

Analysis of solar urticaria in Thai patients

Narumol Silpa-archa, Chanisada Wongpraparut and Vichit Leenutaphong

Summary

Background: Solar urticaria (SU) is an uncommon photodermatosis characterized by erythema and whealing within minutes to a few hours after exposure to sunlight or an artificial light source.

Purpose: To determine the clinical features, photobiological characteristics and treatment outcomes in Thai SU patients visiting a tertiary referral hospital.

Method: A retrospective analysis of 13 patients with SU was conducted. Demographic data, disease characters, phototesting results, laboratory investigations, treatment and outcome were evaluated.

Results: Of the 13 patients diagnosed with SU from 2000 to 2012, most patients were female (10, 77%). The mean age of onset was 29 years (15-51). The mean duration of SU was 46 months (6-120) at presentation. The most common affected location was the upper extremities (92%), followed by head and neck (77%). The responsible action spectra were visible light in 8 patients (61.5%), ultraviolet A (UVA) in 1 patient (8%), and both visible light and UVA in 4 patients (31%). The median course from disease onset to disease resolution was 63 months (95% confidence interval 30-95). After 13 months and 55 months from the onset of symptoms, 23% and 49% of patients, respectively, were predicted to recover from their symptoms.

Conclusion: Solar urticaria is a rare condition in Thailand. The common eliciting spectra of SU were visible light and UVA. Management of SU remains challenging. (*Asian Pac J Allergy Immunol* 2016;34:146-52)

Key words: solar urticaria, visible light, ultraviolet, phototesting, clinical course

Introduction

Solar urticaria (SU) is an uncommon photodermatosis, defined as itching, erythema and whealing within minutes to a few hours after exposure to ultraviolet (290-400 nm) or visible light (400-700 nm) or, rarely, infrared radiation (>700 nm).¹ The severity of the reaction depends on various factors such as the photosensitivity of the patient, the duration of exposure and the intensity of solar radiation. Sporadically, this can be a life-threatening disease.² The prevalence of SU accounts for 0.3-0.4% of events in urticaria patients.^{3, 4} The mechanism of SU has been hypothesized to be an IgE-mediated hypersensitivity to a photoallergen created from a skin chromophore after exposure to the causal wavelength.⁵ The diversity of the action spectra is mainly due to differences in the chromophore.⁶ Previously, Harber et al. classified SU into six types based on the action spectrum.⁷ In 1989, Leenutaphong et al. proposed two types of solar urticaria:⁸ type I, an IgE-mediated hypersensitivity to specific photoallergens which form only in SU patients and type II, an IgE-mediated hypersensitivity to non-specific photoallergens which form in both SU and normal patients. This troubling condition can affect the quality of life in patients who are usually active outdoors.⁹ To date, there have been only a few studies on SU from Asia.^{10, 11} In the present study, the authors focused on clinical features, photobiological characteristics and treatment in Thai SU patients visiting a tertiary referral hospital.

Methods

This study was approved by the Siriraj Institutional Review Board, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand. We retrospectively reviewed the medical records of SU patients who visited the dermatology clinic at the Department of Dermatology, Faculty of Medicine, Siriraj Hospital from January 2000 to December 2012. The collected data included demographic data (age, age onset, gender, skin type, atopy history, familial history of SU), disease

From Department of Dermatology
Faculty of Medicine Siriraj Hospital, Mahidol University
2 Wanglang Road, Bangkoknoi, Bangkok, THAILAND 10700
Corresponding author: Chanisada Wongpraparut
E-mail: chanisada@hotmail.com
Submitted date: 17/2/2015
Accepted date: 8/9/2015

characters (disease duration, exposure time, location of rash, associated symptoms), phototesting and laboratory investigations, treatment, and outcomes.

