Journal of the Turkish Academy of Dermatology
eISSN 1307-394X

Case Report DOI: 10.6003/jtad.1482c5

Photocontact Dermatitis due to *Hypericum perforatum*

Belma Türsen,[1] MD, Erdinç Terzi,[2] MD, Tamer İrfan Kaya,[3] MD, Ümit Türsen,[3]* MD

Address: [1]Mersin State Hospital, Department of Dermatology, Mersin, Turkey, [2]Sakarya State Hospital, Department of Dermatology, Sakarya, Turkey, [3]Mersin University, School of Medicine, Department of Dermatology, Mersin, Turkey

E-mail: utursen@mersin.edu.tr

** Corresponding Author:* Dr. Ümit Türsen, Mersin University, School of Medicine, Department of Dermatology Mersin, Turkey

Published:
J Turk Acad Dermatol 2014; **8 (2)**: 1482c5
This article is available from: http://www.jtad.org/2014/2/jtad1482c5.pdf
Key Words: Photocontact dermatitis, hypericin

Abstract

Observations: Hypericin, originating from *Hypericum perforatum*, is a potent photosensitizer known to induce skin phototoxicity when given systemically. *Hypericum perforatum* is a botanical extracts with anti-inflammatory and antibacterial effect. Photocontact dermatitis is a common cutaneous reaction by various herbs. We describe a 54-year-old female patient with *Hypericum perforatum* associated photocontact dermatitis shortly after topical application therapy for knee pain due to osteoarthritis. Hypericum perforatum therapy was stopped and the patient was treated with topical corticosteroids and systemic antihistamines. The eruption resolved within ten days. Photocontact dermatitis induced by *Hypericum perforatum* has been reported as second case in English literature. We propose that photocontact dermatitis is a side-effect of topical *Hypericum perforatum*.

Introduction

Photocontact dermatitis is a pattern of skin reaction caused by various drugs and botanical extracts. The incidence of photocontact dermatitis caused by a specific drug and herbals depends on the frequency of its use. Hypericum perforatum (Saint John's wort) extracts are used mainly as oral antidepressants. Depending on source, the extracts contain various amounts of phenylpropanes, flavonol derivates, biflavones, proathocyanidines, xanthones, phloroglucinoles, some amino acids, naphtodianthrones (hypericines) and essential oil constituents. The therapeutic use of Hypericum perforatum extracts however is limited by their phototoxic potential. Among the tested flavonoids quercitrin was found to be cytotoxic, while rutin unexpectedly demonstrated phototoxicity whereas quercitrin was effective to control the phototoxic activity of Hypericum perforatum extracts. Recently, with roughly one report per 300,000 cases treated with extract of Hypericum perforatum reversible phototoxic skin reactions, such as delayed erythema, blistering, and hyperpigmentation, are the most common pharmacovigilance case reports documented. Hypericum perforatum extract has been used to treat a variety of conditions, especially psychovegetative disorders, depressive disorders, anxiety, and/or nervous agitation. The main bioactive components of Hypericum perforatum extract for treatment of depression were thought to be hypericin and hyperforin [**1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11**]. We describe a patient with severe photocontact dermatitis caused by shortly after starting topical Hypericum perforatum therapy for osteoarthritis. Hypericum perforatum is a common specimen plant in the Turkey. The diagnosis of photocontact dermatitis produced by plants that are indigenous to a particular country is more

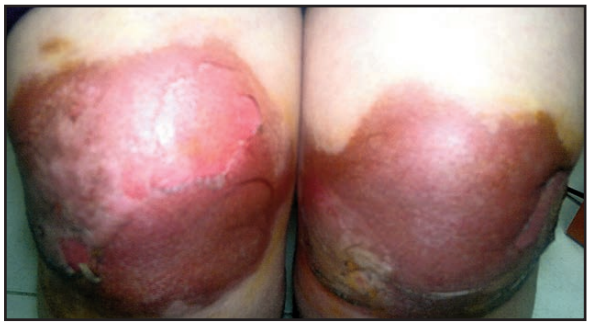

Figure 1. Confluent erythematous and eroded rash on the legs, sharply demarcated above the knees, with multiple erosions and crusting

likely to be delayed, as well as mistaken for cellulitis and burns.

