Letter in reply: Pericarditis and peripheral edema in a healthy man on low-dose oral minoxidil therapy

To the Editor: In the recent article titled "Pericardial, pleural effusion and anasarca: A rare complication of low-dose oral minoxidil for hair loss," Dlova et al[1] reported a case of a previously healthy 40-year-old black woman who developed pericardial and pleural effusions after 3 weeks of low-dose oral minoxidil (LDOM) for frontal fibrosing alopecia. The report is an important contribution to the literature as it is the first to highlight serious potential adverse effects of LDOM. As acknowledged by Dlova et al,[1] minoxidil at hypertensive dosages (10-40 mg) is associated with severe cardiopulmonary adverse effects, including pericardial effusions in 3% of patients.[2] In the United States, the Food and Drug Administration issued a black-box warning for pericardial effusion, cardiac tamponade, and electrocardiogram (EKG) changes for oral minoxidil therapy. The potential for these adverse events explains its indication for only severe, treatment-resistant hypertension. Despite these warnings, recent reviews support the theory that LDOM (0.25-5 mg) possesses a mild side-effect profile.[3,4] The case described by Dlova et al[1] raises legitimate concerns that this may not be true in all patients.

We would like to extend the discussion by commenting upon a case of a 52-year-old athletic man who developed pericarditis and peripheral edema after 2 weeks of LDOM therapy (2.5 mg daily) for androgenic alopecia. He had a medical history significant for idiopathic pericarditis complicated by pericardial effusion 5 years prior but was otherwise healthy without coexisting cardiac, hepatic, or renal disease. Following his normal regimen of high-intensity exercise, he developed an acute episode of sharp chest pain that worsened in the supine position but improved with sitting and leaning forward. His medical evaluation was significant for low-grade fever (101.6) and laboratory values of elevated erythrocyte sedimentation rate 97 mm/h (ref: 0-24), C-reactive protein 216 mg/L (ref: 0-7.9), ferritin 593.5 ng/ml (ref: 20-300), and white blood cell count 16,000/μL (ref: 4500-11,000). He was on no other medications, denied illicit drug use, had no recent symptoms of viral illness, and had received no recent vaccinations. He had an unremarkable rheumatologic and infectious disease workup, including multiple negative tests for COVID-19, full viral panel, and negative antinuclear antibody and rheumatoid factor. EKG revealed diffuse ST elevation and PR depression across leads. An echocardiogram and cardiac magnetic resonance imaging were within normal limits with no signs of pericardial effusion or heart failure. Following discontinuation of oral minoxidil and initiation of ibuprofen and colchicine, inflammatory markers and EKG normalized, suggesting LDOM was responsible for his presentation. His symptoms of chest pain and peripheral edema resolved within 1 week. He completed a 3-month course of colchicine, resumed high-intensity exercise and has remained symptom free 6 months later.

As an antihypertensive medication, minoxidil is a potent peripheral vasodilator, reflexively activating the sympathetic nervous system and the renin-angiotensin-aldosterone pathway. By this mechanism, patients with preexisting fluid balance disorders (eg, chronic kidney disease, cirrhosis, congestive heart failure) on LDOM may be at especially high risk of developing serious adverse effects in a dose-dependent manner. Therefore, it seems reasonable for Dlova et al[1] to adjust their treatment strategy to include every other day treatment for 1 month and then adjust to daily. We would like to emphasize that despite these observations, the Food and Drug Administration black-box warning does not discuss issues of dose dependency. The optimal dosages to avoid these adverse effects are currently unknown, considering they have now been observed in even low-dose formulations. Owing to the seriousness of these cardiac complications, we emphasize the need for caution when prescribing LDOM, particularly for patients with high-risk medical histories.

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Key words: androgenic alopecia; edema; low-dose oral minoxidil; pericarditis.

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Conflicts of interest

All authors declare that they have no commercial or other associations that might pose a conflict of interest.

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