To identify SU patients, we performed phototesting with ultraviolet A (UVA), ultraviolet B (UVB) and visible light using the following light sources; polychromatic UVA (SUPUVASUN 3000, Mutzhas, Munich, Germany), 5-45 J/cm²; polychromatic UVB (UVB 800, Walmann, Villiger-Schwenningen, Germany), 50-280 mJ/cm² and 30 minutes of visible light (Kodak Carousel S-AV 2020 projector, Kodak AG, Stuttgart, Germany). For visible light testing, a glass of water was placed in front of the projector to avoid excessive heat. An IL-1700 radiometer (International light Inc. Newburyport, MA, USA) was used to measure UVA and UVB irradiance. The inhibition and augmentation spectra were assessed in one patient. Phototesting was carried out in covered areas, generally on the middle or lower back. Wheals and flares were assessed during irradiation, immediately, 10 minutes, 30 minutes and 1 hour after phototesting. The patients were asked to discontinue antihistamines for at least one week and systemic corticosteroids for at least two weeks before phototesting.

During the follow-up, the patients reported the severity of symptoms and the response to the treatment, as experienced by the patient. Resolution of disease was defined as no cutaneous symptoms after sun exposure, whether the patients had taken the medication or not. The disease duration was calculated from the onset of SU to resolution.

Descriptive statistics (e.g., mean, median, minimum, maximum, frequencies and percentages) were applied to describe demographic data and photobiological characteristics. The Kaplan-Meier survival curve was applied to determine the clinical course. SPSS for Windows version 10 (SPSS, Chicago, IL, USA) was used to analyze all statistical data.

Results

Of the 13 patients diagnosed with SU from 2000 to 2012, most were female (10, 77%); only three patients were male (23%). The mean age onset of SU was 29 years (15-51). Two patients (15%) had a personal history of atopy, most likely allergic rhinitis. All of the patients had Fitzpatrick skin type IV. None of the patients had solar angioedema or anaphylaxis. A familial history of SU was not detected. One patient had SU combined with chronic

idiopathic urticaria and one patient had SU combined with cholinergic urticaria. None of the patients had a history of medication use associated with SU. The median duration of urticarial symptoms before physician presentation was 24 months (6-120). The most common location of SU was the upper extremities (2%), followed by the head and neck (77%), the lower extremities (54%) and the trunk (15%). One patient developed wheals only on particular areas of the arms and forearms; therefore, fixed SU was suspected. Other investigations such as anti-nuclear antibody and porphyrin tests were done in SU patients to exclude other photosensitive diseases; the results were negative.

Phototesting were carried out in all patients. Eight patients (61%) reacted only to visible light and one patient (8%) reacted only to UVA. Four patients (31%) reacted to both visible light and UVA. None of the patients reacted to UVB. In the patient suspected of fixed SU, phototesting on his back revealed a negative result. Hence, phototesting was performed on his right arm and right forearm, which had been previously affected. Urticarial lesions were observed after irradiation and a diagnosis of fixed SU was given. This patient was previously reported.¹² One patient had an inhibition spectrum at 400-500 nm.

All of the patients received a combination of H-1 antihistamines, physical photoprotection and broad spectrum sunscreen; most of them had a satisfactory response. Five (38%) patients required both second and third generation H-1 antihistamines and two patients (15%) received a two-fold higher dosage of a second generation H-1 antihistamine. One patient was recalcitrant and failed on a combination of H-1 antihistamines, narrowband UVB (NB-UVB) hardening, psoralen plus UVA (PUVA) hardening, and six sessions of plasmapheresis. This patient was previously reported.¹³

Regarding the clinical course, the median disease duration from the onset of symptom to clinical resolution was 63 months (95% confidence interval: 30 to 95 months). Three patients reported no symptoms after the cessation of medication. The probability of resolution is shown in a Kaplan-Meier survival curve (Figure 1). At 13 months and 55 months from the onset of symptoms, 23% and 49% of SU patients, respectively, recovered from their symptoms.



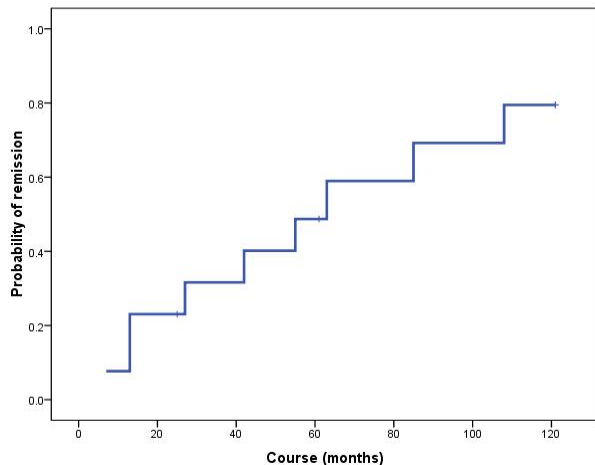


Figure 1. A Kaplan-Meier survival analysis demonstrates the probability of clinical resolution in solar urticaria patients (n=13). After 13 months and 55 months from the onset of symptoms, 23% and 49% of patients respectively, recovered from the symptoms.

