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A Case Report on Peau'd Orange induced by Macitentan

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ABSTRACT

The incidence of pulmonary arterial hypertension (PAH) is increasing day by day. Newer advances in the management of PAH are being developed. The efficacy and safety of these agents is monitored by applying these in clinical practice. Here is a case of a 34yr old female diagnosed with severe PAH, RV dysfunction, heart failure with multiorgan dysfunction, diabetes mellitus and congestive heart failure. She was on sildenafil and ambrisentan+tadalafil combination for PAH. Initially ambrisentan was withheld due to complaints of fluid retention. Later macitentan which is known to cause comparatively less edema was started as a substitute for ambrisentan along with sildenafil. After 10 days patient developed generalised edema and weight gain of about 10kg. The skin developed orange peel-like (peau'd orange) appearance. Macitentan was withheld on the following day and the problem was resolved. Her clinical condition improved, she was ambulated and discharged on O_2 support. Need for a vigilant monitoring when using newer drugs is very essential for improving patient safety.

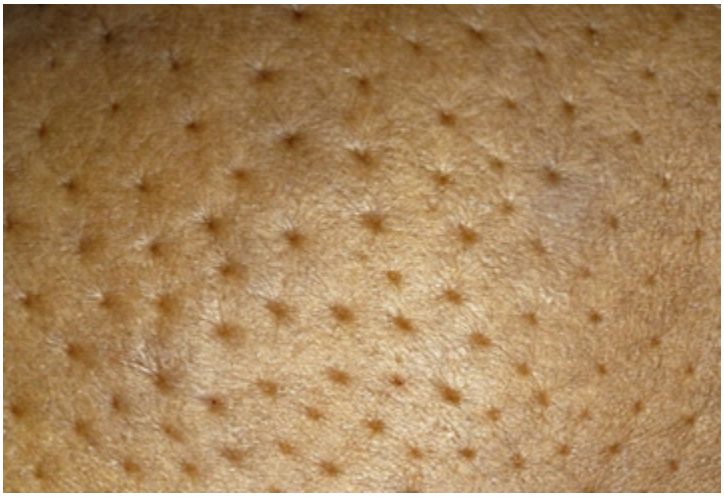
INTRODUCTION

PAH is defined as a chronic, progressive damage to the lung vasculature which results in right sided heart failure and ultimately death if left untreated[(1)]. Important advances in PAH therapy have been made, including the development of endothelin-receptor antagonists (ERAs).

Macitentan is a novel drug considered to be dual ERA exhibiting sustained receptor occupancy. The established safety profile of macitentan appears to be superior than bosentan and ambrisentan respectively, considering hepatic safety and fluid retention. The pharmacokinetics of macitentan in patients with renal or hepatic impairment does not require dose adjustments. Thus, based on the above mentioned features, macitentan is an important addition to the therapeutic armamentarium in the long term treatment of PAH[(2)]. Endothelin receptor antagonists, phosphodiesterase type 5 inhibitors and prostacyclin and its anlogues have been approved for treatment of PAH. Long term usage of macitentan had shown significant decrease in the prevalence of morbidity and mortality among PAH patients in the SERAPHIN (Study with an Endothelin Receptor Antagonist in Pulmonary Arterial Hypertension to Improve Clinical Outcome) trial[(3)].

CASE REPORT

A 34 year old female presented with swelling of legs and body since 1 month. She was a known case of primary pulmonary hypertension and was on warfarin, combination of ambrisentan and tadalafil. Ambrisentan was stopped due to fluid retention and the edema resolved. She was admitted and initiated on O_2, IV diuretic, LMWH and other medications. Patient had breathing difficulty with saturation drop and chest X-Ray showed left lower zone haziness. She continued to be O2 dependent. Instead of tab.ambrisentan, a different drug from the same class tab.macitentan 5mg which is less likely to cause edema was started in addition to sildenafil. After 10 days, patient developed generalised edema with orange peel-like skin appearance (peau'd orange) associated with a weight gain of 10 kg. The observed edema was non-pitting with indurations. The edema was



Representational Image

generalised but more prominent on the immobilised parts of the body. The patient also gained weight about 10 kg. The serum urea and creatinine values indicated normal renal function. Serum potassium levels were 3.5,3.3,3.7,3.6,4.3mg/dl on consecutive days of hospital stay which indicated hypokalemia. Also patient was found to be hyponatremic with serum sodium levels 128mg/dl and 132mg/dl. Peau'd orange describes a phenomenon in which hair follicles become buried in edema, giving the skin an orange peel appearance.

The edema got resolved with discontinuation of the drug. After the withdrawal of the agent, the excess weight gain got reverted which also improved the exercise capacity of the patient. The patient was discharged with home oxygen therapy. The patient was continued on sildenafil for management of pulmonary hypertension. Also the patient was asked to limit the fluid intake to 1.5L/day, avoid pregnancy and review after 1 month. On follow up, after 1 month she complained of early morning giddiness. Tab.metolazone once weekly was prescribed. Also the patient was started on tab.selexipag 200mcg ½-0-½ for better control of PAH.

DISCUSSION

A proper evaluation of the possible differential diagnoses was also discussed. The real photograph of the observed reaction could not be captured as the patient was not willing. PAH has become one of the major diseases to be addressed seriously. Until recently treatment options for PAH were very limited. Proper understanding of the disease etiology and pathophysiology has led to the emergence of newer agents that can improve pulmonary function and quality of life of the patients[4]. The paradigm for treatment of PAH continues to advance rapidly. Recent advances like endothelin receptor antagonists (ambrisentan, macitentan) should be used by weighing benefits and risks. These factors should be properly assessed before prescribing the drug into a wider population.

Advance in the development of these agents raises new questions about first line treatment and combination therapies. In the mean time, as more data becomes available, the treatment algorithm will continue to evolve in accordance with the evidence based approach [5].

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