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RESEARCH ARTICLE

Metoprolol Induced oral Lichen planus in An adult Female Patient – A Case Report

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ABSTRACT:

The prevalence of oral lichen planus (LP) in Indian population is 2.6% with more female predilection. LP is considered idiopathic but there are anecdotal reports of various medications like β-blockers, nonsteroidal anti-inflammatory drugs (NSAIDs), methyldopa, penicillamine, quinidine, quinine and angiotensin-converting enzyme (ACE) inhibitors.Metoprolol is rarely being reported to cause oral lichen planus despite its common usage. A 25 years old female patient developed bilateral oral lichen planus after administration of metoprolol, which was given for treatment of postpartum dilated cardiac myopathy with atrial fibrillation. Diltiazem was prescribed in place of metoprolol and patient was improved. Increased awareness of prescribers, close monitoring with immediate withdrawal of the culprit drug can reduce the complexity of management that occur due to development of such adverse drug reaction.

KEYWORDS: Metoprolol, Beta blockers, Oral lichen planus.

INTRODUCTION:

Lichen planus is an immune-mediated oral and cutaneous inflammatory disease, found in Indian population 0.5% to 2.6% of general population[1]. The prevalence of oral lichen planus in Indian population is 2.6% with more female predilection[2]. Oral lichen planus (OLP) is considered as a potentially malignant disorder with malignant transformation rate of 0.5% to 2%[3]. Skin lichen planus is the cutaneous counterpart of oral lichen planus affecting stratified squamous epithelium. Oral lesions are usually bilaterally distributed and appear as white streaks on erythematous areas. Buccal mucosa, tongue, and gingiva are the common sites affected by oral lichen planus[4]. Skin lesions appear as pruritic flat-topped violaceous papules of ankles, wrist, and genitalia.

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There are six recognized Oral lichen planus: reticular, papular, plaque, atrophic, erosive and vesiculo-bullous type[5]. Reticular lichen planus (RLP) presents Wickham's striae with erythematous margins. Erythematous lichen planus and atrophic lichen planus lesions exhibit erythematous back ground with radiating white striae. Plaque lichen planus appears as white plaque lesions whereas bullous lesions present as intraoral bullae[6]. The exact etiology of oral lichen planus is uncertain. Autoimmunity, immunodeficiency, food allergies, stress, trauma, diabetes and hypertension are considered as som e of the etiological factors for lichen planus[7].

Drugs causing Lichen planus like nonsteroidal anti-inflammatory drugs (NSAIDs), methyldopa, penicillamine, quinidine, quinine and angiotensin-converting enzyme (ACE) inhibitors. Metoprolol is a commonly used cardiovascular drug whose wide spread use can be attributed to its generic and affordable short

and long-acting formulations and its established safety and efficacy in treating a variety of cardiovascular disorders such as hypertension, arrhythmias, angina pectoris, acute coronary syndromes and congestive heart failure[8]. Metoprolol is rarely being reported to cause oral lichen planus despite its common usage. Metoprolol having previously reported ADRs like fatigue, insomnia and giddiness.

Case report:

25 years old adult female patient presented to medicine outpatient department of Sir Takhtasinhji General Hospital, Bhavnagar, Gujarat, India on regular basis follow up visit with complain of oral ulcer and pain over neck. Patient was known case of postpartum dilated cardiomyopathy with atrial fibrillation and hypothyroidism since two years. Patient was on following treatment, Tablet. Digoxin 0.25mg ½; 24 hourly, Tablet.Levothyroxine 100mcg 1 ½; 24 hourly, Tablet Alprax (Alprazolam) 0.25mg 1; 24 hourly, Tablet. Lasix (Furosemide) 40mg 1; 24 hourly, Tablet.Aldectone (Spironolactone) 25mg 2; 24 hourly, Tablet.Metoprolol 25mg 1; 12 hourly, Tablet. MVBC (multivitamin with B - complex) 1; 12 hourly, Tablet.Folic acid (800mcg) 1; 12 hourly and B. folcin (Choline salicylate) mouth ulcer gel 12 hourly.

Patient was referred to otorhinolaryngology and dermatology department for stomatitis. In otorhinolaryngology outpatient department, patient was advised Tablet. MVBC (multivitamin with B - complex) 1; 12 hourly, Tablet. Folic acid 1; 12 hourly, Tablet. Vitamin C (Ascorbic acid) 1; 24 hourly for 15 days. In dermatology outpatient department, patient was diagnosed to be suffering from oral Lichen planus possibly due to metoprolol. Patient was advised to use Triamcinolone oral gel 12 hourly, mucaine viscous gargle 12 hourly, betamethasone ointment local application 12 hourly, Tablet. Vitamin C (Ascorbic acid) 1; 24 hourly, Tablet. Metronidazole 400mg 1; 8 hourly and referred back to medicine department for alternative of metoprolol (β-blocker) in this particular case.

On same day patient came to medicine outpatient department and shifted to Tablet. Diltiazem 30 mg 1; 8 hourly as alternative to Tablet. metoprolol. After 03 months - patient admitted to medicine ward for atrial fibrillation with high ventricular rate which was reverted by Injection. Diltiazem. On discharge dose of Tabet. Diltiazem was increased to 1½; 8 hourly then patient was on monthly regular follow up.

After discontinuation of Tablet. Metoprolol for 03 months when patient came to medicine outpatient department on follow up day, lesions of oral lichen planus were resolving on left buccal mucosa and resolved to near normal buccal mucosa on right side.

WHO scale for causality assessment of suspected adverse drug reaction was "**PROBABLE**"[9]. Naranjo scale showed that the relationship between oral lichen planus and Metoprolol drug was "**PROBABLE**" **(SCORE 8)**[10].

According to Modified Schumock and Thronton's criteria, this reaction was definitely "**PREVENTABLE"**[11]. As per Modified Hartwig and Siegel's scale reaction was "**MODERATE (LEVEL 3)"**[12].

Figure 1:-Lesion on left side buccal (oral) lichen panus

Figure 2:-Lesion on left side buccal (oral) lichen panus after drug withdrawn

DISCUSSION:

Generally, β-blockers are known to be associated with Lichenoid drug eruption, affecting the oral cavity in 0.5% to 2% patients[13]. The peak age with oral lichen planus was found to be 30-60 years for both males and females. β-blockers may have a site-specific effect in patients with vulval Lichen Planus. This association was not found in patients with oral lichen planus. One proposed mechanism of action relies on the fact that there are β_2 receptors broadly present in the skin. Cyclic adenosine monophosphate (cAMP) is an intracellular messenger that stimulates proteins and is responsible for keratinocyte differentiation and inhibition of its proliferation. β -blockers are known to block cAMP

levels, therefore reduced cAMP levels result in upregulation of keratinocyte proliferation, reduced differentiation and increased lymphocyte motility[14].

The pathogenesis of β-blocker-induced lichenoid drug eruption is unclear but it may involve the blockade of β -adrenoreceptors. The β_2 subclass of receptors is present on epidermal keratinocytes, Langerhans cells, and dendritic cells[15]. These cells also possess pattern recognition receptors (PRR), whose role is to detect pathogen-associated molecular patterns (PAMP). Rises in inflammatory cytokines and antigen-specific plasmacytoid dendritic cells are necessary for the pathologic cascade of lichenoid tissue reactions that occur when skin is exposed to a non-selective β -blocker and a peptidoglycan (a PAMP)[16]. This suggests that the dermal adrenergic system may have a role in controlling the T helper-1(TH-1) response of pathogens that is recognized by the PRRs and thus its blockade with a β -blocker may potentially lead to a T helper-1-sustained skin inflammatory process such as a lichenoid tissue reaction[17].

The β -adrenergic system has been suggested to play a role in cutaneous homeostasis and in the pathogenesis of a number of inflammatory dermatoses[18]. In wound healing, the β-adrenergic system influences extracellular signal regulated kinases, which in turn affect keratinocyte migration[15]. The involvement of the cutaneous β-adrenergic system in multiple dermal processes may also suggest a more complex pathogenesis cascade in β-blocker-induced lichen planus.

The incidence of systemic illness associated with lichen planus included hypertension, diabetes mellitus, hypersensitivity reactions (asthma, allergy, gastritis, and arthritis), hyperthyroidism and skin vesiculo bullous lesions. About 71% of OLP cases were associated with systemic illness. Incidence of OLP is more common in females and in age group 30 – 60 years [19]. In this case, age of the female patient was 25 years. She was known case of hypertension and hypothyroidism and she also received β-blocker, which were the probable reasons of developing oral lichen planus.

So, healthcare professionals are expected to watch for rare adverse reactions like this and report them.

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