RESEARCH ARTICLE

Comorbidities of rosacea

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ABSTRACT

Objective: Rosacea is a common chronic, inflammatory skin disease and some comorbid diseases often accompany the disease. We evaluated the relationship between rosacea and systemic comorbidities in our study.
Methods: Our study is a retrospective descriptive study. From Çanakkale Onsekiz Mart University Faculty of Medicine Hospital's patient information system, 18 years and older-aged, a total of 114 adult patients who were diagnosed with rosacea with at least 2-3 months of follow-up in the period between 2012-2018 were included in the study.
Results: Of the 114 patients included in the study, 76.3% (n=87) were female and 23.7% (n=27) were male. The mean age of the patients was 46.5±10.9 years, the median age was 45.0 years (range 21-72). Hypertension 19.3% (n=22), gastroesophageal/dyspepsia 14.9% (n=17), hyperlipidemia 13.2% (n=15), diabetes mellitus 13.2% (n=15), hypothyroidism 10.8% (n=12), obesity 9.6% (n=11), and depression 9% (n=10) were found to be the most frequently related to such diseases in our rosacea patients.
Conclusion: Rosacea can be easily diagnosed by dermatological examination. And it may be a clue to dermatologists in screening comorbid diseases related to rosacea.

Keywords: Rosacea, comorbidity, inflammation, hypertension, dyspepsia, hyperlipidemia

Rozasea'nın komorbiditeleri

ÖZET

Amaç: Rozasea kronik, inflamatuvar bir deri hastalığıdır ve Bazı komorbid hastalıklar sıklıkla hastalığa eşlik edebilir. Çalışmamızda rozasea ile sistemik komorbiditeler arasındaki ilişkiyi değerlendirdik.
Yöntem: Çalışmamız, retrospektif bir tanımlayıcı çalışmadır. Çalışmaya, Çanakkale Onsekiz Mart Üniversitesi Tıp Fakültesi Hastanesi hasta bilgi sisteminden, 18 yaş ve üstü, 2012-2018 yılları arasında en az 2-3 ay takip edilen rozasea tanısı alan toplam 114 yetişkin hasta dahil edildi.
Bulgular: Çalışmaya dahil edilen 114 hastanın %76.3'ü (n=87) kadın, %23.7'si (n=27) erkekti. Hastaların yaş ortalaması 46.5±10.9 yıl, ortanca yaş 45 yıldı (aralık 21-72). Rozasea hastalarımızda; hipertansiyon %19.3 (n=22), gastroözofageal/dispepsi %14.9 (n=17), hiperlipidemi %13.2 (n=15), diabetes mellitus %13.2 (n=15), hipotiroidi %10.8 (n=12), obezite %9.6 (n=11) ve depresyon %9 (n=10) gibi hastalıklar en sık ilişkili olduğu bulundu.
Sonuç: Rozasea dermatolojik muayene ile kolayca teşhis edilebilir. Ve rozasea ile ilişkili komorbid hastalıkların taranmasında dermatologlar için bir ipucu olabilir.

Anahtar kelimeler: Rozasea, komorbidite, kronik inflamasyon, hipertansiyon, dispepsi, hiperlipidemi

INTRODUCTION

Rosacea is a common chronic inflammatory skin disease in people of all ethnic backgrounds. It is more common in people with light skin (skin phototype 1 and 2) and women over 30 years of age. The etiopathogenesis of rosacea is complex and still not fully understood. Many factors have been charged such as abnormalities in innate immunity, inflammatory reactions to cutaneous microorganisms, ultraviolet damage, and vascular dysfunction [1]. Some environmental triggering factors (such as Demodex, UVR, temperature change, alcohol consumption, and spicy foods) can stimulate the release of various cytokines, especially antimicrobial peptides such as cathelicidin. The adaptive immune system in which T helper (Th) 1 and Th17 cell infiltration is dominant can be activated [2]. Besides, the expression of some matrix metalloproteinases (MMP's) in rosacea has also increased [3].