Case Report

A 54-year-old female patient presented with a 2 days history of erythematous to violaceous eroded lesions on the knees. The lesions were sharply demarcated and moderately pruritic (**Figure 1**). She was treated for osteoarthritic pain with topical Hypericum perforatum, of 5 days duration. She had a negative history of any other drug intake. The result of routine complete blood cell count, urinalysis, erythrocyte sedimentation rate, liver and kidney function tests were within normal limits. At that time, a possibility of photocontact dermatitis was raised. Topical Hypericum perforatum treatment was stopped and the patient was treated with topical corticosteroids and systemic antihistamines. The eruption resolved within ten days.

Discussion

Potential patients in the developed world are increasingly turning to treatment with herbs. One of the most popular herbs taken for depression is Hypericum perforatum, which contains the potential photosensitizer hypericin. 'Hypericism' is a term used to describe a state of skin sensitivity to visible light in animals following ingestion of hypericin-containing plants and feed [**1, 2**] Recent investigations suggest an anti-inflammatory and antibacterial effect of hyperforin, which is a major constituent of Hypericum perforatum. In a half-side comparison study, it was assessed the efficacy of a cream containing Hypericum extract standardized to 1.5% hyperforin (verum) in comparison to the corresponding vehicle (placebo) for the treatment of subacute atopic dermatitis. The study design was a prospective randomized placebo-controlled double-blind single center study. Hypericum cream was significantly superior to its vehicle in the topical treatment of mild to moderate atopic dermatitis [**10**]. The therapeutic efficacy of the Hypericin, originating from Hypericum perforatum, is a potent photosensitizer known to induce skin phototoxicity when given systemically. In a study, it was assessed the time course and skin histopathology of the phototoxic response after a single topical application of hypericin and hypericin acetate, and subsequent irradiation. The results indicate that hypericin is an effective photosensitizer not only after systemic administration, but also after topical application, especially when applied as its precursor acetate ester [**6**]. A patient who developed a severe phototoxic reaction to laser light at 532 nm and also an exaggerated and unexpectedly severe response to pulsed dye laser light at 585 nm is described. It subsequently transpired that the patient was taking Hypericum perforatum at the time of laser treatment [**9**]. Hypericum perforatum extracts are used mainly as oral antidepressants. Depending on source the extracts contain various amounts of phenylpropanes, flavonol derivates, biflavones, proathocyanidines, xanthones, phloroglucinoles, some amino acids, naphtodianthrones (hypericines) and essential oil constituents. The therapeutic use of Hypericum perforatum extracts however is limited by their phototoxic potential. Hypericum perforatum extracts demonstrated cytotoxicity and photocytotoxicity in a dose and UVA-dose dependent manner. Hypericine itself also evoked severe phototoxic effects and was thus identified as the main phototoxic constituent. Among the tested flavonoids quercitrin was found to be cytotoxic, while rutin unexpectedly demonstrated phototoxicity whereas quercitrin was effective to control the phototoxic activity of Hypericum perforatum extracts [**7, 8**].

Observational studies with preparations of Hypericum perforatum have recorded an incidence of adverse events among those treated of between 1 and 3%. This is some ten times less than with synthetic antidepressants. The most common adverse events (1 per 300000 treated cases) among the spontaneous reports in the official register concern reactions of the skin exposed to light. Extracts of Hypericum perforatum are used in the treatment of depression. They contain the plant pigment hy-

pericin and hypericin derivates. These compounds have light-dependent activities [**11**]. Dry skin is associated with a disturbed skin barrier and reduced formation of epidermal proteins and lipids. During recent years, skin-barrier-reinforcing properties of some botanical compounds have been described. Hypericum perforatum can specifically improve skin barrier and/or promote keratinocyte differentiation in vivo after topical application [**5**]. Botanical extracts and single compounds are increasingly used in cosmetics but also in over-the-counter drugs and food supplements. Topical Hypericum appear promising for atopic dermatitis. Topical Dynamiclear is a topical formulation containing copper sulfate and Hypericum perforatum and also only single dose application may provide a more effective and convenient treatment option for symptomatic management of HSV. The Dynamiclear formulation was well tolerated, and efficacy was demonstrated in a number of measured parameters, which are helpful in the symptomatic management of HSV-1 and HSV-2 lesions in adult patients. Remarkably, the effects seen from this product came from a single application [**3**]. The naphthodiantrones hypericin and pseudohypericin, ingredients of hypericum extracts, are known as potent photosensitizers that may cause phototoxic effects in grazing animals after excessive ingestion of hypericum species and in some cases in higher concentrations of hypericum extracts oder pure hypericin in humans as well [**2**].

