Granuloma annulare likely induced by Solifenacin

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Abstract: Background: Granuloma annulare (GA) is a benign inflammatory skin disease with unknown etiology. It is a relatively common disease that can affect patients of different age groups. Granuloma annulare is characterized clinically by annular erythematous papules and plaques. It is self limited but it can be chronic and of significant discomfort. Solifenacin is a medication that is used to treat overactive bladder. Objectives: To report a 53 year old male who developed generalized granuloma Annulare after initiating Solifenacin for overactive bladder. Case report: 53 year old male with history of benign prostatic hyperplasia presented to dermatology clinic with annular erythematous eruption appeared 2 weeks after initiating Solifenacin to treat overactive bladder associated with BPH. Patient has no other medical problems aside from BPH and was not taking any medication prior to initiation of Solifenacin. He was seen at the dermatology clinic 3 weeks after appearance of this rash. Biopsy was taken from one of the lesions and it showed dermal infiltrate of palisading histiocytes and lymphocytes with degenerated collagen in the center. Patient was treated with topical corticosteroids for 2 weeks with no improvement. Solifeacin was discontinued and Lesions resolved 10 days after discontinuing the medication. Conclusion: After reviewing published data of reported cases of drug induced granuloma annulare, this is believed to be the first reported case of drug induced granuloma annular caused by Solifenacin. The clear temporal relationship between appearance of the rash after starting Solifenacin and resolution of rash after discontinuing the medication makes the possiblity of Solifenacin as the culprit of inducing granuloma annular in this patient very likely.

Keywords: Granuloma annulare, Solifenacin

Introduction:
Granuloma annulare is a relatively common benign self limiting skin disease that can affect patients of different age groups. Granuloma annulare (GA) can be associated with systemic diseases such as diabetes mellitus, thyroiditis, AIDS and malignancy,. GA can be associated with the use of certain medications like Allopurinol, Amlodipines, diclofenac. Solifenacin is a competitive muscarinic receptor antagonist which mainly works on M3 receptors. It is approved by US Federal and Drug Administration (FDA) for treatment of overactive bladder.

Histopathology of a biopsy taken from the lesion on left upper arm showing mid dermis with central mucin deposition and degenerated collagen surrounded by palisading histiocytes and lymphocytes.

Case Report: We report a 53 year-old male with past medical history of benign prostatic hyperplasia and overactive bladder. Patient was started on Solifenacin for overactive bladder at a dose of 5 mg po q day. 3 weeks after starting Solifenacin patient presented with annular erythematous non scaly plaques over dorsal hands, legs and arms. Rash appeared first on dorsal hands and then spread to dorsal feet, legs, arms and the back Rash was associated with burning sensation. Aside from Solifenacin, patient denied taking any other medication including over the counter medications. To confirm diagnosis, a 4 mm punch biopsy was taken from the lesion on right dorsal hand. Histopathology showed degenerated collagen in mid dermis surrounded by palisading histiocytes and lymphocytes consistent with the diagnosis of granuloma annulare. He was prescribed clobetasol ointment to affected areas twice a day for 14 days. Laboratory tests were done including complete blood count, basic metabolic profile and thyroid function tests and results came back normal. Patient was seen for follow up and he had no improvement after 2 weeks of using Clobetasol ointment to affected areas. Given close time association between the initiation of Solifenacin and appearance of GA, we thought this could be drug induced GA. After discussing our findings with the patient’s urologist, he agreed to discontinue Solifenacin. 3 weeks later, patient was seen at the dermatology clinic and skin lesions were completely resolved. Solifenacin was never restarted again and patient was disease free at 3 months follow up.
Left upper arm with annular erythematous non scaly plaque at presentation.

Left dorsal hand with annular erythematous plaque consistent with GA at first visit.

Left dorsal hand with complete resolution of GA 3 weeks after discontinuing Solifenacin.

Left dorsal hand with complete resolution of GA 3 weeks after discontinuing Solifenacin.

Discussion:
Drug induced GA is recently described entity with the first case reported in 1980. Several medications reported to induce GA including gold, allopurinol (3), diclofenac (4), amlodipine (1) and topiramates (2).

After reviewing published cases of drug induced GA, this will be the first reported case of Solifenacin induced GA.
Solifenacin is a competitive muscarinic receptor antagonist that is approved by FDA for the treatment of overactive bladder with symptoms of urge urinary incontinence, urgency, and urinary frequency. Side effects of Solifenacin includes dry mouth, blurred vision, constipation, urinary retention, angioedema, QT prolongation and renal impairment.

In conclusion, we think that GA like eruption that appeared in our patient is most likely induced by Solifenacin given the close temporal relationship between initiating the medication and appearance of the rash. Also that fact that the patient despite using strong topical corticosteroids, did not notice any improvement until Solifenacin was discontinued. And to our knowledge, this will be the first reported case of Solifenacin induced GA like eruption.

References: