

CLINICAL REPORT

Somatic and Psychiatric Comorbidity in Patients with Chronic Pruritus

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It has been reported that 10–50% of patients with pruritus but no skin rash have an underlying systemic disease and up to 70% a psychiatric one. The aim of this retrospective study was to review the records of a large number of patients with chronic pruritus for concomitant diseases and treatment options. Medical records of 139 patients (52 males, 87 females) with chronic pruritus who visited the outpatient dermatological clinic during a 17-month period were reviewed. Itch was the presenting symptom in 6 of 47 patients with systemic disease and in 17 of 31 patients with psychiatric disease. Twenty-four patients had neuropathic itch and 37 patients had pruritus of unknown origin. The most severe and long-lasting itch was found in patients with multiple systemic diseases and in those with pruritus of unknown origin. Pruritus of the scalp and face was most common in psychogenic pruritus. Phototherapy was found to be a useful therapeutic option. In conclusion, systemic diseases are unlikely to cause chronic pruritus in patients consulting a dermatology department. Key words: itch; cofactors; psychiatric; systemic; pruritus of unknown origin; therapy.

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Itch has been reported to be the dominating skin complaint in the general population.

In a recent population study based on postal questionnaires in Norway, 27% of the 18,770 respondents reported itch (1). In a previous population study in London, UK, based on postal questionnaires and additional home visits, the prevalence of itchy skin conditions was estimated to be 8.2% (2). As a symptom of skin disease, itch is often described in medical records but is not normally allocated a code from the International Statistical Classification of Diseases (ICD-10); the code for the skin disease is used instead. However, itch occurring in skin that appears to be normal, or in skin with secondary reactive conditions such as excoriations, lichenification or prurigo, qualifies for a principal diagnosis of its own: L29.9 (pruritus), L29.8 (other pruritus) or L28.1 (prurigo). The prevalence of pruritus as a diagnosis in a Danish acute outpatient clinic at a university hospital was found to be 2.5% (3). However, this number may

be an underestimation as the patients were emergency referrals from other hospital departments, private dermatologists and general practitioners. Chronic pruritus, i.e. pruritus with duration of 6 weeks or more, is likely to be referred to dermatology departments via other more planned routes (4).

Chronic pruritus can be a disabling disease, associated with suffering and social isolation. Several retrospective studies on patients with chronic pruritus have been performed, and these have revealed a great variation (13–50%) in the coexistence of chronic pruritus and systemic diseases (5–13). These data originate from dermatological departments. However, pruritus patients with systemic diseases may also be managed by their internists, and the majority never see a dermatologist.

A high incidence of psychiatric illness (70%) has also been described in dermatology inpatients with chronic itch (14). Also, negative life events, especially where social support is lacking, have been shown to be associated with occurrence of itch (2). However, psychiatric diseases or negative life events do not in themselves motivate a diagnosis of psychogenic pruritus. A chronological relationship of the occurrence of pruritus with one or several life events, and improvement in pruritus with psychotropic drugs or psychotherapies, may confirm the diagnosis (15). Pruritus with no skin rash is often not only a diagnostic, but also a therapeutic, challenge (16).

The aim of this retrospective study was to investigate the occurrence of systemic and psychiatric disease in patients with chronic pruritus and no skin rash and to assess a possible chronological relationship with life events. In addition, the outcome of common treatment options was evaluated.

MATERIALS AND METHODS

Medical records were reviewed for 149 patients diagnosed with pruritus, and with no visible primary skin disease, who visited the Department of Dermatology at Lund University Hospital between January 2005 and May 2006. The inclusion criteria were: pruritus UNS (ICD code L29.9), and other pruritus (L29.8) with duration of 6 weeks or longer.

The majority of patients visited the department several times during this period and many of them had older medical records. The following data was obtained from the patient's medical history: (i) localization of itch, (ii) status of the skin, (iii) laboratory findings, (iv) occurrence of other diseases, and (v) different treatment regimes.

Information about the occurrence of other medical illness was based on the patient's own reports or on the laboratory findings at our department and not on medical diagnoses from the medical records of other departments.

In addition, data on previous psychiatric disease was based on the patient's own reports or on referral records. The diagnosis psychogenic pruritus was made by a psychologist (M. Sterner) using the diagnosis criteria of the French Psychodermatology Group (15).

The duration of itch was classified into three groups: < 1 year, 1–5 years and > 5 years. In the few cases for which duration of itch was not stated, a duration of < 1 year was assumed.

Severity of itch was seldom stated in the medical records. As scratching often parallels the severity of itching, the status of the skin was classified as: (i) normal skin, (ii) excoriated skin or (iii) prurigo or lichen simplex. In the few cases where the status was not described; normal skin was considered.

Laboratory investigation included as a minimum: blood count, differential blood count, platelets, serum iron, blood glucose, creatinine, liver transaminases, bilirubin, alkaline phosphatase, and thyroid function tests. Investigation to exclude a malignancy was performed in cases of anaemia, fatigue or reduction in weight.

RESULTS

Ten patients were excluded because further medical records explained pruritus to be secondary to scabies in five patients, nummular eczema in two patients, and toxicoderma, psoriasis, and Grover's disease in one patient each.

A total of 139 patients (52 men and 87 women) were included in the study. The age distribution in the whole study material is shown in Fig. 1 and the distribution of males/females per diagnosis is shown in Table I. Sixty patients complained of general itch, while the rest reported itch at several locations, and 38 complained of genital itch. However, the most troublesome locations are shown in Table II. The duration of itch per diagnosis as well as itch intensity are shown in Table III. A majority of patients with multiple internal diseases, pruritus of unknown origin (PUO), kidney

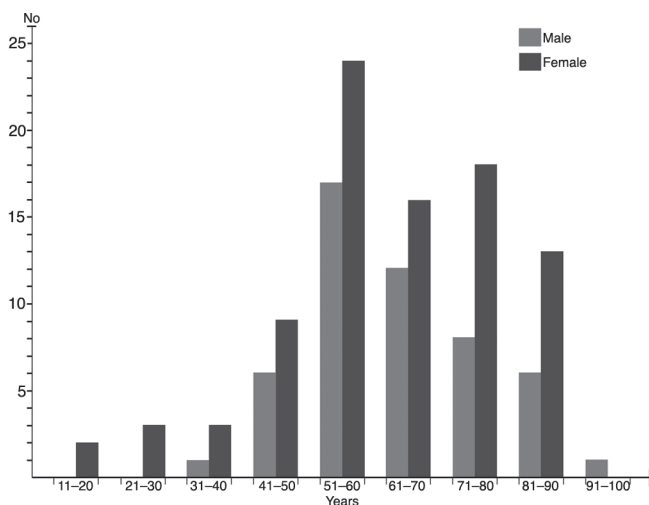


Fig. 1. Age distribution of the study material.

Table I. Distribution of the patients according to diagnoses

Diagnosis	Males	Females
Neuropathic (n=24)		
Brachioradial pruritus	3	8
Notalgia paraesthetica + fibromyalgia	3	10
Systemic (n=47)		
Chronic kidney disease	4	0
Diabetes + haematological disease	6	4
Thyroid + liver disease	6	9
Malignancy	4	2
Multiple systemic diseases	3	6
Drugs	3	0
Psychiatric disease	9	22
Pruritus of unknown origin	10	27

diseases and thyroid diseases had severe itch with secondary reactive skin lesions such as excoriations or prurigo (Table III).

Patients with systemic disease

Forty-seven patients (26 males, 21 females, mean age 67 ± 14 years) had one systemic disease and nine patients had two or more internal diseases. Three patients had had new drugs (methadone, etanercept and influenza vaccine) introduced at the time when itch started. In total, 13 patients had chronic kidney disease, 15 suffered from diabetes, 10 from levothyroxine-substituted hypothyroidism, 2 from hyperthyroidism, 11 from iron deficiency, 6 from cholestasis (one was pregnant), 5 from a solid malignancy and one had polycytemia vera and lymphoma. In five cases of malignancy, the disease was stable and the patients had no treatment. One patient was diagnosed with pulmonary carcinoma 2 years after the start of itch. In only three patients with internal disease was itch diagnosed at the time of investigation: two cases of hyperthyroidism and one case of cholestasis secondary to pregnancy. Pruritus improved upon antipruritic therapy before the thyroidea function was normalized. Also, the pregnant woman improved upon treatment and itch disappeared upon delivery. In all other cases, the internal diseases were known for years and did not correlate to pruritus.

Of the 15 patients with diabetes 10 had well-regulated disease and five had high levels of blood sugar at the time of the first presentation of itch. Eleven patients with chronic itch showed iron deficiency, but the supplement of iron was insufficient to cure itch, even if it was partly reduced in some patients. Only one of the patients with chronic kidney disease was on dialysis and two were transplanted.

Nine patients had more than one internal disease and constitute a separate group in the tables and figures – “multiple diseases”.

