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A Multidirectional Interrelationship: Iron Deficiency Anemia Begets Angular Cheilitis and Atrial Fibrillation, Atrial Fibrillation Begets Heart Failure and Heart Failure Begets Atrial Fibrillation and Anemia

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Angular cheilitis is a specific type of cheilitis characterized by inflammatory affecting the vermilion and surrounding skin of the lips. Various systemic conditions that cause stress, lower immunity, and increase mucosal susceptibility to infection can contribute to the development of angular cheilitis. One significant factor is iron deficiency, which results from a decrease in hemoglobin levels and erythrocyte concentration. This report describes a case of angular cheilitis associated with complex cardiac interrelationships.

A 74-year-old woman presented with a history of chest palpitations. She followed a vegetarian diet and complained of fatigue and decreased exercise tolerance. On examination, she had red, dry, scaly lips resembling lip rouge, along with koilonychia, conjunctival pallor, and pale skin (Figure 1). An electrocardiogram demonstrated atrial fibrillation, and blood tests revealed iron at 25 mcg/dl, hemoglobin at 8.3 g/dl, and ferritin 4 mcg/ml, with normal reticulocyte and platelet levels. She was not on antiplatelet or anticoagulant medications. Endoscopy, colonoscopy, and pelvic ultrasound results were normal. Additionally, echocardiography indicated an ejection fraction within the normal range of 55%. Parameters such as septal and lateral annular peak early diastolic velocities, tricuspid regurgitation velocity, left atrial size, and left ventricular mass index were all within normal limits. In this patient with atrial fibrillation, the N-terminal pro-brain natriuretic peptide (NT-proBNP) level was 600 pg/ml, compared to a normal value of 500 pg/ml. The diagnoses were heart failure with preserved ejection fraction, atrial fibrillation, angular cheilitis, and iron-deficiency anemia. The patient was started on a regimen of 20 mg of rivaroxaban and 20 mg of furosemide daily.

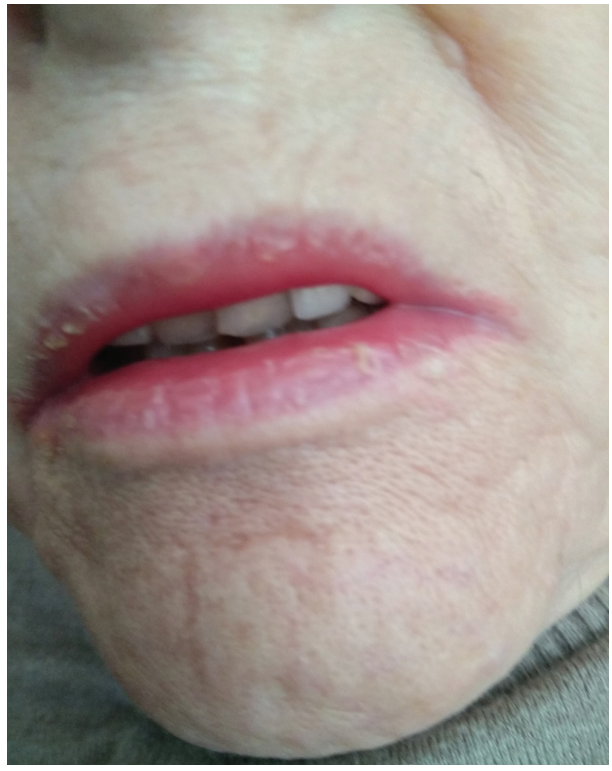

FIG. 1. The patient had red, dry, scaly lips resembling lip rouge, along with koilonychia, conjunctival pallor, and pale skin.

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After 3 months of iron therapy, her anemia and cheilitis improved, and her levels of fatigue and discomfort decreased. The NT-proBNP level was reduced to 500 pg/ml.

The described patient developed angular cheilitis associated with iron deficiency, atrial fibrillation, and heart failure with preserved ejection fraction. In patients with normal left ventricular function, anemia itself may cause high-output heart failure.[1] Iron deficiency can induce atrial fibrillation through arrhythmogenic substrates, such as oxidative stress, ion channel remodeling, and improper calcium handling.[2] Correction of severe anemia in these patients leads to a rapid and complete regression of high-output heart failure. Anemia exacerbates cardiac dysfunction due to tachycardia and increased stroke volume, creating a vicious cycle in which anemia leads to heart failure, which then further exacerbates anemia and cardiac function, contributing to kidney damage. Patients with heart failure and preserved ejection fraction may experience increased systemic vascular resistance, left ventricular afterload, and decreased left ventricular ejection fraction if their hemoglobin levels are elevated.[3] Heart failure can arise from any structural or functional heart issue,[4] potentially explaining the inverse relationship between hemoglobin levels and left ventricular ejection fraction observed in some studies.[1]

Atrial fibrillation is one of the most common clinically significant arrhythmias[5] and is linked to higher ventricular rates and stress, increasing the risk of developing heart failure, known as tachyarrhythmia-induced cardiomyopathy. Atrial fibrillation commonly develops in patients with heart failure. Left ventricular overload, transferred to the atria through the mitral valve,[6] causes atrial stretch and fibrosis, resulting in atrial fibrillation in advanced stages of heart failure. Moreover, NT-proBNP is a better biomarker for atrial fibrillation than for heart failure in stable outpatients with cardiovascular risk factors. It should not be used to diagnose chronic heart failure in patients with atrial fibrillation or heart failure with preserved ejection fraction. If heart failure is absent and NT-pro-BNP levels are elevated, screening for atrial fibrillation should be considered.[7]

Conversely, heart failure can cause atrial fibrillation due to elevated cardiac filling pressures, abnormal intracellular calcium homeostasis, and impaired autonomic and neuroendocrine function. Chronic anemia can lead to left ventricular hypertrophy, exacerbating heart failure and causing cardiac cell death through apoptosis. This further perpetuates kidney damage,[8] as the kidneys produce erythropoietin, a protein necessary for red blood cell production. Low erythropoietin levels due to renal dysfunction can result in anemia, creating a vicious cycle between heart failure and anemia.

In our patient, the primary clinical manifestation of iron deficiency anemia was angular cheilitis. This condition was linked to atrial fibrillation and heart failure, emphasizing the importance of examining these interrelated conditions in individuals without a clear underlying cause. Cardiovascular disorders are often accompanied by anemia, particularly in the context of heart failure and coronary artery disease. This association warrants careful consideration across various medical fields, including internal medicine, pediatrics, dentistry, geriatrics, dermatology, cardiology, and primary care.[9]

Informed Consent: Informed consent was obtained from all cases.

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