Characteristics and Prognosis of Idiopathic Solar Urticaria

A Cohort of 87 Cases

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Background: As little has been published on the course of idiopathic solar urticaria (SU) patients cannot receive comprehensive prognostic advice.

Objective: To determine the prognosis and photobiological characteristics of idiopathic SU.

Design: Historical cohort study, with inception cohort followed up from time of diagnosis. Follow-up for a median of 4 years (range, 3 months to 26 years) after diagnosis.

Setting: Tertiary referral center for the investigation of photodermatoses in Scotland.

Patients: The study included 87 patients, 61 (70%) of whom were female, with phototest-confirmed idiopathic SU between 1975 and 2000. Sixty patients (69%) were followed up clinically, and 25 patients (29%) were phototested on 2 or more occasions.

Interventions: Investigations at time of diagnosis included monochromator phototesting. Further monochromator phototesting was performed in those patients in whom it was clinically indicated (select subgroup), and all patients who could be traced received a follow-up questionnaire.

Main Outcome Measures: Characteristics of SU, responsible wave bands, and prognosis for clinical resolution.

Results: The prevalence of idiopathic SU in Tayside, Scotland, is estimated to be 3.1 per 100,000. Action spectra were typically broad, with 63% reacting to more than 1 wave band, and the most common provoking wavelengths were the longer UV-A and the shorter visible ones. The majority of subjects were affected perennially (68%), by radiation transmitted through glass (83%) and thin clothing (76%). Coexistent polymorphic light eruption occurred in 20 patients (23%), and another photodermatosis occurred in 6 patients, 3 of whom had chronic actinic dermatitis. In those with SU alone, the mean age at onset was 41 years. The probability of clinical resolution at 5 and 10 years after diagnosis was 0.12 (95% confidence interval, 0.06-0.24) and 0.26 (95% confidence interval, 0.15-0.43), respectively.

Conclusion: Idiopathic SU is a chronic disease. The majority of this cohort was still affected after 5 and 10 years.

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IDIOPATHIC SOLAR urticaria (SU) is an uncommon photodermatosis. The published literature consists mainly of single case reports and, recently, a small number of cohort studies. Solar urticaria is characterized by the early onset of itching, erythema, and whealing after exposure to UV-A (320-400 nm), visible (400-600 nm), less commonly UV-B (280-320 nm), and, rarely, infrared (>600 nm) radiation. It may occur as a result of drug use, porphyria, lupus erythematosus, or the topical application of tar but is otherwise idiopathic. It is hypothesized that a phototoallergen, produced from a skin “chromophore” on absorption of radiation of an appropriate wavelength, is recognized by specific IgE that binds to mast cells, causing degranulation with release of histamine and other mediators. Chromophores, detected in serum samples from some patients who react to intradermal injection of their own irradiated serum (intradermal test), have been isolated but not yet identified. Each has a characteristic absorption spectrum. The action spectrum of SU is usually broad but can vary widely between patients and within an individual over time. With such heterogeneity, it would appear that a range of chromophores is responsible.

Clinical features are also diverse. The severity of symptoms and signs, and the exposure time necessary to provoke them, can vary over time and relate to season, latitude, altitude, and reflection. Most patients develop urticaria within minutes of
exposure, which resolves within an hour, occasionally showing delayed onset and resolution.\textsuperscript{21,22} Other sources of radiation capable of provoking SU include UV-A sunbeds\textsuperscript{24} and halogen and fluorescent bulbs.\textsuperscript{23} Management includes behavioral avoidance of triggering wavelengths and the use of dark clothing of tight weave, sunscreens, and systemic antihistamines, which are of benefit in approximately two thirds of patients.\textsuperscript{20} Although prevalence or incidence figures are lacking, SU accounts for 0.4% of all cases of urticaria.\textsuperscript{27} As few data exist on the natural history of SU and none for prognostic indicators, clear advice to patients on disease outcome has not been possible.

We report the clinical features, photobiological characteristics, response to therapy, and natural history of 87 cases of idiopathic SU and examine identifiable factors at diagnosis, which may predict disease outcome.

