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Mixed Connective Tissue Disease and Papillary Thyroid Cancer: A Case Report

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Patient: Female, 58
Final Diagnosis: Papillary thyroid carcinoma
Symptoms: Cough • shorthness of breath
Medication: —
Clinical Procedure: Fine needle aspiration and a near total thyroidectomy
Specialty: Rheumatology

Objective: Rare co-existance of disease or pathology

Background: Mixed connective tissue disease (MCTD) is a connective tissue disorder characterized by high titers of distinct antibodies: U1 ribonucleoprotein with clinical features seen in systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), dermatomyositis (DM), polymyositis, and scleroderma. The association of SLE and DM with various cancers of the thyroid has been reported in the literature. However, there have been no reports associating MCTD with thyroid cancer.

Case Report: We present a 58-year-old woman diagnosed with MCTD with co-morbid interstitial lung disease that has remained stable for 10 years, who developed papillary thyroid carcinoma (PTC) 10 years after initial diagnosis.

Conclusions: We theorize that: 1) MCTD may have been a primary diagnosis complicated by PTC, or 2) MCTD may have been an initial presentation of paraneoplastic syndrome of silent PTC, because her symptoms of MCTD significantly improved after total thyroidectomy. To the best of our knowledge, this is the first case report to associate MCTD with PTC. It highlights the importance of maintaining a high index of suspicion for thyroid malignancy in MCTD patients.

MeSH Keywords: Arthritis, Rheumatoid • Dermatomyositis • Lupus Erythematosus, Systemic • Mixed Connective Tissue Disease • Scleroderma, Diffuse • Thyroid Neoplasms

Full-text PDF: http://www.amjcaserep.com/abstract/index/idArt/894176

Background

Mixed connective tissue disease (MCTD) was originally defined as a connective tissue disorder characterized by the presence of high titers of distinct antibodies known as U1 ribonucleoprotein (RNP) complex in combination with clinical features seen in systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), dermatomyositis (DM), polymyositis, and scleroderma [1]. The association of SLE and DM with various thyroid cancers has been described in case reports and a few studies [2-6]. However, the association of MCTD and thyroid cancer has not been described. We report a 58-year-old woman who developed papillary thyroid carcinoma (PTC) 10 years after the diagnosis of MCTD was made. We believe this is the first case report to associate MCTD with PTC.

Case Report

The 58-year-old woman with body mass index 34 kg/m^2 was diagnosed with MCTD in 2002. The initial presentation was with polyarthralgias, edema of the dorsum of the hands (puffy hands), Raynaud's phenomenon, erythematous rash on the face and upper arms, subcutaneous calcifications, bilateral knees synovitis, and gastroesophageal reflux disease. She also developed mild exertional dyspnea with subsequent pulmonary function tests and chest computerized tomography (CT) findings consistent with interstitial lung disease (ILD), which has remained stable until 2012. The patient did not have muscle weakness. Her rash resolved in a few months with residual hyperpigmentation of the skin and no recurrence since the initial presentation. During the course of 10 years, the patient was treated with variable doses of corticosteroid (methylprednisone) for flares of inflammatory polyarthritis and ILD.

The complete blood count, renal function, hepatic functions, thyroid function tests, and urinalysis were normal. Serology studies revealed positive nuclear antibody at a titer of 1:640 with speckled pattern, negative anti-double-stranded DNA and positive antibody against U1-ribonucleoprotein (RNP) multiple times during the course of 10 years. The latest antibody against RNP was >8.0 U. Levels of complements 3 and 4 were normal.

