A Coincidence of Rheumatoid Arthritis, Autoimmune Thyroid Disease and Vitiligo in a Single Patient: A Possible Pathogenetic Linkage

Bir Olguda Romatoid Artrit, Otoimmün Tiroid Hastalığı ve Vitiligo Birlikteliği: Olası Bir Patogenetik Bağlantı?

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Abstract

It has been widely observed that disorders with an autoimmune pathogenesis occur with increased frequency in patients with a history of another autoimmune disease (AD). The numbers of documented cases of a co-occurrence of different autoimmune diseases in a single patient in addition to studies investigating the possible common etiopathogenesis of these diseases have increased in recent years. Available data suggest that the presence of one AD should alert the clinician to the possibility of a second AD. In this report, we aimed to draw attention to these potential coincidences and the possible pathogenetic linkages between three distinct ADs in a single individual diagnosed with rheumatoid arthritis, autoimmune thyroid disease and vitiligo. Further documentation of observations of possible coincidence are required in order to yield results that may shed light on the biological pathways of these diseases.

Keywords: Rheumatoid arthritis, Autoimmune thyroid disease, Vitiligo.

Özet

Otoimmün patogenezi olan hastalıkların bir başka otoimmün hastalık (OH) öyküsü bulunun olgularda artmış sıklıkta geliştiği klinik olarak yaygın bir şekilde gözlenmektedir. Aynı olguda farklı OH'ların birlikteliği üzerine bildirilen verilerin ve bu hastalıkların olası ortak etyopatogenezini araştıran çalışmaların sayısı son yıllarda giderek artmaktadır. Elde edilen veriler, bir OH varlığının klinisyeni bir diğerini de araştırması için uyarması gerektiğini göstermektedir. Bu çalışmada romatoid artrit, otoimmün tiroid hastalığı ve vitiligo sergileyen bir olgu ile üç farklı OH arasındaki olası patogenetik bağlantılara ve koinsidanslara dikkat çekmeyi amaçladık. Bu hastalıklar arasındaki biyolojik bağlantılara ışık tutacak verilerin birikimi için koinsidanslar hakkındaki bu tür gözlemlerin daha fazla dökümantasyonuna gereksinim bulunmaktadır.

Anahtar Kelimeler: *Romatoid artrit, Otoimmün tiroid hastalığı, Vitiligo*

Introduction

Autoimmune diseases (ADs) are conditions under which an individual develops antibodies against their own cells, tissues and/or organ systems. An AD can be either organ-specific or non-organ specific (systemic) in its clinical presentation. The numbers of documented cases of a co-occurrence of different ADs in the same patient in addition to studies investigating the possible common etiopathogenesis of these diseases have increased in recent years [1].

In this report, we aimed to draw attention to the coincidence and possible pathogenetic linkage of three different ADs in a case study that describes an individual diagnosed with rheumatoid arthritis (RA), autoimmune thyroid disease (ATD) and vitiligo.

Case Report

A 34-year-old female patient was admitted to our clinic complaining of pain and swelling in her hands and feet that had persisted over the last four months. This patient also complained of morning stiffness that persists for roughly one hour each day. Eight years ago the patient was diagnosed with RA due to the symmetrical nature of her arthritis in addition to the occurrence of morning stiffness, clinical tests that were rheumatoid factor (RF)-positive and additional radiological findings. In the patient's past medical history, our physicians learned that she had been diagnosed with generalized vitiligo due to depigmented skin lesions observed on her face and extremities. The patient was being administered levotiron upon being diagnosed with ATD due to the observation of abnormal thyroid functions and thyroid antibodies that persisted for two years.

During the patient's physical examination, although there were no systemic abnormalities, some tenderness and swelling were observed during locomotor examination in her left elbow, metacarpophalangeal (MCP) and knee joints (bilaterally). Moreover, patchy losses of pigmentation from the patient's skin upon acrofacial topography examination were observed.

In laboratory investigations, whole-blood analyses and routine biochemical investigations were unremarkable with the exception of a diagnosis of chronic disease anemia. The erythrocyte sedimentation rate (ESR) was 35 mm/h, while the C-reactive protein (CRP) concentration was 1.19 mg/dl. The results of thyroid functional tests were determined to be in the normal range following administration of levotiron. In addition, RF and CCP tests were positive (70.7 IU/ml and 30.8, respectively), while the profiles of antinuclear antibodies (ANA) and extractable nuclear antigens (ENA) were negative. Signs of RA, such as periarticular osteopenia, erosion, cyst formation and a narrowing of the joint space were observed bilaterally in the third and fourth MCP joints during the radiological evaluation. Due to the patient's medical history, the results of the physical examination and the laboratory and radiological findings, the patient was diagnosed with RA, ATD and generalized vitiligo. In addition to levotiron, local corticosteroid administration and doses of Sulfasalazin and Chloroquine were prescribed for the patient.

