**CASE REPORT**

**Pericardial, pleural effusion and anasarca: A rare complication of low-dose oral minoxidil for hair loss**

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**Key words:** alopecia; alopecia treatment; cardiopulmonary side effects; frontal fibrosing alopecia; hair loss; lichen planopilaris; low-dose oral minoxidil; oral minoxidil; pericardial effusion; safety.

**INTRODUCTION**

Topical minoxidil has been used for many years in the treatment of androgenic alopecia and other hair disorders. Although the mechanism of action of topical minoxidil is poorly understood, animal studies have shown that it affects the hair growth cycle by shortening the telogen phase and prolonging the anagen phase.\(^1\,^2\) Lately, there has been growing evidence to support successful use of low-dose oral minoxidil (LDOM) in the treatment of various types of alopecia. The dosing regimens range from 0.25 to 5 mg daily to twice daily, with side effects reported to be dose dependent.\(^3\) We present the case of an African woman with frontal fibrosing alopecia (FFA) in whom pericardial, pleural effusion and anasarca developed 3 weeks after LDOM therapy.

**CASE REPORT**

A 40-year-old, healthy, Black, South African woman with no comorbidities presented with a 2-year history of hairline loss that involved the frontal and temporal hairlines. A dermatoscopic examination and histologic findings confirmed the clinical diagnosis of FFA. The patient was treated with 5% topical minoxidil, tacrolimus ointment 0.1%, clobetasol propionate ointment, 100 mg of doxycycline twice daily, and 0.25 mg of oral minoxidil (OM) daily. She was advised about the adverse effects of all the medications.

The patient consented to the publication of all photographs and medical information provided that is on file with the understanding that this information may be publicly available.

After 3 weeks of treatment, the patient noticed swelling of both lower extremities (Fig 1), which progressively spread to the upper extremities and face (Fig 2). She was advised to stop OM and present herself for follow-up, where she was admitted to the hospital for additional workup and further management by a cardiologist.

Cardiology assessment revealed generalized pitting edema involving the lower limbs, sacrum, and facial and periorbital areas as well as abdominal wall edema, without shifting dullness. Cardiovascular examination showed a regular pulse of 85 beats/min, with no pulsus paradoxus. Her blood pressure was 110/70 mm Hg, and all pulses were palpable. The heart sounds were normal, with no added sounds or murmurs. Respiratory examination yielded normal results. There was no clinical evidence of hepatic insufficiency.

The patient’s laboratory workup was unremarkable and included a comprehensive panel, which showed normal renal, hepatic, and thyroid function as well as normal levels of inflammatory markers. The albumin levels were within the normal range, and there was no indication of protein loss in the urine. Ultrasound showed fluid collections in the pericardium, pleural space, and abdomen. A plural...
effusion measured 31 mm on the right and 17 mm on the left (Fig 3). The portal vein and inferior vena cava were within normal limits. An echocardiogram revealed a small pericardial effusion, 0.6 cm in relation to the apex and 3 cm posteriorly, with no evidence of cardiac tamponade (Fig 4). The cardiac wall motion and valves were normal, with an ejection fraction of 70% (left ventricular internal diastolic diameter, 4.8 cm; left ventricular internal systolic diameter, 3.1 cm; innerventricular septal diameter, 1 cm; posterior wall diameter, 1 cm).

The patient was commenced on 40 mg of intravenous furosemide daily for 4 days with potassium replacement. Generalized edema was alleviated on diuretic treatment, with normalization by the fourth day in the hospital, after which the patient was discharged. Within 1 week after cessation of LDOM, the diuretics were discontinued, without any further recurrence of edema. At follow-up 2 weeks later, complete resolution was observed both clinically and using ultrasound, and the patient is still asymptomatic to date, 1 year later.

Having excluded other causes of pericardial effusion and anasarca in the previously healthy, young woman, we concluded that LDOM was responsible for her clinical presentation.

DISCUSSION

Minoxidil was first developed for the treatment of hypertension in the 1970s as a direct-acting peripheral vasodilator. LDOM has been studied for the treatment of different hair disorders, with the majority of treated cases being androgenetic alopecia. The other conditions include alopecia areata, telogen effluvium, traction alopecia, permanent chemotherapy-induced alopecia, monilethrix, loose anagen hair syndrome, and scarring alopecias (lichen planopilaris and FFA). The use of LDOM in the treatment of FFA is limited to a few case reports. One case described the use of LDOM in a premenopausal 46-year-old woman with FFA, wherein treatment with 0.1 mg of dutasteride daily and 1 mg of minoxidil daily stabilized hair loss. Pirmez and Abraham reported a satisfactory hair growth response after 6 months of LDOM treatment in 7 women with FFA who presented with moderate eyebrow loss.
Randolph and Tosti\(^8\) reviewed 17 studies, including 634 patients on LDOM as the primary treatment for 8 different types of alopecia, with the doses of OM used ranging between 0.25 and 5 mg. The most common adverse effect was hypertrichosis, which was observed in approximately 20% of the patients and was more frequently associated with higher doses of LDOM. Lower limb edema occurred in approximately 3% of the patients, the majority of whom were taking 5-mg dosages of OM. Cardiovascular events were rare and included hypotension and electrocardiography changes, with no severe cardiopulmonary adverse effects noted.\(^8\)

As an antihypertensive agent, OM is typically used at doses between 10 and 40 mg, and at this dosage, it has been shown to be associated with several severe cardiopulmonary adverse effects, with pericardial effusion occurring in 3% of patients.\(^9\) Patients with renal impairment and receiving dialysis are at a higher risk of developing pericardial effusion, although it can be observed rarely in patients without any identifiable cause.\(^9\) The relationship between minoxidil and pericardial effusion has been described to be an idiosyncratic drug reaction, in which the risk is not dose related or necessarily a known pharmacologic effect.\(^10\)

To the best of our knowledge, the occurrence of pericardial, pleural effusion and anasarca with the use of LDOM for alopecia has not been reported in the literature. Our extensive workup of this young, previously healthy patient did not suggest any underlying obvious cause; thus, we concluded that the patient’s presentation was a rare side effect and should be documented to alert other clinicians to look out for this uncommon adverse effect of LDOM. We have since advised patients to start with alternate days of LDOM for 1 month and then increase it to daily dosages thereafter. This case report serves to alert clinicians to be aware of this potential side effect.

**Conflicts of interest**
None disclosed.

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