

# *Doxycycline induce Photo-sensitivity in a 21year old female being treated for recurrent acute cystitis- a case report*

*Akwue Tochukwu Anthony<sup>a</sup> MD, Aneke Chukwuebuka Somto<sup>b</sup> MD*

<sup>a</sup>. Emergency Physician, Department of Emergency Medicine, Abha clinic and Emergency Hospital, Directorate of Health Affairs in Aseer region, kingdom of Saudi Arabia.

<sup>b</sup>. General Physician, Department of Paediatrics, Mosogar General Hospital, Ethiope West LGA, Delta State, Nigeria.

## **Abstract;**

Doxycycline belongs to tetracycline family which are a class of antibiotics that include demeclocycline, doxycycline, and minocycline and their mechanism of action involves binding to the 30s ribosomal subunit of bacteria and inhibiting bacterial protein synthesis <sup>1</sup>.

It is typically recognized as the most tolerable agent within tetracycline family<sup>2</sup>. In addition to that, it is predisposed to adverse drug reactions such as systemic and cutaneous adverse reactions such as photo-sensitivity. Photo-sensitivity to drugs include photo-allergic and photo-toxic reactions, in which the precise mechanism of doxycycline photo-allergy remains elusive<sup>3</sup>. The commonest clinical symptoms of photo-sensitivity ranges from pruritus and burning sensations from mild to moderate erythema of sun-exposed face and extremities <sup>4</sup>. Therefore early recognition and prompt treatment are essentials for better prognosis.

**Keywords:** Doxycycline, Tetracycline, Antibiotics, Photo-sensitivity.

## **Introductions:**

Tetracyclines are broad spectrum bacteriostatic antibiotics that inhibit protein synthesis. They are active against many gram positive and gram negative bacteria including anaerobes, rickettsiae, chlamydiae, mycoplasmas, and L forms and against some protozoa eg; amoeba<sup>5</sup>. They enter micro-organisms in part by passive diffusion and in part by an energy-dependent process of active transport. Susceptible cells concentrate the drug intracellularly and once inside the cell; binds reversibly to the 30s subunit of the bacterial ribosome; blocking the binding of aminoacyl tRNA to the acceptor site on the mRNA- ribosome complex and this process prevents addition of aminoacids to the growing peptide<sup>5</sup>. They are excreted in bile and urine, while doxycycline and minocycline remain as the long acting tetracycline and almost complete absorption and slow excretion which allow for once-daily dosing.<sup>5</sup>

However, doxycycline and minocycline are regarded as the first-line options for the treatment of acne due to their efficacy against propionibacterium acne<sup>6</sup>, and also for the treatment of sexually transmitted infections such as chlamydia<sup>7</sup> as well as tickborne infections including borreliosis, brucellosis, Ehrlichiosis and rickettsial diseases especially rocky mountain spotted fever.<sup>8</sup>

Oral doxycycline is a recommended treatment regimen for adult patient with erythema migrans and has the advantage of its efficacy against anaplasma phagocytophilum in patient with early onset of borreliosis.<sup>1</sup>

Despite its clinical usages, doxycycline has been implicated as one of the causes of photo-sensitivity. Jacob et al enumerated that common cutaneous adverse reactions to doxycycline include photosensitivity and morbilliform exanthema; with less common skin side effects include bullous eruptions, lupus-like eruptions, pigmentary disorders and vasculitis; albeit uncommon doxycycline associated dual cutaneous adverse reactions to the drugs such as the photo-sensitivity and morbilliform exanthema may occur.<sup>9</sup>

In this report, a case of doxycycline induced photosensitivity in a 21 year old female being treated for recurrent acute cystitis is presented.

### ***Case report;***

A 21-year-old woman with a history of recurrent acute cystitis of 2weeks duration presented to the emergency room. She had been evaluated and treated by numerous prior physicians.

Her recent management included systemic metronidazole 500mg thrice daily and topical vaginal insert nocte daily; however, her symptoms and clinical appearance were not improving, which prompted a change in her drug regimen, and doxycycline monohydrate 100 mg daily was started. Within 7 days of initiation of doxycycline, she presented again to the emergency room with a complaint of rash on the face and neck sparing areas covered by her clothing.

One of the skin lesions was limited to sun-exposed areas of the face and neck; it also affected the forearms corresponding to areas not covered by her shirt sleeves.

Dermatological examination findings revealed a pruritic macular erythema rashes on her face, chest as well as the forearm not covered by her clothes. A diagnosis of doxycycline associated photosensitivity reaction was made and management involves discontinuation of doxycycline as well as vaginal insert and metronidazole. Oral antihistamines (loratadine 10mg daily) were started. A short course of oral prednisone was started: 10 mg morning and evening for 3days. Also, bethmethasone 0.1% cream was applied twice daily to all affected areas. She was counseled on reduction of exposure to ultra-violent radiation, the use of sun screen and protective clothing.