Hypericum perforatum dermatitis is rare in the world, it has not been reported previously in Turkey. The most commonly affected sites for phototoxic dermatitis are exposed areas on the arms, legs and face. In our patients, skin lesions were seen on the knees. Dermatitis may have a diffuse, patchy appearance if the sap soaks through the clothing onto the skin. Although the mildest presentation often lacks vesicles, the most severe reaction manifests with bullae and oedema. Without continued or new exposures, Hypericum perforatum dermatitis resolves untreated in 3 weeks. However, due to the severity of inflammation, oral and topical corticosteroids and antihistamines are often used and they do alter the time course of the disease. We used only topical corticosteroid and antihistamines in our patient. The diagnosis of phototoxic dermatitis produced by plants that are not indigenous to a particular country may be delayed, as well as mistaken for cellulitis, burn and especially when patients present to other specialities.

References

1. Boiy A, Roelandts R, van den Oord J, de Witte PA. Photosensitizing activity of hypericin and hypericin acetate after topical application on normal mouse skin. Br J Dermatol 2008; 158: 360-369. PMID: 18047507
2. Schulz HU, Schürer M, Bässler D, Weiser D. Investigation of the effect on photosensitivity following multiple oral dosing of two different hypericum extracts in healthy men. Arzneimittelforschung 2006; 56: 212-221. PMID:16618014
3. Clewell A, Barnes M, Endres JR, Ahmed M, Ghambeer DK. Efficacy and tolerability assessment of a topical formulation containing copper sulfate and hypericum perforatum on patients with herpes skin lesions: a comparative, randomized controlled trial. J Drugs Dermatol 2012; 11: 209-215. PMID: 22270204
4. Reuter J, Merfort I, Schempp CM. Botanicals in dermatology: an evidence-based review. Am J Clin Dermatol 2010; 11: 247-267. PMID: 20509719
5. Casetti F, Wölfle U, Gehring W, Schempp CM. Dermocosmetics for dry skin: a new role for botanical extracts. Skin Pharmacol Physiol 2011; 24: 289-293. PMID: 21709432
6. Bernd A, Simon S, Ramirez Bosca A, Kippenberger S, Diaz Alperi J, Miquel J, Villalba Garcia JF, Pamies Mira D, Kaufmann R. Phototoxic effects of Hypericum extract in cultures of human keratinocytes compared with those of psoralen. Photochem Photobiol 1999; 69: 218-221. PMID: 10048312
7. Schulz V. Incidence and clinical relevance of the interactions and side effects of Hypericum preparations. Phytomedicine 2001; 8: 152-160. PMID: 11315759
8. Wilhelm KP, Biel S, Siegers CP. Role of flavonoids in controlling the phototoxicity of Hypericum perforatum extracts. Phytomedicine 2001; 8: 306-309. PMID: 11515722
9. Cotterill JA. Severe phototoxic reaction to laser treatment in a patient taking St John's Wort. J Cosmet Laser Ther 2001; 3: 159-160. PMID: 12006194
10. Schempp CM, Hezel S, Simon JC. Topical treatment of atopic dermatitis with Hypericum cream. A randomised, placebo-controlled, double-blind half-side comparison study. Hautarzt 2003; 54: 248-253. PMID: 12634994
11. Onoue S, Seto Y, Ochi M, Inoue R, Ito H, Hatano T, Yamada S. In vitro photochemical and phototoxicological characterization of major constituents in St. John's Wort (Hypericum perforatum) extracts. Phytochemistry 2011; 72: 1814–1820. PMID: 21782201