CASE REPORT

Tibolone induced Bullous pemphigoid

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Abstract

We present first ever report of Bullous pemphigoid induced by Tibolone, a STEAR (Selective tissue estrogenic activity regulator) that has progestogenic, some androgenic as well as estrogenic effects prescribed as an alternative to estrogen replacement therapy for treatment of climacteric symptoms in one of the 51 year old postmenopausal women with one and half year duration since menopause with previous history of use of estrogen progesterone pills during her active sexual life. The mechanism for this ADR is not well understood. But possible explanation could be progesterone activity of the drug leading to autoimmunity as reported previously. The present patient was managed by dechallenge of drug, local, oral corticosteroids and injectable, methotrexate, along with folic acid and antibiotic coverage fearing anemia and secondary infections.

Key Words

Tibolone, STEAR, Bullous Pemphigoid

Introduction

Adverse cutaneous drug reactions (ACDR) form an important clinical entity in clinical practice and the severity of such reactions vary from mild to fatal ones. The incidence of ACDR in developed countries range from 1-3% among in patients (1).Whereas, in developing countries like India it range to 2-5% (2). Bullous pemphigoid (BP) is a chronic inflammatory, autoimmune, subepidermal, blistering skin disease. Bullous dermatoses can be debilitating and possibly fatal. The drugs most commonly implicated in causing BP (3) are the antibiotics, especially beta-lactams, macrolides, co-trimoxazole, Furosemide, nonsteroidal anti-inflammatory agents. Although there are reports regarding hormones like, progesterone-induced erythema multiforme (4) and autoimmune progesterone dermatitis (5) in past but no report is available for tibolone induced BP.

Hence, the present case report of BP induced by Tibolone (6), a STEAR (Selective tissue estrogenic activity regulator) that has progestogenic, some androgenic as well as estrogenic effects prescribed as an alternative to estrogen replacement therapy for treatment of climacteric symptoms in one of the 51 year old postmenopausal women with one and half year duration since menopause with previous history of use of estrogen progesterone pills during her active sexual life is worth reporting.

Case

Onset of lesions was abrupt, within 1-5 days after starting the medication. Patients reported a diffuse pruritic or burning painful eruption associated with fever, malaise. The lesions were round to oval in shape, and ranged from skin-colored to erythematous. Nikolsky's sign, was usually positive. The buccal mucosa of the oral cavity was involved. Ruptured bullae leaved painful erosions. Itching was not a common symptom but complaint of hoarseness, dysphagia, and unpleasant mouth odor was present. Physical examination and per abdominal palpation did not reveal any abnormal finding. Cervix and vagina were healthy on per speculum examination without any bleeding from external os. On bimanual examination uterus was multipara sized, anteverted, mobile and fornices were free. Routine investigations, LFT, RFT, lipid profile and blood sugar were within normal limits. Ultrasonography of pelvic organs revealed normal uterus, ovaries and adenxa. TSH, T_4 & T_3 levels were within normal range. Laboratory studies during disclosed

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eosinophilia, leukocytosis, and elevated sedimentation rate. Subsequently she develop electrolyte abnormalities and hypoalbuminemia. Immunofluorescence study antinuclear antibodies, skin biopsy, direct and indirect immunofluorescence studies for linear deposits of IgG and C3 and histopathologic examination were not done due to non availability of test in rural setup and financial constrains on the part of patient. Patch testing of the offending drug was also not done in view of severity of reaction.

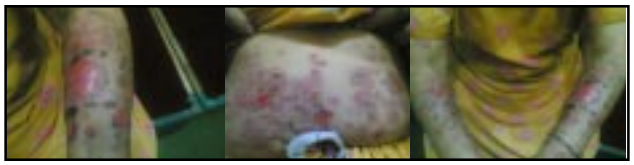

Fig 1: Tibolone induced Bullous pemphigoid (BP)

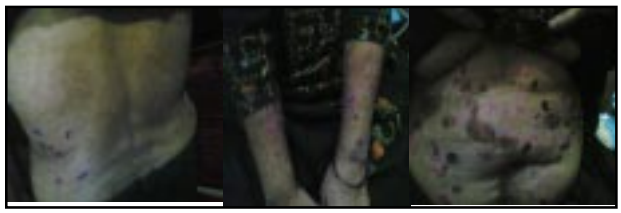

Fig 2: Withdrawal of the offending medication treatment of bullous drug reactions

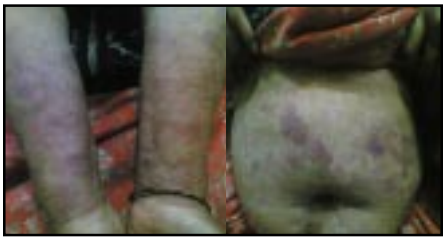

Fig 3: After Treatment

Discussion

No concurrent medicine intake or any pathology was found to be associated. Considering the possibility that tibolone might have some association with ADR, woman was advised to stop using the concerned product. De-challenge resulted in but medical intervention was required as the clinical situation war tented. Re-challenge, would have confirmed our suspicion of association between ADR and the suspected medicine but because of ethical constraints and severity of ADR, it was not done. Dose-response relation of this product with ADR was not studied therefore the type of ADR cannot be specified. Naranjao's adverse drug reactions (ADR) probability scale (7) evaluation was done to assess the likelihood of ADR occurring due to tibolone. It gave a score of 4 indicating a 'possible' relationship, which was further confirmed by WHO- UMC causality assessment criteria (8).

The mechanism for this ADR is not well understood. But possible explanation could be progesterone activity of the drug leading to autoimmunity as reported previously (4, 5). It has been suggested that the synthetic progesterone acts as a stimulus for antibodies which cross-react with natural progesterone leading to autoimmunity. This however needs to be substantiated. Another important aspect to note in this present case report is that women had past history of use of estrogen and progesterone during her active sexual life raising important question that does menopause makes women's more vulnerable for such autoimmune adverse reactions. The present patient was managed by local, oral corticosteroids and injectable, methotrexate, along with folic acid and antibiotic coverage fearing anemia and secondary infections.

Conclusion

Such aggressive or widespread BP with Tibolone is first reported case. The present case pleads for creating awareness among health care professional, especially the physicians to be aware of the possibility of this rare but serious life-threatening event when prescribing this drugs to vulnerable population due to advancing age and advise patients to discontinue use at the earliest possible sign or symptom appears as well as equip them how to treat/ manage such reaction.

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