She was then followed-up after one week of treatment with a significant improvement of the itching and skin lesions and all of her symptoms and lesions resolved after two weeks of therapy.

### ***Discussion;***

Drug Hypersensitivity reactions affect more than 7% of the population and are a common concern for doctors and patients alike.<sup>10, 11</sup> Drug hypersensitivity reactions are common and the skin is by far the most frequently involved organ with a broad spectrum of reaction types.<sup>12, 13</sup>

Furthermore, photo-sensitivity as a component of adverse drug reaction as been described in case of doxycycline therapy as acute phototoxic dermatitis and phototoxic onycholysis on sun-exposure.<sup>3, 14, 15, 16</sup>

Women are often affected than men and possibly as a result of more frequently exposed to the sun than men.<sup>4</sup>

The precise mechanism of doxycycline photoallergy is not fully understood.<sup>3</sup> However, the photosensitization (phototoxicity or photoallergy) is usually caused by UVA radiation, because UVA penetrates deeper into the skin and most of the offending drugs absorb UV radiation in the UVA spectrum of 320–400 nm, e.g. tetracycline at 289–342 nm.<sup>17</sup> Following UV irradiation and photon absorption, drug molecules in an excited energy state cause chemical reactions when they return to their energetic base level, resulting in the synthesis of photoproducts that act as a haptens or antigens, generating an allergic reaction.<sup>18</sup>

In addition to doxycycline, other antibiotics are also associated with photo-sensitivity reactions such as fluoroquinolones, and sulfonamides, being the most commonest agent<sup>19, 20, 21, 22</sup> but cephalosporins and penicillins have also been rarely observed to cause photo-sensitivity reactions.<sup>23, 24</sup>

Yap et al described a case of tetra-cycline induced solar urticaria that developed within 5mins of patient exposure to sunlight.<sup>25</sup> The follow-up phototesting as a diagnostic challenge revealed light induced eruptions while these reactions were resolved within a week of drug discontinuation.<sup>25</sup>

Also, Jacob et al reported a case of doxycycline associated dual cutaneous adverse reactions to the drug with concurrent photosensitivity and morbilliform exanthema in a 51 year old woman who was placed on doxycycline monohydrate for rosacea and within 9 days of therapy, developed two different simultaneous skin rashes; a photo-toxic reaction and a morbilliform drug eruption.<sup>9</sup>

Diagnosing and managing drug hypersensitivity is challenging because there are no clear limits between different types of drug reactions.<sup>26</sup> When many people use a drug, adverse reactions can occur, conditioned by diverse genetic profiles, viral infections or concomitant therapy,<sup>26</sup> and the management usually involves discontinuation of the offending agents, reduction of exposure to ultra-violet radiation, the use of sun screen and protective clothings<sup>9</sup> as well as the use of oral anti-histamines and cortico-steroid therapy as in the case of index patient.

### **Conclusion:**

Doxycycline can induced photosensitivity which can include photoallergy and photo-toxicity in sun exposed part of the body manifesting as itching, burn sensation, redness, and sometimes morbilliform exanthema, ranging from benign eruption to more severe form. Therefore, prompt recognition and stoppage of offending agent are a surest means of achieving a better prognosis. All clinicians should be on alert when prescribing the medications to susceptible individuals.

**Sponsorship or Financial Inducement:** None

**Conflict of interest:** None

### **References:**

1. Ashourian N, Cohen PR: Chapter 4: Systemic antibacterial agents. Comprehensive Dermatologic Drug Therapy. Stephen E. Wolverson (ed): Saunders/Elsevier, Philadelphia, PA; 2007. 39-74.
2. Leslie A. H, Anthony JG; Tetracycline Allergy; *Pharmacy* **2019**,7, 104; doi:10.3390/pharmacy7030104 [www.mdpi.com/journal/pharmacy](http://www.mdpi.com/journal/pharmacy)
3. Alexander V K, Peter W, Michael J F, Thomas R, Joerg C P; Photoallergic Erythroderma due to Doxycycline Therapy of Erythema Chronicum Migrans; Journal Compilation, 2011 Acta Dermato-Venereologica, 91, ISSN 0001-5555; doi: 10.2340/00015555-1161
4. Velusek M, Bajrovic FF, Franc S, Stupica D; Doxycycline induced photosensitivity in patient treated for Erythema Migrans; BMC infectious diseases J, 2018, 18:365.
5. Katzung BG, Susan BM, Trevor AJ; Basic and Clinical Pharmacology; Mc Graw Hill Pub, 11ed, 2009; 796-799.
6. Zaenglein, A.L.; Pathy, A.L.; Schlosser, B.J.; Alikhan, A.; Baldwin, H.E.; Berson, D.S.; Bowe, W.P.; Graber, E.M.; Harper, J.C.; Kang, S.; et al. Guidelines of care for the management of acne vulgaris. *J. Am. Acad. Dermatol.* 2016, 74, 945–973.

7. Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. *MMWR Recomm. Rep.* 2015, 64, 1–140.
8. Centers for Disease Control and Prevention. Tickborne Diseases of the United States: A Reference Manual for Healthcare Providers, 5th ed. Available online: <https://www.cdc.gov/ticks/tickbornediseases/TickborneDiseases-P.pdf> (accessed on 4 June 2019).
9. Jacob J S, Cohen P R (November 18, 2020) Doxycycline-Associated Dual Cutaneous Adverse Reaction to the Drug (CARD): Case Report of Concurrent Photosensitivity and Morbilliform Exanthem to Doxycycline. *Cureus* 12(11): e11546. DOI 10.7759/cureus.11546
10. Demoly P, Adkinson NF, Brockow K, Castells M, Chiriac AM, Greenberger PA, et al. International consensus on drug allergy. *Allergy.* 2014;69:420-437.
11. Gomes ER, Demoly P. Epidemiology of hypersensitivity drug reactions. *Curr Opin Allergy Clin Immunol.* 2005;5:309-316.
12. Bigby M. Rates of cutaneous reactions to drugs. *Arch Dermatol.* 2001;137:765-770.
13. Knut Brockow, Michael R A J, Maja M, Wener A, Annick B, Jean-Christoph C, Radoslaw S, Marie JT, Charlotte GM; EAACI Position Paper on how to classify Cutaneous Manifestations of drug hypersensitivity; John Wiley and Sons Pub; *Allergy*, 2019;74:14-27
14. Frost P, Weinstein GD, Gomez EC. Phototoxic potential of minocycline and doxycycline. *Arch Dermatol* 1972; 105: 681–683.
15. Frank SB, Cohen HJ, Minkin W. Photo-onycholysis due to tetracycline hydrochloride and doxycycline. *Arch Dermatol* 1971; 103: 520–521.
16. Moore DE. Drug-induced cutaneous photosensitivity: incidence, mechanism, prevention and management. *Drug Safety* 2002; 25: 345–372
17. Palmer RY, White IR. Phototoxic and photoallergic reactions. In: Frosch PJ, Menne T, Lepoittevin J-P, editors. *Contact dermatitis*. 4<sup>th</sup> edn. Berlin: Springer Verlag, 2006: p. 309–317.
18. Ping-Kai H, Wai-Kwong F. Identification of tetracyclines by second-derivate ultraviolet spectrophotometry. *Analyst* 1991; 116: 751 -752.
19. Urbina F, Barrios M, Sudy E: Photolocalized purpura during ciprofloxacin therapy . *Photodermatol Photoimmunol Photomed.* 2006, 22:111-112. 10.1111/j.1600-0781.2006.00210.x
20. Dawe RS, Ibbotson SH, Sanderson JB, Thomson EM, Ferguson J: A randomized controlled trial (volunteer study) of sitafloxacin, enoxacin, levofloxacin and sparfloxacin phototoxicity. *Br J Dermatol.* 2003, 149:1232-1241. 10.1111/j.1365-2133.2003.05582.x
21. De D, Dogra S, Kaur I: Dapsone induced acute photosensitivity dermatitis; a case report and review of literature. *Lepr Rev.* 2007, 78:401-404.
22. Frost P, Weinstein GD, Gomez EC: Phototoxic potential of minocycline and doxycycline . *Arch Dermatol.* 1972, 105:681-683. 10.1001/archderm.1972.01620080011005

23. Vinks SA, Heijerman HG, de Jonge P, Bakker W: Photosensitivity due to ambulatory intravenous ceftazidime in cystic fibrosis patient. *Lancet*. 1993, 341:1221-1222. 10.1016/0140-6736(93)91058-t
24. Delaunay J, Chassain K, Sarre ME, Avenel-Audran M: A drug not recognized as a photosensitizer? . *Contact Dermatitis*. 2019, 81:143-144. 10.1111/cod.13265
25. Yap, L.M.; Foley, P.A.; Crouch, R.B.; Baker, C.S. Drug-induced solar urticaria due to tetracycline. *Australas. J. Dermatol*. 2000, 41, 181–184.
26. Javier Fernandez & Inmaculada Doña (2017): Diagnosing and managing patients with drug hypersensitivity, *Expert Review of Clinical Immunology*, DOI: 10.1080/1744666X.2018.1410059