PATIENTS AND STUDY METHODS

The study was performed at the Scottish National Photodermatology Unit in Dundee, Tayside, a tertiary referral center for the investigation of photodermatoses. It included patients who had been diagnosed as having idiopathic SU clinically and on phototesting between 1975 and 2000, forming a defined inception cohort. Those with secondary SU were excluded.

Patient information was retrieved from a departmental database and from written records. We recorded age at onset and diagnosis, sex, atopic status (as determined by a history of eczema, asthma, or hayfever), family history of photosensitivity, presence of other photodermatoses (with definitions as stated in the next section), skin phototype, medications, and medical history. Disease characteristics and results of hematologic tests, phototests, intradermal tests, and other investigations were retrieved. Severity was determined by the minimal urticaria dose at an affected wavelength divided by the lowest normal population minimal erythema dose at that wavelength (<0.1 indicated very severe photosensitivity). Prevalence was calculated by the number of known patients affected as a proportion of the population of Tayside in 1999.

A telephone interview of all patients who were available for follow-up from the original cohort was conducted. Hospital records from our own unit and from the referring hospital, the recorded general practitioner, and telephone directories were used to track the patients. Patients who were not contacted by telephone, but for whom a recent address was available, were sent a questionnaire by mail. We determined clinical resolution by asking, “Do you feel that you are still abnormally sensitive to sunlight?” If the answer was no, they were asked, “Do you feel that you are completely back to normal?” Those who thought that they were “still abnormally sensitive to sunlight” or that they were “not completely back to normal” were asked to state the exposure time now required to provoke urticaria; they were also asked if they felt they were improving, not changing, or getting worse with time. All patients were asked, irrespective of reported resolution, if they regularly used sunscreen and/or antihistamines and actively avoided sunlight. The results of further phototesting if carried out were also determined.

QUESTIONNAIRE-BASED DEFINITIONS

Complete clinical resolution referred to patients who reported that they were no longer abnormally sensitive to sunlight, had returned completely to normal, and were no longer using sunscreen, taking antihistamines, or avoiding sunlight; clinical resolu-

PHOTOTEST INVESTIGATIONS

At the time of initial assessment, all patients underwent phototesting (with 305±5 [wavelength±half-maximum bandwidth], 335±30-, 365±30-, 400±30-, 450±30-, 460±30-, 500±30-, and 600±30-nm wave bands) with a xenon arc lamp (XBO [1600 W]; Osram GmbH, Munich, Germany) coupled to a monochromator, using a standard technique.\textsuperscript{26} Irradiance was measured using a calibrated thermopile and digital voltmeter. A UV-A source (Blue Light 2000 [400 W]; Dr Honle, Graefelfing, Germany) at 25 J/cm\textsuperscript{2} was successfully used to induce urticaria in 2 patients with negative results on monochromator phototesting. In 1 other patient, broadband solar-simulated radiation produced by a xenon arc 150-W filtered source was required. Infrared testing was conducted using an infrared lamp (InfraPhil HP3690 [150 W]; Royal Philips Electronics, Amsterdam, the Netherlands) in 8 patients who reported heat provocation. Idiopathic SU was diagnosed only in those in whom urticaria was provoked.

LABORATORY AND OTHER INVESTIGATIONS

Serologic tests for antinuclear antibodies and anti-Ro and -La antibodies to exclude lupus erythematosus and a plasma porphyrin scan to exclude porphyria, as well as routine biochemical analysis and a full blood cell count, were performed in all patients. Fifteen patients with more severe disease who were considered to be possible candidates for plasmapheresis underwent intra-dermal testing with autologous irradiated serum. One serum sample was irradiated using the minimal urticaria dose and another using a dose 4 times greater than the minimal urticaria dose at the most sensitive wave band. Both irradiated serum samples and a dark control serum sample were then injected intradermally (0.1 mL of each) in a forearm, labeled, and observed for 30 minutes. A skin biopsy was performed in patients with CAD (n=3) and lymphocytoma cutis (n=3).