Persistent erythema affecting the central facial region of the face, persistent erythema, papules, pustules, telangiectasia, phymatous skin changes, cutaneous edema, burning or stinging sensation, and flushing are the characteristic cutaneous manifestations affecting the facial region of the face are characteristic cutaneous manifestations of rosacea [4].
It has also been reported to be related to many diseases such as chronic inflammatory bowel diseases, metabolic diseases, malignancies, autoimmune diseases, allergic diseases and urogenital, diseases with rosacea [5]. However, the reasons for the relationship of rosacea with these diseases are unclear. The chronic inflammatory structure of rosacea may have played a major role in the development of systemic comorbid diseases such as the relationship between systemic inflammation in psoriasis and the development of comorbidities.

It is thought that systemic inflammation plays a common role in the relationship between rosacea and cardiovascular diseases [6]. The aim of our study was to evaluate the relationship between rosacea what is a chronic inflammatory disease, systemic comorbid diseases and to present an idea of whether or not rosacea patients should be investigated for systemic diseases. Thus, better management of the disease will be ensured by monitoring more effective approaches in the follow-up and treatment of the disease.

MATERIALS and METHODS

Our study is a retrospective descriptive study, approved by the ethics committee on 03.10.2018. The study was performed between 27.10.2018-27.07.2019. From Çanakkale Onsekiz Mart University Faculty of Medicine Hospital's patient information system, 18 years and older-aged, adult patients who were diagnosed with rosacea with at least 2-3 months of follow-up in the period between 2012-2018 were included in the study. And patient's recorded information (age, gender, ocular involvement, presence or absence of feminine skin changes, and related diseases) were examined from the patient information system. Statistical analysis was performed using the summary statistics method.

Statistical Analysis

The obtained data were analyzed using descriptive statistics method. All the analyses were performed by SPSS 23.0 for Windows. Numbers, percentages, means, standard deviations, medians, and ranges were used in the presentation of descriptive data.

RESULTS

A total of 114 adult patients aged between 18-20 years and older, who were diagnosed as rosacea with at least 2-3 months of controls, were included in the patient information system of Çanakkale Onsekiz Mart University Medical Faculty Hospital. Of the 114 patients, 76.3% (n=87) were female and 23.7% (n=27) were male. The mean age of the patients was 46.5±10.9 years, the median age was 45.0 years (range 21-72). Disease groups frequently related to rosacea patients: hypertension 19.3% (n=22), gastroesophageal/dyspepsia 14.9% (n=17), hyperlipidemia 13.2% (n=15), diabetes mellitus 13.2% (n=15), hypothyroidism 10.8% (n=12), obesity 9.6% (n=11), and depression 9% (n=10) (Table 1). The data of patients are shown in Table 1.

DISCUSSION

Recent studies on rosacea have shown that rosacea has an important relationship with cardiovascular, gastrointestinal, and psychiatric diseases that can affect morbidity and mortality. However, the pathogenesis of rosacea is not well understood and the causal relationship between these diseases and rosacea is still not fully understood. Recent data suggest that adaptive immune system activation and proinflammatory cytokines are effective in the development of the disease. Due to these recent data, the relationship between rosacea and comorbid diseases may also be similar. We found cardiovascular diseases (CVD), obesity, gastrointestinal tract diseases, autoimmune diseases, and psychiatric disorders as frequent diseases related to rosacea and discussed the

Table 1. Distribution of patients with comorbidities in the study group.