We were able to establish a chronological relationship between pruritus and internal diseases in only six cases: in two cases each of hyper-thyroidism and cholestasis (one of them being induced by pregnancy), in one case

Table II. Distribution of the most troublesome itch according to diagnoses

Diagnosis	General	Extremity	Trunk	Scalp	Face	Genital
Total	67	29	13	16	7	2
Brachioradial pruritus	0	11	0	0	0	0
Notalgia paraesthetica	0	0	8	1	0	0
Chronic kidney disease	1	2	1	0	0	0
Fibromyalgia	3	0	0	1	0	0
Diabetes	4	0	0	2	0	0
Haematological disease	2	1	1	0	0	0
Thyroid disease	4	2	0	1	1	0
Liver disease	6	1	0	0	0	0
Malignancy	5	0	1	0	0	0
Multiple systemic diseases	6	1	1	0	0	0
Drugs	2	1	0	0	0	0
Psychiatric disease	9	3	3	5	5	2
Pruritus of unknown origin	17	7	6	6	1	0

of pulmonary carcinoma, and in one case of lymphoma and polycythemia vera.

Many older individuals were on some kind of drug therapy. At the presentation of itch, most patients suspecting itch as a side-effect of drugs contacted their physician and treatment was withdrawn or changed. In only two patients was the itch found to be induced by drugs: etanercept and a vaccine against influenza.

Patients with neuropathic pruritus

Of 24 patients with neuropathic itch (6 males, 18 females, mean age 57 ± 13 years) ten patients had brachioradial pruritus, nine had notalgia paresthetica and four had both of these two diagnoses, with one predominating in intensity as shown in Table II. One patient had itch in one foot, digitalgia paresthetica (this female patient was incorporated in the group of brachioradial pruritus in the table) and four patients suffered from fibromyalgia (6). While patients with

fibromyalgia had general pruritus, itch in the other patients was localized to scapula in notalgia paresthetica, arms or shoulders in brachioradial pruritus and foot in digitalgia paresthetica, respectively.

Patients with psychiatric disease

This group included thirty-one patients (9 males and 22 females, mean age 56 ± 15 years). Thirteen patients had a previous psychiatric diagnosis: seven had depression, five suffered from psychosis and two from psychological stress. All patients were either on medication or psychotherapy. There was no chronological relationship between the psychiatric disorder and the occurrence of pruritus. In 17 patients we could confirm an association between itch and psychiatric illness: seven with parasitophobia, six with depression, two with psychosis, one with trichotillomania and one with dysmorphophobia. Ten patients reported occurrence of itch at a time of one or several life events, including divorce, immigration to Sweden, childbirth, sexual intercourse with a prostitute, and severe disease of a close relative.

A large number of patients with psychiatric disease had pruritus of the scalp (16.7%) and face (16.7%) compared with non-psychiatric patients (10.1% and 1.8%, respectively) (Table II). The occurrence of pruritus of the face was significantly more common in psychogenic pruritus ($p < 0.005$).

Patients with pruritus of unknown origin

In the remaining 37 patients (10 males and 27 females, mean age 66 ± 15 years), no systemic cause, neuropathic disease or psychiatric disorder was found, which resulted by exclusion in the diagnosis PUO. All but one of the patients were older than 40 years and 24 of them were older than 65 years. Four patients aged 84, 85, 86 and 90 years, respectively, were diagnosed with dementia.

Table III. Duration and intensity of itch, judged from the status of the skin

Diagnosis	Duration of itch			Severity of itch as reflected in the skin status		
	<1 year	1–5 years	>5 years	Normal	Excoriated	Prurigo
Total	50	55	34	69	45	25
Brachioradial pruritus	6	4	1	6	4	1
Notalgia paraesthetica	3	4	2	7	1	1
Chronic kidney disease	1	1	2	1	3	
Fibromyalgia	1	1	2	2	1	1
Diabetes	3	2	1	2	3	1
Haematological disease		2	2	2	2	
Thyroid disease	3	5	1	5	3	1
Liver disease	3	1	2	2	2	2
Malignancy	1	4	1	3	2	1
Multiple systemic diseases	3	3	3	2	1	6
Drugs	2	1		2	1	
Psychiatric disease	12	13	6	20	9	2
Pruritus of unknown origin	12	14	11	15	13	9

Treatment outcomes

Sedating antihistamines were prescribed as night medication to 72 patients; 26 improved from the medication, 33 patients had to stop the medication because of fatigue, and for 13 patients, no follow-up was reported. Non-sedating antihistamines were tried in 70 patients; 34 benefited from the medication, 17 did not respond and 19 were not followed up. Patients with dry skin were almost always treated with moisturizers. Elderly patients were also treated with corticosteroids, group 2 or 3. Thirty patients (5 with normal skin, 15 with excoriations and 10 with prurigo) were treated with local steroids with good results. Phototherapy was given to 44 patients. Thirty patients were treated with narrowband ultraviolet B (UVB), all but one with good effect. Seven patients were treated with broadband UVB, two with UVA/UVB and two were treated with psoralen plus ultraviolet A (PUVA), all with good results. Topical capsaicin (0.025%) was helpful in 11 patients with neuropathic itch and gabapentin was helpful in one patient.

