DIAGNOSIS OF JUVENILE SYSTEMIC LUPUS ERYTHEMATOSUS IN ADOLESCENTS WITH HASHIMOTO'S THYROIDITIS: TWO CASE REPORTS

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Abstract

Objectives: To report the unusual diagnosis of juvenile systemic lupus erythematosus (JSLE) in two adolescents with a previous diagnosis of Hashimoto's thyroiditis (HT).

Case reports: Case # 1: An 11 year-old girl was diagnosed with HT. One year later, she presented with generalized edema, pericardial and pleural effusion, positive ANA, thrombocytopenia, increased anti-cardiolipin IgG and nephritis, being diagnosed with JSLE. (Case # 2): A 13 year-old girl was diagnosed with HT at the age of 10 years. Two years later, she presented with weight loss, knee and elbow arthritis, alopecia, leukopenia, and positive ANA and dsDNA autoantibody confirming the diagnosis of JSLE. The first patient was treated with prednisone and cyclophosphamide, and the second with prednisone and hydroxychloroquine with both achieving relief of the lupic symptoms.

Conclusion: In spite of the known association between autoimmune diseases and thyroid disorders, the occurrence of JSLE in patients with a previous diagnosis of HT is rare. It is important to bear in mind this possibility when following patients with HT in order to not delay the diagnosis and treatment of a serious systemic autoimmune disease such as JSLE.

Keywords: Adolescent; Hashimoto's Thyroiditis; Systemic Lupus Erythematosus.

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Introduction

The autoimmune diseases can be classified as systemic or organ-specific[1]. Hashimoto's thyroiditis (HT) is an organ-specific autoimmune disease in which production of thyroid antibodies occurs along with thyroid lymphocytic infiltration. Systemic lupus erythematosus (SLE) is an autoimmune systemic disease, characterized by autoantibodies and deposition of immune complexes in several organs and tissues. The diagnosis of autoimmune thyroid disease in patients with SLE is well-known, especially in adults, with few case reports involving children and adolescents[2]. However, the literature is scarce in studies showing the opposite, that is, the occurrence of SLE in previously diagnosed HT patients[3-5].

As there is little data about this theme, the authors describe two adolescents who developed SLE one year after the diagnosis of Hashimoto's thyroiditis.

Case Report

Patient #1

An 11 year-old girl was diagnosed with HT at the age of 10 years-old, based on free thyroxine [FT4]: 0.22 ng/dL (0.75–1.80), thyrotropin [TSH]: 135 mIU/mL (0.3–5.0); antiperoxidase antibody (TPO): 263 IU/mL (< 35) and antithyroglobulin antibody: 51 IU/mL (< 40). One year later, she presented with generalized edema, mucosal bleeding and hematuria. Physical examination showed: T 36.5 °C (97.7 °F); HR: 108 bpm; RR 26 ipm; BP: 136/95 mmHg; height: 121 cm; weight: 30.2 Kg and absence of arthritis or butterfly rash. Laboratory evaluation (reference values in parenthesis) demonstrated: hemoglobin: 7.1 g/dL, leukocytes: 8,800/mm^3, platelets 4,800/ /mm^3 (145,000–450,000), BUN: 54.2 mg/dL (6-20), creatinine: 1.2 mg/dL (0.4 – 1.1), sodium: 138 mEq/ /L (136–148), potassium: 6.1 mEq/L (3.5–5.5), albu-

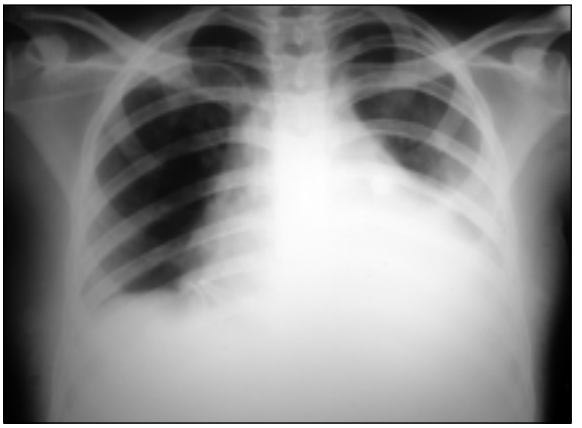

Figure 1. Chest X-ray revealing bilateral pneumonia, right pleural effusion and pericardial effusion

