Hypoestrogenic state in postmenopausal women has a wide array of effects on the cardiovascular system. Significant gender-based differences in coronary artery disease, left ventricular hypertrophy and cardiac remodeling post myocardial infarction have been well documented. Hormone replacement therapy (HRT) has been shown to reduce coronary heart disease and ameliorate vasomotor symptoms related to hypoestrogenism including hot flashes and palpitations. In this case we present a 56-year-old woman with a history of hyperlipidemia, resolved mild COVID-19 infection, latent tuberculosis and hypothyroidism who presented to the clinic with three weeks of palpitations. Review of symptoms was notable for persistent fatigue after COVID-19 infection and light-headedness associated with palpitations; she has not experienced syncopal symptoms, shortness of breath, or chest pain. The patient’s medications include levothyroxine 75mcg for hypothyroidism, omeprazole 20mg twice daily, estradiol-norethindrone acetate 1-0.5mg daily for post-menopausal vasomotor symptoms. She was also started on rifampin 600mg daily for treatment of latent tuberculosis two months prior. ECG in the clinic showed normal sinus rhythm with frequent premature atrial contractions. Rifampin is a well-known potent inducer of the cytochrome P-450 oxidative enzymes. The first step of estrogen metabolism in the liver is hydroxylation, mediated by cytochrome P450 enzymes. In this patient who was recently started on rifampin for treatment of latent tuberculosis, it can be reasonably postulated that plasma estrogen levels were decreased due to more rapid metabolism. HRT should be optimally titrated in these patients to obtain improved outcomes while on rifampin therapy, as was recommended in this patient with close gynecologic follow up. Palpitations in postmenopausal women on HRT should be carefully investigated for potential drug-drug interactions especially when starting P450 inducers, like rifampin.