and inflammation is usually successful, and only in some cases is thyroid support with levothyroxine needed. Influenza vaccine prevents thousands of deaths each year. Therefore, the suspension of vaccine applications is not justified.

Immunological and genetic studies are needed in the follow-up of patients with a similar history of

thyroiditis, to better understand the correlation that exists between these events.

CONCLUSION

Acute thyroiditis is a self-limiting illness, with a viral etiology in most of the cases. However, it becomes increasingly important to identify vaccination against influenza as a probable trigger to develop subacute thyroiditis. Suspicion is needed when exposure to the vaccine correlates in time and no previous history of infection can be found. This correlation has been reported in less than a dozen cases. Cases are usually self-limited and without consequences for the patient. Therefore, the suspension of vaccine applications is not justified.

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