Below the Surface

New research continues to suggest rosacea is more than just a skin disease with increased risk of other systemic diseases.

New studies are now revealing potential associations between rosacea and increased risks of cardiovascular disease, gastrointestinal disease, certain types of cancer, and many other systemic illnesses.

“Recently, there have been a growing number of reports associating rosacea with a variety of potentially serious diseases,” said Dr. Richard Odom, professor of dermatology at the University of California-San Francisco in a National Rosacea Society (NRS) release. “Although it’s important to note that causal relationships between rosacea and these other diseases have not been demonstrated, this provides further reason for people who suspect they may have rosacea to seek diagnosis and appropriate treatment.”

EVALUATING SYSTEMIC DISEASE RISK FOR PATIENTS WITH ROSACEA

Researchers in Taiwan investigated the associations of rosacea with cardiovascular disease risk factors and cardiovascular diseases from a nationwide population-based database. A total of 33,553 patients with rosacea and 67,106 age- and gender-matched control subjects were identified from the National Health Insurance Research Database in Taiwan from 1997 to 2010. Multivariate logistic regressions were performed to compare the odds of comorbidities between the 2 groups. The researchers found that those patients with rosacea had a 41 percent greater risk of high cholesterol, a 35 percent higher risk of coronary artery disease, and a 17 percent greater risk of high blood pressure than people without rosacea, according to the published findings in the Journal of the American Academy of Dermatology (JAAD).¹

The NRS also refers to the well-known Nurses Health Study II as research pointing to increased health risks among patients with rosacea. In this study, an ongoing biennial questionnaire on the medical history of 116,000 nurses since 1989, the more than 6,000 women diagnosed with rosacea, according to the published findings in the Journal of the American Academy of Dermatology (JAAD).²

Among 130 participants (65 patients/65 control subjects), the researchers observed a significant association between rosacea and allergies (airborne, food), respiratory diseases, gastroesophageal reflux disease, other gastrointestinal diseases, hypertension, metabolic and urogenital diseases, and female hormone imbalance. Compared with mild rosacea, moderate to severe rosacea was significantly associated with hyperlipidemia, hypertension, metabolic diseases, cardiovascular diseases, and gastroesophageal reflux disease.

Study authors noted that the study was limited because it was a case-control study with moderate sample size, and associated medical conditions were self-reported and could not always be confirmed by medication use and medical records.

The researchers concluded that rosacea is associated with numerous systemic comorbid diseases in a skin severity-dependent manner and that physicians should be aware of these associations to provide comprehensive care to patients with rosacea, especially to those with more severe disease.

Other recent studies have found increased risks of inflammatory bowel disease in people with rosacea, according to the NRS.

ROSACEA AND NEUROLOGIC SYMPTOMS

According to a nationwide cohort study in Denmark, rosacea may increase risk for glioma. The findings, published online in JAMA Dermatology,³ suggest that an increased focus on neurologic symptoms in patients with rosacea may be warranted.

Exactly how the two conditions are linked is not fully understood. “This association may be mediated, in part, by mechanisms dependent on matrix metalloproteinases,” study authors write. Rosacea has a poorly understood pathogenesis in which increased matrix metalloproteinase activity might play an important role. Glioma accounts for 80 percent of all primary malignant tumors in the central nervous system, and these tumors also show upregulation of certain matrix metalloproteinases, they note.

All Danish citizens 18 years or older from January 1, 1997, to December 31, 2011, were eligible for inclusion in the cohort study. A total of 5,484,910 individuals were eligible for analysis; of these, 68,372 had rosacea and 5,416,538 constituted the reference population. Data were analyzed from July 14 to August 10, 2015. Of the 5,484,910 individuals in the study population, 21,118 individuals developed glioma during the study period, including 20,934 of the 5,416,538 individuals in the reference population (50.4

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percent women; mean [SD] age, 40.8 [19.7] years) and 184 of the 68,372 patients with rosacea (67.3 percent women; mean [SD] age, 42.2 [16.5] years). The incidence rate of glioma was 3.34 (3.30-3.39) in the reference population and 4.99 (4.32-5.76) in patients with rosacea. The adjusted incidence rate ratio of glioma in patients with rosacea was 1.36 (1.18-1.58) in the primary analysis. The adjusted incidence rate ratio was 1.82 (1.16-2.86) when analyses were limited to patients with a primary diagnosis of rosacea by a hospital dermatologist (n = 5,964), the study showed.

Another new study suggests that rosacea may be linked to an increased risk of dementia—in particular Alzheimer’s disease.

This risk was highest in older patients and in patients where rosacea was diagnosed by a hospital dermatologist. The new findings are published in the Annals of Neurology. As with glioma, exactly how dementia and rosacea are linked is unknown, but it is known that rosacea is characterized by elevated expression of certain proteins—including matrix metalloproteinases and antimicrobial peptides—that are also involved in various neurodegenerative disorders such as Alzheimer’s disease and other forms of dementia.

Researchers, led by Alexander Egeberg, MD, PhD, a dermatologist at the University of Copenhagen in Denmark, investigated the association between rosacea and dementia in Danish registers. There were 5,591,718 Danish citizens aged ≥18 between 1997 to 2012, including 82,439 patients diagnosed with rosacea. Individuals were followed until December 31, 2012, migration, a diagnosis of dementia, or death from any cause, whichever came first. A total of 99,040 individuals developed dementia, of which 29,193 were diagnosed with Alzheimer’s disease.

After adjustments for potential confounding factors, patients with rosacea had a seven percent increased risk of dementia and a 25 percent increased risk of Alzheimer’s disease compared with individuals without rosacea. Women had a 28 percent increased risk of Alzheimer’s disease and men had a 16 percent increased risk if they had rosacea. When analyses were stratified by age at study entry, the risk of Alzheimer’s disease was only significantly increased in individuals ≥60 years (who had a 20 percent increased risk). When analyses were limited to patients with a hospital dermatologist diagnosis of rosacea only, the increased risks of dementia and Alzheimer’s disease were 42 percent and 92 percent, respectively, the study showed.

“A subtype of patients have prominent neurological symptoms such as burning and stinging pain in the skin, migraines, and neuropsychiatric symptoms, suggesting a link between rosacea and neurological diseases,” explains Dr. Egeberg in a news release. “Indeed, emerging evidence suggests that rosacea may be linked with neurological disorders including Parkinson’s disease and now also Alzheimer’s disease.”

Further research is warranted to examine whether treating rosacea may also modify patients’ risk of developing dementia.

DEPRESSION, ANXIETY, AND ROSacea

The Danish cohort study also investigated the relationship between rosacea and new-onset depression and anxiety disorders. The investigation comprised a total of 4,632,341 individuals, including 30,725 and 24,712 patients with mild and moderate-to-severe rosacea, respectively. The study results found that rosacea was associated with a disease severity-dependent, increased risk of depression and anxiety disorders. The findings may call for increased awareness of psychiatric morbidity in patients with rosacea, the authors concluded.

2. Li WQ, Zhang M, Dang WY, Yan J, Qureishi AA. Personal history of rosacea and risk of incident cancer among women in the US. Br J Cancer. 2015;113:520-523.