Discussion

SU is a rare photodermatosis in Thailand. In a recent survey of 1,200 urticaria patients over five years in Thailand, only four patients (0.3%) were diagnosed with SU.³ Regarding the demographic data, the present study showed a female preponderance (86.7%), which was similar to previous studies in Scotland and Japan that reported a female preponderance of 70% and 60%, respectively.^{1,10} This is contrast to a series in Singapore that showed a male preponderance of 79%.¹¹ Different ethnic backgrounds can affect the results regarding gender. The mean age of onset in this study was in the second decade of life (29 years), was younger than previously published studies from Japan,¹⁰ Belgium² and France¹⁴. A lower incidence (15%) of atopy was observed in this study compared to the studies reported by Ryckaert et al. (48%) and Monfrecola et al. (47%).^{2,15} For the affected sites, the upper extremity was the commonest site of SU compared to the head and neck, which tend to have more regular sun exposure. This was supported by the series from Singapore showing that 58% of SU patients developed lesions on the arms and forearms.¹¹ One patient with fixed SU was observed in this study. This condition is extremely rare and was first described in 1990.¹⁶ In this condition, the urticarial wheal specifically occurs in a fixed location after repeated sun exposure. To diagnose this condition, phototesting

should be carried out in the previously affected area. This condition is thought to occur based on variations in the mast cell distribution or mast cell population and the response of these cells to irradiation.¹⁷

The wavelengths that activate SU can be in the ultraviolet, visible light or infrared range. In Asian patients, the most common action spectra are visible light and UVA.^{10, 11} We found that visible light, followed by UVA, was the responsible action spectra for SU in this study. Thirty-one percent of patients had a reaction to both spectra while none of the patients was induced by UVB. Conversely, in a series of 25 patients from Belgium, 6 (24%) and 3 (12%) patients reacted to UVA and UVB, respectively, while 5 patients (20%) had reaction to visible light.² Negative phototesting to UV and visible light has been reported in the literature.^{11, 15, 18} A study from the United States demonstrated negative phototesting (minimal erythema dose (MED)-A, MED-B and visible light) in 216 out of 319 patients with suspected photodermatosis. Among this negative phototesting group, 19 patients (8.8%) were diagnosed with SU.²¹ In suspected SU patients, heat-induced urticaria (heat contact urticaria and cholinergic urticaria) should be differentiated. Heat contact urticaria is typically well-defined, limited to the area of heat exposure, develops within a few minutes after heat contact and resolves after 1 to 3 hours.¹⁹ Cholinergic urticaria presents with a pruritic erythematous punctate wheal following an increase in body temperature, and can be actively (exercise) or passively (hot bath) induced.¹⁹ Another explanation for negative phototesting is infrared- induced SU, which is a rare condition.²⁰ Monfrecola et al. reported that 3 (5.3%) out of 57 SU patients reacted to natural sunlight.¹⁵ Ultimately, it should be noted that clinical history and physical examination are still important in the diagnosis of photodermatoses, especially in negative phototesting patients.

Antihistamine is the mainstay treatment for SU, based upon the hypothesis that IgE specific for an photoallergen binds to mast cells. The combination of antihistamines and sunscreen in SU has a synergistic effect.²² Sunscreens can increase the minimal urticarial dose (MUD) while antihistamines can suppress the urticarial symptoms.²² Antihistamines combined with a leukotriene receptor antagonist (cetirizine 20 mg/day, loratadine 20 mg/day, fexofenadine 240 mg/day and montelukast 10 mg/day) showed effective results