ANALYSIS

Kaplan-Meier analysis was used to determine, as a function of time, the proportion of patients who had resolution both clinically and on phototesting. Univariate exploratory analyses to estimate the prognostic value of a number of variables were carried out using a proportional hazards model. The variables assessed included age at diagnosis, coexistence of PLE, duration...
A total of 87 patients were identified as having idiopathic SU confirmed by phototesting, and 60 (69%) of the 87 patients were included in the follow-up study.

PATIENT CHARACTERISTICS

Of the 87 patients, 20 had coexistent PLE and 2 of the 20 patients with coexistent PLE also had lymphocytoma cutis. Six patients had other coexistent solar-provoked dermatoses: 3 with CAD, 1 with lymphocytoma cutis, 1 with actinic prurigo, and 1 with undefined photosensitivity. Three patients also had chronic idiopathic urticaria, and 1 patient had cholinergic urticaria and urticarial vasculitis. All patients diagnosed as having a coexistent photodermatosi s had phototest and/or clinical evidence of both the photodermatosi s and SU, and those with CAD or lymphocytoma cutis also had histologic evidence of both. Those with CAD had multiple contact allergies on patch testing.

Overall, 61 patients (70%) were female: 41 (67%) of the 61 with SU alone, 19 (95%) of the 20 with coexistent PLE, and all 3 with lymphocytoma cutis. All patients with CAD were male. Previous skin type was recorded in 60 patients: 18 (30%) were skin type I, 29 (48%) were skin type II, 11 (18%) were skin type III, and 2 (4%) were skin type IV. Background population skin type distribution represented by 2371 patients with psoriasis who were skin type IV. Background population skin type distribution represented by 2371 patients with psoriasis who were skin type II, 11 (18%) were skin type III, and 2 (4%) were skin type IV. Background population skin type distribution represented by 2371 patients with psoriasis who were skin type II, 11 (18%) were skin type III, and 2 (4%) were skin type IV. Background population skin type distribution represented by 2371 patients with psoriasis who were skin type II, 11 (18%) were skin type III, and 2 (4%) were skin type IV.

The age distribution at the time of diagnosis was broad (Figure 1). In all cases, the median age at onset was 35 years (range, 3-89 years; interquartile range [IQR], 22-51 years). The presence of another photodermatosi s complicated both presentation and clinical features of the disease. For those with SU alone (n=61) and hence more reliable history, the median age at onset was 41 years (range, 14-75 years; IQR, 29-53 years) and at diagnosis 43 years (range, 15-85 years; IQR, 33-56 years). The median age at onset of SU in those with concomitant PLE (n=20) was 23 years (range, 3-40 years; IQR, 11-34 years), and at presentation 39 years (range, 14-58 years; IQR, 31-47 years), with PLE generally preceding SU by years. For those with SU and another photodermatosi s (n=6), the median age at onset was 50 years (range, 5-89 years; IQR, 27-59 years) and at presentation 60 years (range, 12-89 years; IQR, 53-65 years).

DISEASE CHARACTERISTICS

Patients with SU in isolation presented with a median dura- tion of disease of 2 years (range, 0.3-43 years) in comparison with those with PLE (median, 11.5 years; range, 0.5-49 years) or another photodermatosi s (median, 4.5 years; range, 0.5-30 years). The majority were severely affected, with less than 5 minutes of sunlight exposure provoking urticaria in 42 subjects (48%), 5 to 15 minutes in 25 subjects (29%), and up to 30 minutes in 12 subjects (14%). Exposure times of 45 to 60 minutes or more were necessary in 2 and 3 subjects, respectively. The majority of patients with solitary SU (95%) reported symptom resolution within 24 hours. The duration of symptoms in those with concomitant PLE or another photodermatosi s was unreliable. Fifty-nine patients (68%) were affected perennially in the United Kingdom, 13 (15%) from spring until fall, 8 (9%) in spring and summer, 3 (3.5%) in summer and fall, and 4 (4.5%) in summer alone. Only 12 (14%) noticed “hardening” as the summer progressed, 55 (63%) did not notice hardening, and 20 (23%) were unsure. Of the 87, 6 (7%) also reacted to artificial light and 7 (8%) to radiant heat. Symptoms were provoked by a conventional UV-A sunbed in 5 patients, 1 of whom had developed systemic symptoms. Seventy-two patients (83%) reacted to light transmitted through window glass and 66 (76%) through light clothing.