In 2012, she had developed increased shortness of breath and coughs. A chest CT was done showing no significant changes; however, there was an incidental thyroid nodule present. The thyroid-stimulating hormone was 1.86 mIU/ml. A thyroid ultrasound later revealed a 12×11 millimeter complex nodule in the middle part of the right lobe. Fine-needle aspiration findings were consistent with PTC. A near total thyroidectomy was subsequently done. The pathology showed a total thyroidectomy of 11 grams of tissue measuring 5×3.5×2 cm, with the right lobe measuring 3.5×2×1 cm, the left lobe measuring 3.5×2×1 cm, and the isthmus measuring 2×1.5×0.5 cm. The capsule was thin and inked black. Sectioning revealed red-brown, homogenous thyroid tissue with a single 1×0.7×0.5 cm, gray-white nodule in the right lobe. The pathology confirmed the diagnosis of PTC of 1.1 cm involving the right lobe. Post-surgery, the patient received Iodine-131 (30 mCi) ablation therapy and was placed on thyroid hormone suppression therapy. The patient has been compliant with thyroxine treatment. Her, thyroglobulin, and thyroglobulin antibody have remained negative. After near thyroidectomy with I-131 ablation, her symptoms of MCTD, including photosensitive facial rash, arthralgia, arthritis, and Raynaud phenomenon, were significantly improved. Corticosteroid dose was tapered to prednisone 10 mg daily without evidence of MCTD flare-up.

Discussion

MCTD is a connective tissue disorder characterized by the presence of high titers of anti-U1 RNP with clinical features of SLE, RA, DM, polymyositis, and scleroderma [1]. The most common initial clinical manifestations of MCTD are Raynaud's phenomenon, joint pain, hand swelling, fever, erythema nodosum, and trigeminal neuropathy [7]. The joints most often involved are metacarpophalangeal and proximal interphalangeal, wrists, metatarsophalangeal, knee, elbow, and ankle. Symmetrical joint involvements mimic that of RA [7].

The diagnosis of MCTD is not always easy as this is an overlapping syndrome. Sharp et al., Kasukawa et al. and Alarcón-Segovia et al. have proposed several different criteria for diagnosis, with different sensitivity and specificity [8–10]. Alarcon-Segovia et al. reported the study comparing the above 3 criteria in 593 patients and concluded that the criteria of Alarcón-Segovia to have a high sensitivity and specificity [11].

There are reports supporting the association between autoimmune diseases, especially SLE and DM, and an elevated risk of malignancy. In a large international cohort study, Bernatsky et al. reported an increased risk of malignancy in SLE patients, including hematologic, lung, vulva, and thyroid malignancies [2]. Similarly, Parikh-Patel et al. reported an elevated risk of lung, kidney, thyroid, and hematologic malignancies in patients with SLE [3]. Moreover, Antonelli et al. reported a high prevalence of PTC (3.2%) in patients with SLE [4]. Also, a number of case reports show the association of DM and PTC [5,6].

Unlike DM and SLE, there have been no statistically significant studies to suggest the association between MCTD and malignancies. Only Black et al. reported an association of MCTD with an increased risk of cancer, but the sample size was relatively small, and may be biased in favor of the inclusion of patients

from MCTD with complications [12]. To date, there have been case reports of MCTD being associated with malignancies: lung cancers, lymphoma, ovarian cancer, non-Hodgkin's lymphoma, thymic carcinoma, hepatocellular carcinoma, and in one case, gastric and uterine cervix cancers [12–17]. None have reported an association of MCTD with thyroid cancers.

In our case, the patient was diagnosed with MCTD based on findings of swollen fingers, Raynaud's phenomenon, bilateral knees synovitis, subcutaneous calcifications, gastroesophageal reflux disease, and positive anti-U1 RNP, along with ILD. She has been diagnosed with MCTD for 10 years and has been managed with only corticosteroids. Subsequently, an incidental finding of a thyroid nodule was found on CT scan. Biopsy result and surgical biopsy confirmed the diagnosis of PTC. We theorize that: 1) MCTD may be a primary diagnosis complicated by PTC in this patient with a body mass index of 34 kg/m^2 because obesity is a proposed risk factor for development of thyroid cancer [18]; and 2) Her initial symptoms may be contributed to by a paraneoplastic component of the spectrum of DM of MCTD that had been significantly improved after total thyroidectomy, especially her DM symptoms. However, the exact pathogenesis of the association between DM and malignancy remain unclear [19]. The epidemiologic evidence of MCTD as a paraneoplastic syndrome of PTC is also very limited.

Conclusions

This case highlights the importance of maintaining a high index of suspicion for thyroid malignancy in MCTD patients, especially since PTC can remain quiescent for several years before symptoms arise.

Thyroid survey should be included in malignancy investigations particularly in patients over 50 with mixed connective tissue disease.

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Conflict of interest

The authors have no conflicts of interest to declare.

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