Table 1. Characteristics of solar urticaria from reported case series

Authors/ country	No. of patients	Age range (years)	Female: Male ratio	Atopy history	Action spectrum No. (%)	Treatment modalities	Clinical course/remission
Ravits et al./United States ³³	12	10-50	5:1	NR	VIS 5 (41.6) VIS+UVA 3 (25) UVA 3 (25) UVA+UVB+VIS 1 (8.3)	H-1Antihistamines, sunscreen, beta carotene, UVB/PUVA hardening	NR
Ryckaert et al./Belgium ²	25	17-71	1:1	48%	VIS 5 (20) VIS+UVA 6 (24) UVA 6 (24) UVB 3 (12) UVA+UVB 3 (12) UVA+UVB+VIS 1 (4) Natural light 1 (4)	H-1Antihistamines, broad spectrum sunscreens, PUVA hardening	NR
Monfrecola et al./ Italy ¹⁵	57	9-65	1.3:1	47%	VIS 38 (67) UVA 16 (28) Natural light 3 (5.3)	H-1Antihistamines, PUVA hardening	Nearly half are free of disease within 5 years.
Uetsu et al./ Japan ¹⁰	40	13-76	1.5:1	NR	VIS 24 (60) VIS+UVA 1(2.5) UVA 4 (10) UVB 4 (10) UVA+UVB 3 (7.5) UVA+UVB+VIS 4(10)	H-1Antihistamines, broad spectrum sunscreen, PUVA hardening	No completely cured patient, most of the patients had gradual improvement.
Beattie et al./Scotland ¹	87	3-89	2.3:1	40%	VIS 26/84 (31) VIS+UVA 35/84 (42) UVA 5/84 (6) UVB 1/84 (1.1) UVA+UVB+VIS 17/84 (20)	H-1Antihistamines, broad spectrum sunscreen	Probability of resolution at 5, 10, 15 years after diagnosis are 12%, 26%, 36%, respectively.
Stratigos et al./Greece ¹⁸	26	14-74	2.7:1	23%	VIS 10/23 (43.4) VIS+UVA 1/23 (4.3) UVA 3/23 (13) UVB 4/23 (17.3) Normal MED 6/23 (26)	H-1Antihistamines, broad spectrum sunscreen, PUVA/UVB hardening	NR

Table 1. Characteristic of solar urticaria from reported case series (Continued)

Authors/ country	No. of patients	Age range (years)	Female: Male ratio	Atopy history	Action spectrum No. (%)	Treatment modalities	Clinical course/remission
Eguino et al./Spain³⁴	20	19-63	1.5:1	NR	VIS 18 (90) UVA 12 (56) UVB 5 (26)	H-1Antihistamines, photoprotection, UVA/sunlight hardening	Complete remission in 40% of patients.
Chong and Khoo/Singapore¹¹	19	7-46	0.27:1	32%	VIS 12 (63) VIS+UVA 5 (27) UVA 1 (5) Natural light 1 (5)	H-1Antihistamines, broad spectrum sunscreen	All patients had partial improvement.
Du-Thanh et al./ France¹⁴	61	4-74	2.4:1	29%	VIS 9 (14.7) UVA 30 (49.2) UVA+UVB 15 (24.6)	H-1Antihistamines, photoprotection UVA/UVB hardening, antimalarial, carotenoids	Three patients had complete remission after 4-11 years.
This study/Thailand	13	17-53	3.3:1	15%	VIS 8 (61) VIS+UVA 4 (31) UVA 1 (8)	H-1Antihistamines, broad spectrum sunscreen, PUVA/NB-UVB hardening, plasmapheresis	Probabilities of remission after 13 months and 55 months from onset were 23% and 49%, respectively.

VIS, visible light; UVA, ultraviolet A; UVB, ultraviolet B; NR, not reported; PUVA, psoralen plus UVA; NB-UVB, Narrowband ultraviolet B; MED, minimal erythema dose