PREVALENCE

Of the 87 patients seen over 25 years, 14 were from the Tayside region, where all cases suspected by a dermatologist are investigated. Of these, SU had resolved in 2 and continued in 8 by 1999, while 4 were not available for follow-up. Assuming these 4 were still affected, the point prevalence is 3.1 per 100 000 of the Tayside population.

RESULTS OF INVESTIGATIONS

In all patients, the results of porphyrin screening were negative and the hematologic and biochemical parameters were normal. In 4 patients, serologic tests were weakly positive for antinuclear antibodies but were negative for anti-Ro and anti-La antibodies; therefore, the results were considered to be unremarkable. The results of intradermal testing were positive in 5 of 15 patients tested.

WAVELENGTH SENSITIVITY

Patients assessed from 1975 to 1980 had only broad wave band sensitivity data available. After 1980, narrower wave
bands and more precise minimal urticaria doses were recorded. Of 87 patients, 84 had urticaria provoked by monochromator testing, 2 by broadband UV-A only, and 1 by broadband solar-simulated radiation only. Idiopathic SU was provoked by the broadband UV-A source in 12 of 20 subjects and by infrared source in 5 of 8 subjects. Wave band data were available for all 84 subjects, the majority exhibiting broad-spectrum sensitivity. One subject had sensitivity to UV-B alone; 5 (6%) to UV-A alone; 17 (20%) to UV-B, UV-A, and visible wave bands; 35 (42%) to UV-A and visible wave bands; and 26 (31%) to visible wavelengths only. Of the 78 subjects assessed after 1980, 18 (23%) were sensitive at 305±5 (wave-length ± half-maximum bandwidth) nm, 35 (45%) at 335±30 nm, 46 (59%) at 365±30 nm, 62 (79%) at 400±30 nm, 60 (77%) at 430±30 nm, 47 (60%) at 460±30 nm, and 39 (50%) at 600±30 nm.

**FOLLOW-UP**

We followed up 60 patients: 40 (66%) of the 61 with solitary SU, 14 of the 20 with coexistent PLE, and all 6 with another photodermatosis. All patients contacted responded. The median duration of disease at follow-up was 10 years (range, 0.5-61 years) from onset and 4 years (range, 0.2-26 years) from diagnosis. We were unable to obtain addresses for 24 subjects, and 3 had died.

**CLINICAL COURSE**

Fifteen (25%) of 60 subjects reported complete clinical resolution, which was less likely in those with additional PLE (2/20) and not reported in those with another photodermatosis. Patients with another photodermatosis could not usually recall the SU onset. We therefore also looked at those with solitary SU, whose probability of resolution was 15% (95% CI, 7%-31%), 24% (95% CI, 12%-43%), and 46% (95% CI, 28%-69%) at 5, 10, and 15 years from onset, respectively. At 5, 10, and 15 years after diagnosis in all patients, the probability of resolution was 12% (95% CI, 6%-24%), 26% (95% CI, 15%-43%), and 36% (95% CI, 18%-49%), respectively (Figure 2).

Nineteen subjects (32%) thought that they had improved significantly with time; 21 (39%) reported that their symptoms had not changed; and 5 (8%) said that they were worse. Of these, the majority were still severely affected, with less than 5 minutes of exposure still capable of provoking the rash in 21 subjects (47%), 5 to 15 minutes in 5 subjects (11%), and 15 to 30 minutes in 7 subjects (16%). A significant number of subjects, however, appeared to be less severely affected than at presentation, with 45 to 60 minutes of exposure necessary in 6 (14%) and more than 60 minutes in 5 (11%), reflecting the clinical impression of a third of these subjects.

At follow-up, the patients were less likely to be affected perennially (58%) or from spring through fall (8.9%) and were more likely to be affected only in spring and summer (13%), summer (15.5%), or winter (4.4%). More patients (24 [40%]) at follow-up reported hardening during the summer months.