Comorbidities	n (%)
Ocular involvement	5 (4.4)
Rhinophyma	5 (4.4)
Diseases of the gastrointestinal tract	23 (20.3)
Inflammatory bowel disease	2 (1.8)
Irritable bowel syndrome	2 (1.8)
Gastroesophageal reflux/Dyspepsia	17 (14.9)
Lactose intolerance	1 (0.9)
Recurrent aphthous stomatitis	1 (0.9)
Hypertension	22 (19.3)
Hyperlipidemia	15 (13.2)
Diabetes mellitus	15 (13.2)
Autoimmune diseases	13 (10.6)
Celiac disease	1 (0.9)
Hashimato thyroiditis	7 (5.3)
Alopecia areata	1 (0.9)
Vitiligo	1 (0.9)
Rheumatoid arthritis	3 (2.6)
Hypothyroidism	12 (10.8)
Psychiatric disease	12 (10.8)
Depression	10 (9)
Major depression	1 (0.9)
Obsessive compulsive disorder	1 (0.9)
Allergic diseases	11 (9.9)
Atopic dermatitis	1 (0.9)
Allergic rhinitis	6 (5.4)
Asthma	2 (1.8)
Urticaria	2 (1.8)
Obesity	11 (9.6)
Venous insufficiency	8 (7)
Fibromyalgia	8 (7)
Female hormone disorder	6 (5.3)
Hyperprolactinaemia	2 (1.8)
Hirsutismus	1 (0.9)
Polycystic ovary syndrome	3 (2.6)
Arthralgia	6 (5.4)
Pituitary adenoma	4 (3.5)
Epilepsy	3 (2.6)
Carpal tunnel syndrome	3 (2.6)
Hyperthyroidism	2 (1.8)
Urogenital disease	2 (1.8)
Cerebrovascular disease	2 (1.8)
Chronic obstructive pulmonary disease	2 (1.8)
Psoriasis	2 (1.8)
Sacroiliitis	2 (1.8)
Familial Mediterranean fever	1 (0.9)
Gallstone	1 (0.9)
Coronary artery disease	1 (0.9)
Deep vein thrombosis	1 (0.9)
Parathyroid adenoma	1 (0.9)
Suprarenal mass	1 (0.9)
Parkinson's disease	1 (0.9)
Vertigo	1 (0.9)
Malignancy (endometrial cancer)	1 (0.9)

possible mechanisms between these diseases and rosacea in our retrospective study [7].

Rosacea is one of the inflammatory skin diseases. The chronic inflammatory nature of rosacea is similar to many other chronic inflammatory skin diseases such as psoriasis. Inflammation plays a prominent role in atherosclerosis [8]. And many studies have reported that there is a relationship between psoriasis and CVD [9]. In a study, it has been suggested that chronic inflammation in rosacea may be systemic [6]. Systemic inflammation may cause structural changes in lipoproteins and this event may also negatively affect their ability to take cholesterol [8]. Paraoxonase-1 is a high-density antioxidant enzyme related to lipoprotein. It has been shown that serum paraoxonase-1 activity was significantly decreased in patients with rosacea just as in dyslipidemic patients [10]. In our study, we found a high rate of hyperlipidemia 13.2% (n=15), and hypertension 19.3% (n=22), which is one of the risk factors for CVD by the literature. The most important causal factor in the rosacea frequent related to CVD may be Systemic inflammation

Besides, another condition that we detected was obesity in our patients with rosacea. In some studies, patients with rosacea were found to be overweight [11]. This may be related to the chronic inflammatory structure of rosacea. Similarly, it has been shown that obesity prevalence increased, and this condition was in parallel with the severity of the disease in psoriasis patients, who are considered to be a systemic inflammatory disease [12]. Tumor necrosis factor alpha, an important proinflammatory cytokine that plays a role in the pathogenesis of psoriasis is present at an increased level in both psoriasis and obesity and is produced by adipose tissue [13]. Other cytokines and bioactive products produced by adipose tissue such as interleukin-6, leptin, resistin, and adiponectin (also known as adipokines or adipocytokines) may also trigger psoriasis [14]. The relationship between rosacea and obesity may be similar. So, rosacea patients may be obese due to the chronic inflammatory nature of the disease and obesity may aggravate the clinical status of rosacea due to the increased inflammatory substances produced by adipose tissue.

In the literature, the relationship between rosacea and gastrointestinal system diseases is controversial [5,15,16]. For example, in a Danish study that includes more than 49,475 patients with rosacea and more than 4.3 million control patients, a modestly increased relationship was found between various gastrointestinal diseases including rosacea and celiac disease. Also, in a study evaluating 113 patients with rosacea, it was shown that the prevalence of excessive bacterial growth in the small bowel was higher in the patients with rosacea, and a complete regression was achieved in the cutaneous lesions by eradication of this condition [16]. It has been reported that there was no relationship between excessive bacterial proliferation with rosacea in the small intestine at another study in which 90 rosacea patients were evaluated. Besides, some studies have shown that the prevalence of Helicobacter pylori in patients with rosacea has increased [15]. In our study, gastroesophageal/dyspepsia 14.9% (n=17) was found to be the highest frequency relationship among gastrointestinal diseases. We found that inflammatory bowel disease 1.8% (n=2), irritable bowel syndrome 0.9% (n=1) and celiac disease 0.9% (n=1) was less than other diseases. The relationship between rosacea and diseases affecting our gastrointestinal tract which is one of our barrier tissues makes us think that it may be a factor in the pathogenesis of rosacea in dysbiosis.