with no short-term side effect in one case series.²³ Unfortunately, in visible light-sensitive patients, organic sunscreen agents usually offer no protection as their absorption spectrum is limited to the UVB and UVA spectra. Inorganic sunscreens based on non-microfine zinc oxide, titanium dioxide or physical protection could be somewhat beneficial.^{24,25} Iron oxide, another inorganic sunscreen, showed promising results in a pigmentary disorder induced by visible light.²⁶ Further studies of iron oxide in SU and other photodermatoses should be performed. Induction of tolerance by subsequent UVA or UVA1 phototherapy is another effective method; however, this is time-consuming and unavailable in some institutions.^{27,28} Plasmapheresis can be used in patients with circulating photoallergens in the serum.²⁹ Novel treatments include afamelanotide, a potent synthetic analog of α -melanocyte-stimulating hormone (α -MSH), which is a regulatory protein that stimulates melanogenesis and melanocyte proliferation. An increase in melanization may protect from ultraviolet and visible light penetration, which are most commonly the responsible wavelengths in SU.³⁰ Haylett et al. reported on the efficacy of a single dose afamelanotide 16 mg implant subcutaneously in 5 SU patients during the winter months. A significant increase in melanin density was observed starting from day 7, peaked at day 15 and persisted to day 60 post-implantation. The MUD was increased compared to baseline, along with significantly decreased wheal formation.³⁰ With this promising result, a larger study should be conducted and the potential risk of dysplastic nevi and melanoma, which have not been observed so far, should be monitored.^{31,32} In this present study, the combination of H-1antihistamines, broad spectrum sunscreen and physical protection showed beneficial results, except in one recalcitrant patient.

The clinical course of SU is chronic and the data regarding prognosis factors are sparse. Beattie et al. reported 15% and 46% of SU patients experienced resolution at 5 and 15 years, respectively. Studies from Japan and Singapore showed no completely cured patients.^{10,11} In the present study, 23% and 49% of patients were predicted experience the resolution of symptoms at 13 months and 55 months, respectively. Clinical resolution was calculated based on the definition that included patients with no urticarial wheal while patients were taking medication. The characteristics of SU in the present study compared to other reported studies are summarized in Table 1.

In summary, SU is an uncommon photodermatosis with a chronic course. Management is still challenging. This study emphasized the clinical features, photobiological characteristics and clinical course of SU based on tertiary hospital care.

References

1. Beattie PE, Dawe RS, Ibbotson SH, Ferguson J. Characteristics and prognosis of idiopathic solar urticaria: a cohort of 87 cases. *Arch Dermatol.* 2003;139:1149-54.
2. Ryckaert S, Roelants R. Solar urticaria. A report of 25 cases and difficulties in phototesting. *Arch Dermatol.* 1998;134:71-4.
3. Silpa-Archa N, Kulthanan K, Pinkaew S. Physical urticaria: prevalence, type and natural course in a tropical country. *J Eur Acad Dermatol Venereol.* 2011;25:1194-9.
4. Champion RH. Urticaria: then and now. *Br J Dermatol.* 1988;119:427-36.
5. Horio T, Minami K. Solar urticaria. Photoallergen in a patient's serum. *Arch Dermatol.* 1977;113:157-60.
6. Kojima M, Horiko T, Nakamura Y, Aoki T. Solar urticaria. The relationship of photoallergen and action spectrum. *Arch Dermatol.* 1986;122:550-5.
7. Harber LC, Holloway RM, Wheatley VR, Baer RL. Immunologic and Biophysical Studies in Solar Urticaria. *J Invest Dermatol.* 1963;41:439-43.
8. Leenutaphong V, Holzle E, Plewig G. Pathogenesis and classification of solar urticaria: a new concept. *J Am Acad Dermatol.* 1989;21:237-40.
9. Jong CT, Finlay AY, Pearse AD, Kerr AC, Ferguson J, Benton EC, et al. The quality of life of 790 patients with photodermatoses. *Br J Dermatol.* 2008;159:192-7.
10. Uetsu N, Miyauchi-Hashimoto H, Okamoto H, Horio T. The clinical and photobiological characteristics of solar urticaria in 40 patients. *Br J Dermatol.* 2000;142:32-8.
11. Chong WS, Khoo SW. Solar urticaria in Singapore: an uncommon photodermatosis seen in a tertiary dermatology center over a 10-year period. *Photodermatol Photoimmunol Photomed.* 2004;20:101-4.
12. Tuchinda C, Leenutaphong V, Sudtim S, Lim HW. Fixed solar urticaria induced by UVA and visible light: a report of a case. *Photodermatol Photoimmunol Photomed.* 2005;21:97-9.
13. Insawang M, Wongpraparut C. Recalcitrant solar urticaria induced by UVA and visible light: a case report. *J Med Assoc Thai.* 2010;93:1238-41.
14. Du-Thanh A, Debu A, Lalleve P, Guillot B, Dereure O, Peyron JL. Solar urticaria: a time-extended retrospective series of 61 patients and review of literature. *Eur J Dermatol.* 2013;23:202-7.
15. Monfrecola G, Masturzo E, Riccardo AM, Balato F, Ayala F, Di Costanzo MP. Solar urticaria: a report on 57 cases. *Am J Contact Dermat.* 2000;11:89-94.
16. Leenutaphong V BH, Holzle E, Plewig G. Fixed solar urticaria (abstract). *Arch Dermatol Res* 1990;281:545-6.