**PHOTOTEST RESOLUTION**

Of the 87 subjects, 25 underwent further phototesting at least 1 year after diagnosis. Six showed resolution, all with SU alone. The probability of phototest resolution at 5 and 10 years after diagnosis was 30% (95% CI, 12%-64%), and at 15 years it was 65% (95% CI, 24%-98%) (Figure 3). Of interest is that 1 patient who had resolution on phototesting reported that she had clinical improvement, and 2 others reported that their symptoms were unchanged. Of the 23 patients who were still photosensitive at their second visit, the action spectrum was unchanged (or no further wavelengths were tested) in 8, broadened in 9, and narrowed in 6.

**PROGNOSTIC VARIABLES**

Of all prognostic variables assessed (Table), none predicted complete clinical resolution. There was a suggestion of poorer prognosis in the subjects who were older than 40 years at diagnosis, in those with concomitant PLE, and in those with greater disease duration at presentation, which did not reach statistical significance. No patients with a positive intradermal test result showed resolution of SU, although the numbers were small.

**MANAGEMENT**

Of the 45 subjects who did not have complete clinical resolution, 34 (75%) took antihistamines: 15 daily throughout the year, 6 throughout the season that they were affected, and 4 intermittently (2 when it was sunny,
and 2 when they were symptomatic); the other 9 failed to answer the question. Of the 34 subjects who took antihistamines, 12 (35%) obtained very good benefit, 12 (35%) had some symptom control, and 10 (30%) felt that benefit was doubtful.

Thirty-eight (84%) of the 45 subjects used a broad-spectrum sunscreen to control their symptoms: 12 (32%) of them daily throughout the year, 12 (32%) throughout the season that they were affected, and 13 (34%) when it was sunny (1 did not answer). The majority (26/45, 68%) thought that sunscreens were of great benefit in controlling symptoms, and 9 (30%) thought that they were of some benefit; 28 subjects (62%) also actively avoided sunlight despite sunscreen and antihistamine use.

This study describes the clinical features, photobiological characteristics, and natural history of idiopathic SU in a cohort of patients diagnosed in a Scottish tertiary referral center over a 25-year period. Although previous studies1,2 have found a slight female preponderance (56%-60%), this finding was much greater in our study. Most articles have not addressed, or given only a passing mention to, the coexistence of other photodermatoses, including PLE, which was found in 23% of this cohort, reflecting the background prevalence in the population of the United Kingdom.20 Three cases of CAD were seen in our study population, a photodermatitis that has not previously been described in association with SU. The point prevalence of SU was estimated to be 3.1 per 100,000 of the Tayside population. As CAD has been estimated to have a prevalence of 1 per 6000 in this population,30 we would not expect this finding to occur by chance. This may reflect diagnostic ascertainment bias rather than a shared cause. The presence of another photodermatosis was found to complicate the presentation and clinical features of the disease, resulting in later presentation and apparent delayed onset and resolution of the rash. Our prevalence figure is likely to be an underestimate, as patients developing SU after another photodermatosis may attribute their symptoms to the underlying disorder, and many other patients initiate sun avoidance and sunscreen use without seeking a diagnosis.

Italian1 and Japanese2 studies of 57 and 40 patients found that 45% and 54%, respectively, were aged 20 to 30 years. By contrast, we found a mean age of 41 years at onset in those with solitary SU and, in the cohort as a whole, of 37 years, along with a much broader age distribution: 46 (53%) were aged 21 to 50 years and only 13 (15%) fell within the 21- to 30-year age group. We failed to detect an association with atopy.

We found a much longer median duration of disease in the subjects with concomitant PLE than in those with solitary SU. However, those with PLE and SU generally thought that the PLE had been present for many years before the onset of SU, and only 3 had been able to distinguish the onset of a separate disease. This may explain the perceived younger age at onset reported by that group.

These results highlight the severity of the disease in the majority of patients. Few case reports have documented delayed onset and resolution of SU.21-23 We found exposure times of an hour or more required for provocation in 6% and delayed resolution of the rash in 5%, suggesting that delayed onset and resolution are common. Atypical presentations and possible coexistence of other photosensitive disease highlight the need for phototesting.