Discussion

From a clinical perspective, it has been widely observed that disorders with an autoimmune pathogenesis occur with increased frequency in patients characterized by a history of previously diagnosed AD, and this tendency to develop another AD has been estimated to occur in approximately 25% of cases of patients with ADs. In recent years, there have been a growing number of reports of the co-occurrence of multiple ADs in the same patient with the aim of trying to clarify the biological pathways of these diseases' possible common pathogenesis [1].

RA is a chronic and systemic inflammatory disorder that may affect numerous tissues and organs, but primarily attacks the joints of the body, producing inflammatory synovitis that often progresses to the destruction of articular cartilage. Although the cause of RA is unknown, autoimmunity plays a pivotal role in its chronicity and progression. ATDs, Hashimoto's thyroiditis and Graves' disease are all organ-specific ADs characterized by the presence of antibodies against thyroglobulin, thyroid peroxidase, or thyrotropin receptor autoantigens, respectively. The relationship between RA and the thyroid gland has been studied extensively, with several studies demonstrating the autoimmune nature of thyroid dysfunctions in RA [2,3]. In a previous study, thyroid dysfunction was found to be three times more prevalent in women with RA than in women with non-inflammatory rheumatic diseases [2]. In a systematic review analyzing the results of 54 studies that investigated the coexistence of ADs within individuals and 9 studies that examininiged within-family associations, these data supported an increased prevalence of ATDs among patients with RA [4]. In a separate study investigating the frequency of rheumatic diseases in patients suffering from ATDs, various rheumatic diseases were detected in 62% of patients with ATDs, two of which were vitiligo and RA [5]. In this study, the authors concluded that an initial evaluation and regular testing for rheumatic diseases in patients suffering from ATD should be recommended due to the higher frequency of rheumatic diseases in these patients. In a separate study investigating the prevalence and distribution of ADs in 368 RA families, the authors reported that the most frequent ADs among relatives of patients with RA were ATDs and vitiligo [6].

Generalized vitiligo is defined as an acquired, non-contagious disorder in which progressive, patchy loss of pigmentation from the skin, overlying hair, and oral mucosa results from the loss of the melanocytes in the involved areas [7]. Vitiligo involves the complex interactions of several factors that ultimately contribute to melanocyte destruction, resulting in the characteristic depigmented lesions. Generalized vitiligo has been considered to be an AD of multifactorial origin that results from a combination of multiple inherited genetic risk factors and environmental stimuli. Studies on generalized vitiligo have led to the recognition that vitiligo is part of a broader, genetically determined autoimmune/autoinflammatory diathesis [7]. In addition, affected members of families diagnosed with vitiligo show elevated frequencies of

other Ads, such as ATD and RA [7]. In a study evaluating vitiligo in multiple autoimmune syndromes, the data confirmed the important association between vitiligo and ATDs [8]. Furthermore, the authors concluded that the female gender and the acrofacial topography of skin lesions could predict associations with other ADs in patients with vitiligo. In agreement with this results, our patient was female and possessed the acrofacial topography with skin lesions of vitiligo.

These studies indicate that the possibility of three or more ADs occurring in the same patient is unlikely to be due to a chance event and thus suggests a pathogenic relationship between the diseases [9]. Although the pathogenesis of the co-occurrence of different ADs in the same patient has not yet been clarified, genetic, infectious and immunologic factors have been implicated, and abnormalities in both humoral and cell-mediated immunity have been described [1]. The genetic predisposition of an individual seems to be a reliable linkage between these entities. Similar environmental triggers in a genetically susceptible individual may lead to the co-occurrence of different ADs in the same patient. Several candidate genetic linkages, such as the HLA B8 phenotype, the DR3 and DR5 genes or GM and KM immunoglobulin allotype interactions with HLA antigens have been suggested as potential factors in various Ads, including RA, ATDs and vitiligo [9,10].

In conclusion, the presence of one AD in a patient should alert the clinician to the possibility of additional ADs. The increasing number of reports of the co-occurrence of ADs indicates the need for continued surveillance for the development of new ADs in predisposed patients. Further documentation of such co-occurrences are needed to yield results that shed additional light on the biological pathways of these diseases.

Conflict interest statement The authors declare that they have no conflict of interest to the publication of this article.

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