17. Reinauer S, Leenutaphong V, Holzle E. Fixed solar urticaria. *J Am Acad Dermatol.* 1993;29:161-5.
18. Stratigos AJ, Antoniou C, Papathanakou E, Daboudi M, Tranaka K, Tsara K, et al. Spectrum of idiopathic photodermatoses in a Mediterranean country. *Int J Dermatol.* 2003;42:449-54.
19. Abajian M, Schoepke N, Altrichter S, Zuberbier T, Maurer M. Physical urticarias and cholinergic urticaria. *Immunol Allergy Clin North Am.* 2014;34:73-88.
20. Mekkes JR, de Vries HJ, Kammeyer A. Solar urticaria induced by infrared radiation. *Clin Exp Dermatol.* 2003;28:222-3.
21. Que SK, Brauer JA, Soter NA, Cohen DE. Normal minimal erythema dose responses in patients with suspected photosensitivity disorders. *Photodermatol Photoimmunol Photomed.* 2012;28:320-1.
22. Faurschou A, Wulf HC. Synergistic effect of broad-spectrum sunscreens and antihistamines in the control of idiopathic solar urticaria. *Arch Dermatol.* 2008;144:765-9.
23. Grundmann SA, Stander S, Luger TA, Beissert S. Antihistamine combination treatment for solar urticaria. *Br J Dermatol.* 2008;158:1384-6.
24. Horio T. Solar urticaria-idiopathic? *Photodermatol Photoimmunol Photomed.* 2003;19:147-54.
25. Deleo V. Sunscreen use in photodermatoses. *Dermatol Clin.* 2006;24:27-33.
26. Castanedo-Cazares JP, Hernandez-Blanco D, Carlos-Ortega B, Fuentes-Ahumada C, Torres-Alvarez B. Near-visible light and UV photoprotection in the treatment of melasma: a double-blind randomized trial. *Photodermatol Photoimmunol Photomed.* 2014;30:35-42.
27. Beissert S, Stander H, Schwarz T. UVA rush hardening for the treatment of solar urticaria. *J Am Acad Dermatol.* 2000;42:1030-2.
28. Lim HW, Silpa-Archa N, Amadi U, Menter A, Van Voorhees AS, Lebwohl M. Phototherapy in dermatology: A call for action. *J Am Acad Dermatol.* 2015;72:1078-80.
29. Collins P, Ahamat R, Green C, Ferguson J. Plasma exchange therapy for solar urticaria. *Br J Dermatol.* 1996;134:1093-7.
30. Haylett AK, Nie Z, Brownrigg M, Taylor R, Rhodes LE. Systemic photoprotection in solar urticaria with alpha-melanocyte-stimulating hormone analogue [Nle4-D-Phe7]-alpha-MSH. *Br J Dermatol.* 2011;164:407-14.
31. Lim HW, Grimes PE, Agbai O, Hamzavi I, Henderson M, Haddican M, et al. Afamelanotide and narrowband UV-B phototherapy for the treatment of vitiligo: a randomized multicenter trial. *JAMA Dermatol.* 2015;151:42-50.
32. Nitiyarom R, Wongpraparut C. Hydroa vacciniforme and solar urticaria. *Dermatol Clin.* 2014;32:345-53, viii.
33. Ravits M, Armstrong RB, Harber LC. Solar urticaria. Clinical features and wavelength dependence. *Arch Dermatol.* 1982;118:228-31.
34. Eguino P, Lasa O, Gardeazabal J, Diaz-Perez JL. [Solar urticaria. Study of 20 cases]. *Actas Dermosifiliogr.* 2005;96:25-9.