Rosacea Comorbidities

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KEYWORDS

• Rosacea • Comorbidities • Depression • Cardiovascular diseases • Malignancies • Autoimmune • Neurologic disorders

KEY POINTS

- Several comorbidities have been found to be associated with rosacea, including cardiovascular diseases, depression, gastrointestinal disorders, malignancies, neurologic diseases, and autoimmune conditions.
- Although the exact etiologic factors of rosacea remain to be elucidated, the physiopathology of rosacea is multifactorial, and numerous cell and molecular mechanisms may contribute to the development of rosacea and its comorbidities.
- A chronic inflammatory state may be the underlying mechanism that accounts for its association with cardiovascular diseases.
- Upregulation of matrix metalloproteinases and antimicrobial peptides is the proposed link for rosacea and neurodegenerative disorders.
- Transient receptor potential vanilloid channels are the proposed mediators of neurogenic inflammation that contributes to the physiopathology of rosacea, depression, and migraine.

INTRODUCTION

Rosacea is a common chronic skin disorder characterized by erythema, telangiectasias, flushing, pustules, and fibrosis affecting the central face.[1] Fluctuations in body temperature, psychological factors, ultraviolet exposure, and lifestyle practices, such as alcohol and caffeine intake, are thought to trigger rosacea flares.[1,2] Although the pathogenesis of rosacea is not completely understood, it is regarded as a multifactorial process. Rosacea symptoms are generally thought to be due to an inflammatory process that results from the complex interplay of an aberrant immune system, neurovascular changes, ultraviolet radiation, epidermal barrier dysfunction, and abnormal skin flora.

Rosacea is associated with several comorbidities, including cardiovascular diseases (CVDs), depression, gastrointestinal disorders, malignancies, neurologic conditions, and autoimmune disorders[3–7] (**Fig. 1**). The authors reviewed the literature concerning comorbidities associated with rosacea.

METHODS

A review of English-language articles was performed using PubMed and Google Scholar. Search terms included rosacea, comorbidities, depression, CVD, autoimmune disease, malignancy, and neurologic disorders. Results were categorized by the comorbidity associated with rosacea or by pathophysiologic relationship linking rosacea to a comorbid condition. Results included information since the first description of the association between migraines and rosacea in 1976, as well as more contemporary

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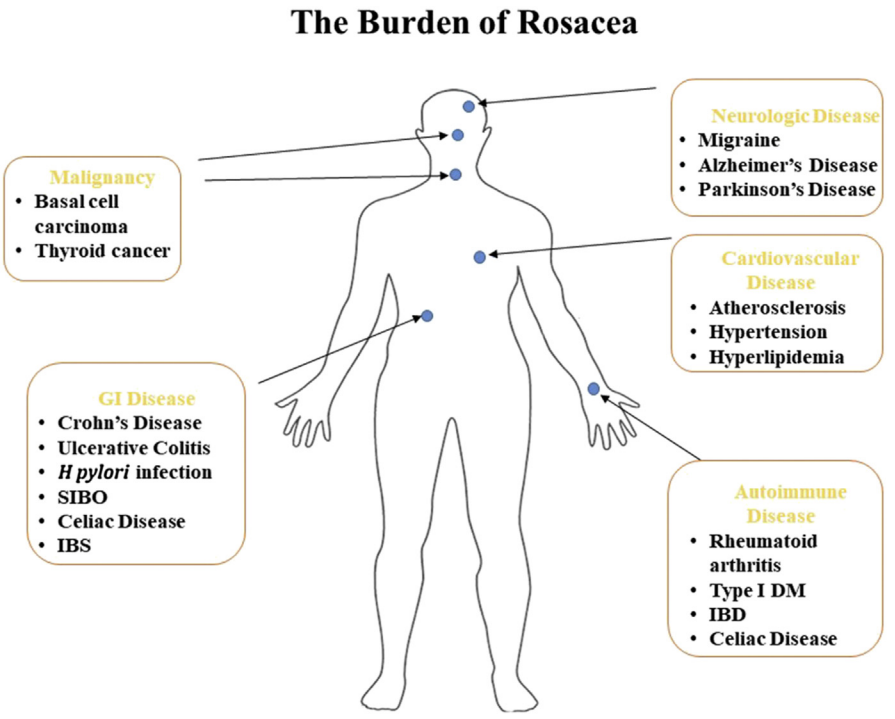

Fig. 1. An overview of comorbidities most commonly seen with rosacea. *H. pylori, Helicobacter pylori*.

epidemiologic data, etiologic data, and retrospective reviews conducted over the past 30 years.

ROSACEA-ASSOCIATED COMORBIDITIES

Cardiovascular Diseases

Inflammation plays a key role in the pathogenesis of rosacea and is an established risk factor in the development of atherosclerosis and its complications. Rosacea and atherosclerosis share the upregulation of cathelicidin in inflammatory cells and low serum paraoxonase-1 (PON-1) activity.[1,8–10] In the skin and vasculature, apart from its antimicrobial activity, cathelicidin functions as an immune modulator, inducing expression of inflammatory genes, leading to cytokine and chemokine liberation from local cells and leukocytes.[8] Injection of mice with cathelicidin peptide fragments from the skin of patients with rosacea produced a rosacea-like dermatitis.[11] Furthermore, cathelicidin-deficient mice were protected against atherosclerosis.[12]

PON-1 is an antioxidant enzyme that protects against atherosclerosis by metabolizing lipid peroxides and preventing the oxidative modification of serum lipoproteins. PON-1–knockout mice developed atherosclerosis faster than their wild-type litter mates on a high-fat diet.[13] In subjects with CVD, PON-1 activity is decreased by half compared with healthy subjects.[14,15] Serum PON-1 enzyme activity was lower in subjects with rosacea than in healthy controls.[10] Altogether, these studies suggest that an increase in cathelicidin and oxidative stress are contributing factors to the pathogenesis of rosacea and atherosclerosis. However, only a few studies have investigated whether patients with rosacea have higher risk of CVD.[7,16–18] One study noted increased prevalence of hyperlipidemia, hypertension, metabolic syndrome, and CVD in patients with rosacea.[17] A retrospective review of National Health Insurance Research Database in Taiwan revealed that patients with rosacea were more likely to have dyslipidemia (odds ratio [OR] 1.41, 95% CI 1.36–1.46), coronary artery disease (OR 1.35, 95% CI 1.29–1.41), and hypertension (OR 1.17, 95% CI 1.12–1.21) compared with controls.[7] Although these studies indicated a higher prevalence of CVD and CVD risk factors in patients with rosacea, the increased frequency of hypercholesterolemia in that patient population may have been confounded by higher incidence of alcohol consumption and smoking.[16] More recently, a Danish population-based study determined that rosacea was not independently associated with CV risk.[18] Future studies are needed to elucidate the relationship between CVD and rosacea.