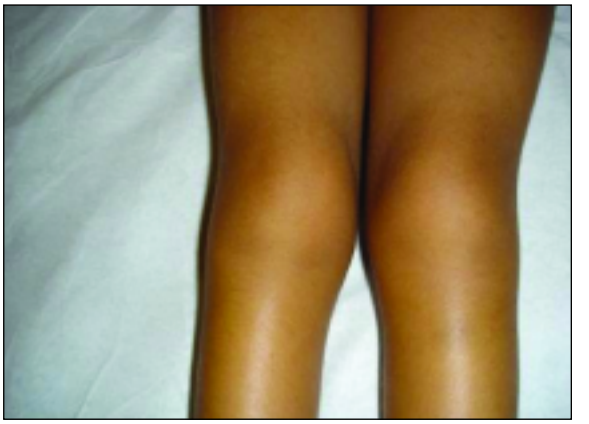

Figure 2. Bilateral knee arthritis

min: 2.5 g/dL (3.5–5.0), aspartate aminotransferase: 15 U/dL (15–37) and alanine aminotransferase: 18 U/dL (30–65). Urine analysis revealed proteinuria and hemoglobinuria. Renal sonogram identified cortex-medullar alterations bilaterally. Chest X-ray revealed bilateral pneumonia, right pleural effusion and pericardial effusion (Figure 1). Myelogram was normal. Serologies were negative to HIV, HTLV and cytomegalovirus. Rheumatologic studies showed: C3: 31 mg/dL (90–207), C4: 1.6 mg/dL (17–52), CH-100: undetected, ANA staining pattern: mixed pattern (homogeneous and speckled), with titles of 1:320 e 1:5.120, extractable nuclear antigens (Ro/SSA, La/SSB, SM), anti dsDNA, P-ANCA and C-ANCA autoantibodies and VDRL were negative. Anti-cardiolipin IgM reactiveness was negative, and the corresponding IgG was moderate reactive. Renal biopsy was compatible to Class IV lupus nephritis. The diagnosis of JSLE was confirmed through the American College of Rheumatology criteria[6]. As there was not a satisfactory response with oral prednisone, intravenous methylprednisolone and cyclophosphamide were added with edema regression, normalization of diuresis and blood pressure levels. She was discharged medicated with cyclophosphamide, prednisone, captopril, levothyroxine and omeprazole.

Patient # 2

A 13 year-old girl was diagnosed with HT at 10 year--old, confirmed by: FT4: 1.38 ng/dL; TSH: 29.72 IU/mL; TPO: 220 UI/mL and antithyroglobulin antibody: 71 UI/mL. Two years later, she developed fatigue, weight loss, arthralgia of the wrists, knee and ankles arthritis and alopecia. Physical examination showed: T: 36,5º C (97.7 °F); HR: 84 bpm; RR: 20 ipm; TA: 85/60 mmHg; height: 166 cm; weight: 44 kg and arthritis in both knees and ankles (Figure 2). Laboratory studies demonstrated: hemoglobin: 9.4 g/dL, leukocytes: 2,800/mm^3, platelets 250,000/mm?, ESR: 71 mm/1st hour (< 20). Renal and liver function tests, electrolytes, proteins, serum lipids, hemoglobin, electrophoresis, urine analysis, echocardiogram, renal ultrasonography and chest X-ray were without abnormalities. Rheumatologic studies showed: C3: 80mg/dL (90-207), C4: 12 mg/dL (17-52), CH-100: 44 mg/dL (> 60); ANA staining pattern: mixed pattern (homogeneous and speckled), with titles of 1:320 e 1:620 and positive dsDNA antibody. The Ro/SSA, La/SSB, anti-SM, anti-cardiolipin IgM and IgG, P-ANCA and C-ANCA autoantibodies, Rheumatoid Factor and VDRL were negative. The diagnosis of JSLE was confirmed by the American College of Rheumatology criteria[6]. The patient was treated with prednisone and hydroxychloroquine with a good clinical response.

Table I summarizes the main clinical and laboratory data of the two patients.