The majority (63%) of subjects had broad-spectrum sensitivity. In contrast, Uetsu et al2 reported that 80% of their patients were sensitive to UV-B, UV-A, or visible wave bands in isolation. Monfrecola et al1 failed to detect UV-B sensitivity; in contrast, 22% of our patients reacted at 305±5 nm. We found a pattern of wavelength sensitivity similar to that found by Ryckaert et al,3 but with a greater proportion sensitive to the long UV-A and short visible wavelengths, thus explaining the high frequency of perennial symptoms (68%) and of induction of SU by sunlight transmitted by window glass (83%) and clothing (76%).

Reports on the natural history of idiopathic SU vary; patients often appear to improve over time, possibly because of improved sun avoidance and the use of antihistamines. Only Monfrecola et al1 reported follow-up data with clinical resolution, defined as being free of symptoms and signs for more than 2 years, in 57.5% of their patients after 5 years. Only 17.5% were still affected after 6 years. In contrast, at 5 years after onset, only 15% of our cohort had clinical resolution, increasing to 24% and 46% at 10 and 15 years, respectively. The difference may have been because their definition of resolution did not require patients to have discontinued therapy; therefore, the patients may have been asymptomatic rather than have had resolution. Patients may continue to use sunscreens and antihistamines out of habit, incorrectly assuming that their condition has resolved. Another possibility is that they were asymptomatic as a result of natural sunlight desensitization of exposed sites, more likely because of their sunnier climate and higher skin types. Patients who had difficulty in distinguishing the onset of SU in relation to existing photosensitivity may also have had difficulty in determining its resolution, resulting in underreporting and explaining why they appear less likely to have clinical resolution. However, no subject who had another photodermatosis showed objective evidence of resolution on phototesting, maybe because the presence of a second skin condition leads to persistence of SU. Failure to detect and report clinical resolution in those patients who con-

<table>
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<th>Variable</th>
<th>Hazards Ratio</th>
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<th>95% Confidence Interval</th>
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<td>Duration at diagnosis</td>
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<td>Concomitant PLE</td>
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<td>.85</td>
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<td>305 ± 5</td>
<td>1.07</td>
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<td>430-600 ± 30</td>
<td>1.05</td>
<td>.95</td>
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Abbreviation: PLE, polymorphic light eruption.
continue to use intervention out of habit may explain the increased probability of objective resolution among those who underwent phototesting a second time. Three of the group who showed resolution on phototesting reported ongoing photosensitivity. Although it is accepted that action spectra change over time, little about the subject has been published. Of the 25 patients who underwent phototesting more than once, the spectra were broadened in 9 and narrowed in 6, suggesting that variation in action spectra with time is common.

No literature on prognostic variables has been published. None of the variables analyzed in this cohort (Table) was of significant predictive value, but it is likely that the numbers were too small to detect even modest associations as significant. That the subjects who reported a longer duration of disease at diagnosis showed a trend toward a poorer prognosis may explain our finding that SU is a more chronic disease than was described in Italy, where more rapid access to a dermatologist may mean that a subset of patients with a faster resolution of SU are seen. No patients with a positive intradermal test result showed resolution of SU, possibly suggesting that the presence of a serum factor might correlate with persistence, but as the numbers were small and this was a selected group with difficult-to-suppress disease, no conclusions can be made.

Sunscreens are generally reported to be of limited benefit, and so our finding that this was the therapy most likely to be considered of long-term benefit by patients is novel. Newer sunscreens with a broader spectrum and a higher sun protection factor provide improved protection. They do not, however, filter visible wavelengths, which 93% of patients were sensitive to, and therefore provide limited protection. For individuals sensitive in this spectral region, the use of a physical sunscreen that filters visible wavelengths is recommended, in conjunction with a broadband-spectrum sunscreen. (The sunscreens used in this study were produced by Tayside Pharmaceuticals.) The finding that 35% of our subjects obtained good benefit and a further 35% some benefit from antihistamines is in keeping with the majority of subjects with a positive intradermal test result showed resolution of SU, possibly suggesting that the presence of a serum factor might correlate with persistence, but as the numbers were small and this was a selected group with difficult-to-suppress disease, no conclusions can be made.

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