The conglomerating of autoimmune diseases is a well-known phenomenon. A case-control study in Denmark was found that the risk of autoimmune diseases such as type 1 diabetes mellitus, celiac disease, multiple sclerosis, and rheumatoid arthritis was increased in rosacea patients [17]. The relationship between these autoimmune diseases and rosacea was found to be stronger in female patients. Indeed, many autoimmune diseases are considered to be more common in women [18]. There is also more female predominance in rosacea. The genome-wide association study, in which the genetic basis of rosacea is evaluated has been shown that rosacea with type 1 diabetes mellitus, celiac disease, multiple sclerosis, rheumatoid arthritis or a combination of these share the same genetic risk locus. [19]. In our study, diabetes mellitus was seen more frequently, other autoimmune diseases such as celiac disease, Hashimoto thyroiditis, and rheumatoid arthritis were found to be more frequently related to in our rosacea patients.

The risk of reduced rosacea was found in patients with advanced-stage diabetes who are using glucose-lowering drugs in a study which is performed in the UK in a clear mismatch with our results [20]. However, in our patient registry system, such a type separation cannot be made concerning the diagnosis of diabetes mellitus. Therefore, our study includes all types of diabetes for the diagnosis of diabetes mellitus in patients with rosacea. The knowledge of these autoimmune comorbidities can generally provide a better understanding of the pathogenesis of rosacea. Autoinflammatory pathways may also contribute to the course of the disease and perhaps may also be related to the clinical presentation of rosacea (erythematotelangiectatic, papulopustular, phymatous, and ocular rosacea).

In another study, a significant relationship was found between major depressive disease and rosacea [21]. In our study, the most common psychiatric disorder in our patients with rosacea was depression. Only one patient was diagnosed with major depression.

Besides, a significant improvement in the quality of life has been reported after using decorative cosmetics in rosacea patients and in skin diseases that make involvement in visible other areas of the body. And this suggestion makes it think that the central facial localization of rosacea is an important cause of the observed relationship between rosacea and

depression [22]. However, rosacea and depression share some mutual inflammatory pathways [2,23]. MMP contribute to the pathology physiology of rosacea and some studies, it was found that serum MMP levels have increased in depressive patients, too [24]. Therefore, further studies are needed to clarify the relationship and underlying mechanisms between rosacea, depression, and anxiety disorders.

It has been reported in studies on psoriasis and comorbidities that the risk of comorbidities has increased due to the increment of the inflammatory load as the severity of the disease increases [25]. Because our study does not include disease severity, more studies are needed to confirm this hypothesis.

In our study, although there is a relationship between rosacea and chronic systemic diseases, pathophysiological connections are complex. These connections may be underlying chronic inflammatory mechanisms such as inflammatory cytokines, metabolic, immune, and endocrine changes.

Our study is a retrospective study and the number of patients included in the study is limited. Also, the database we use does not contain information about clinical subtypes of rosacea, clinical severity of rosacea, and laboratory data. And the data of a certain number of patients recorded in the hospital information system could be only examined. Therefore, prospective studies need to increase the number of patients and record more data.

Our study provides evidence supporting the relationship between rosacea and systemic comorbidities. Rosacea is more associated with hypertension, gastroesophageal/dyspepsia, hyperlipidemia, diabetes mellitus, hypothyroidism, obesity, and depression. Rosacea which can be easily diagnosed as a result of dermatological examination may be a clue for dermatologists in screening comorbid diseases related to. Dermatologists should be aware of these systemic comorbid diseases, which are often related to rosacea to provide better follow-up and treatment for patients with rosacea. Thus, more effective patient management will be provided in rosacea patients.

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