Discussion

There is a consensus about a higher prevalence of autoimmune thyroid diseases and thyroid antibodies among SLE patients[2-7]. Although elevated thyroid antibodies prevalence can be evidenced in some SLE series, the presence of thyroid dysfunction is rare. Blich *et al.*, reported a 4.3 to 21.4 per-

Table I. Overview of clinical and laboratory findings

Variables		Case report # 1	Case report # 2
Age at HT diagnosis		10 year-old	10 year-old
Age at SLE diagnosis		11 year-old	13 year-old
Thyroid Function Tests	TSH (0.3-5.0 IU/mL)	135	29,72
	FT4 (0.75-1.80 ng/dL)	0.22	1.38
	Antiperoxidase antibody (< 35 IU/mL)	263	220
	Antithyroglobulin antiboby (< 40 IU/mL)	51	71
Work-up for SLE diagnosis	C3 (90-207 mg/dL)	31	80
	C4 (17-52 mg/dL)	1.6	12
	CH-100 (> 60 mg/dL)	Undetected	44
	ANA (Negative)	Positive	Positive
	sdDna antibody (Negative)	Negative	Positive
	Anti-cardiolipin IgG (Negative)	Moderate Reactiveness	Negative
	Ro/SSA (Negative)	Negative	Negative
	La/SSB (Negative)	Negative	Negative
	Anti-Sm (Negative)	Negative	Negative
	P-ANCA (Negative)	Negative	Negative
	C-ANCA (Negative)	Negative	Negative
Systemic manifestations	Pancytopenia	+	–
	Arthritis/Arthralgia	+	+
	Renal failure	+	–
	Thrombocytopenia	+	–
	Serositis	+	–

Legend: (HT): Hashimoto's thyroiditis; (SLE): systemic lupus erythematosus; (FT4): free thyroxine; (TSH): thyrotropin; (C): complement; (ANA) antinuclear antibody.

cent prevalence rate of thyroid abnormalities among SLE patients when compared to a 1 percent prevalence rate in the general population[1]. Some studies demonstrated a higher frequency of thyroid abnormalities in children, whereas others did not[8].

However, the current knowledge is limited about if there is a higher prevalence of SLE in autoimmune thyroid disease patients. Besides few case reports, we found two large studies connecting these two conditions: a study from Gaches *et al.* indicated a 13.7 percent prevalence rate of systemic autoimmune diseases among HT patients, particularly SLE and Sjögren's syndrome[9]; and a study by Biró *et al.* demonstrated a 6.5 percent prevalence rate of SLE among patients with HT, compared to 0.05-0.1 percent for the general population[4].

Tektonidou *et al.* suggest as a feasible explanation to the association between HT and systemic autoimmune diseases a polyclonal autoimmune response against organ-specific autoantigens[5]. Biró *et al.* demonstrated the association of HLA-DQA1*0301/DQB1*0401/DRB1*0405 haplotypes with these syndromes, as well as with thyroid autoantibodies cross reaction with several tissues and organs, besides an unbalanced proinflammatory cytokine setting[3]. Picco *et al.* proposed a role of the pubertal hormonal changes in triggering the outburst of these diseases[4]. In their study, the authors revealed a positive ANA two years before overt clinical SLE. However, Eberhard *et al.* mentioned that 30% of the children diagnosed with autoimmune thyroiditis had a positive ANA, although only some of them presented SLE[8]. In the study of Picco *et al.*, similar to the patient presented in the first case, anti-dsDNA and anti-Sm were negatives at the SLE diagnosis[4]. Kramer *et al.* alleged a higher prevalence of hyperprolactinemia among LES patients, which must be considered among the causes of immunologic imbalance[10]. Furthermore, hyper-

prolactinemics patients have a higher prevalence of thyroid antibodies, evidencing an interrelationship among these three syndromes.

It is important to be alert to the unusual possibility of SLE developing in patients with a previous diagnosis of autoimmune thyroiditis. Cohorts studies must be designed in order to clarify the risk factors and the causality between thyroid dysfunction and SLE. For instance: if Hashimoto's thyroiditis and systemic autoimmune diseases share a polyclonal autoimmune response against organ-specific autoantigens, if thyroid autoantibodies cross react with several tissues and organs, and the role of pubertal hormonal changes in triggering the outburst of these diseases.

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