Thirteen patients with a psychiatric disease were treated by psychiatrists; four of them used antidepressants while one used a neuroleptic drug when the pruritus started. Fourteen of the 17 patients for whom we could confirm an association between itch and life events or exacerbation of a psychiatric disease were improved by treatment with psychotropic drugs.

DISCUSSION

Chronic itch, like chronic pain, is often associated with a fear of an underlying malignancy or other systemic disease. How should we investigate these patients? How often should we repeat the investigations? That depends on how often we can expect to discover a previously unknown systemic disease that is responsible for causing pruritus. Previous reports on the association of chronic pruritus with systemic diseases present diverging results. Rajka (10) found systemic causes in 17 of 34 inpatients with pruritus (50%), Beare (9) detected systemic aetiology in 7 of 43 outpatients with pruritus (16%), Kantor & Lookingbill (8) in 6 of 44 (14%) and Zirwas & Seraly (12) in 11 of 50 (22%) and Afifi et al. (13) in 38 of 95 (40%). In some studies, all patients with pruritus as a main diagnosis were analysed, and patients with skin rash as a cause of pruritus were included. In three studies based on large numbers of patients seeking or referred for work-up of pruritus, 24%, 42% and 57% of cases, respectively, were due to dermatoses (5, 6, 11). When the patients with dermatoses are excluded only 31% (18 of 56) of the patients of Lyell (11) and 82% (47 of 57) of the outpatients of Weisshaar et al. (6) are found to have an underlying systemic disease. Sommer et al. (5) considered a systemic disease to be

responsible for pruritus when a clear relationship between onset and course of both pruritus and the disease was reported. They found such an association in 22% (35 out of 153) of the inpatients with pruritus in whom the cutaneous cause of pruritus was excluded.

In the present study we found that, out of 139 reviewed outpatients with chronic pruritus and no skin rash responsible for the pruritus, 39 patients had one systemic disease and nine had several systemic diseases. However, there was clear evidence of an association between chronic pruritus and systemic disease in only six patients (4.3%). Pruritus was the presenting symptom in one case of hyperthyroidism, one case of hypothyroidism, two cases of cholestasis (one of them being induced by pregnancy), one case of pulmonary carcinoma and one case of lymphoma.

In addition, the course of pruritus was not always related to the management of the internal disease. Only one-third of patients with diabetes in the present study had high levels of blood sugar at the time of the first presentation of itch. These data indicate that itch is not directly dependent on blood sugar levels which is in accordance with a previous report (17). Of the six patients with diabetes as the only systemic disease, four had general pruritus and two had pruritus of the scalp.

We found two pruritus patients with fibromyalgia, which is known to alter the perception of pain due to both central and peripheral mechanisms (18). The same mechanisms could explain a pathological transmission of itch.

Itch can accompany advanced malignancies. In our five patients with a history of malignancy, the tumour was in remission, and required no ongoing treatment. It explains why 50% of these patients had normal skin, 50% had excoriations and none had prurigo. There was probably no connection between itch and the previous malignancy. One patient who presented with severe pruritus and prurigo developed lung carcinoma later.

Like Kantor & Lookingbill (8), as well as Sommer et al. (5), we observed that patients with a combination of several internal diseases, such as chronic kidney disease, liver disease, hypothyroidism and iron deficiency, had more severe and more longstanding pruritus.

Thirty-one (22%) of our patients had psychiatric diseases. This low number compared with the study of Schneider et al. (14), who found a psychiatric diagnosis in more than 70% of their patients. Thirteen of our patients had longstanding psychiatric diseases that were treated by psychiatrists, four patients were on antidepressants, while one used a neuroleptic drug when the pruritus started. Although psychiatric medication is used for the treatment of pruritus, it did not provide sufficient protection in our patients (19). This is in line with the finding that pruritus may occur in 32–42% of psychiatric inpatients (20, 21). In the remaining 17 patients (12%) with psychiatric disease, pruritus was the presenting symptom. Fourteen of these patients impro-

ved with psychotropic drugs, supporting the diagnosis of psychogenic pruritus (15). Antidepressants have been described as a successful treatment for pruritus of the scalp (22). This finding is in accordance with our observation that pruritus of the face and scalp was found in 33.4% of our psychiatric patients compared with 11.9% of non-psychiatric patients with pruritus. Pruritus of the face, in particular, was significantly more common in psychiatric patients and suggests a more careful taking of psychiatric history in this group.

Thirty-seven of all patients had PUO. Like the patients with the multiple internal diseases, their itch was severe and longstanding. Eighty percent of the patients with PUO have had itch for more than 1 year and 64% were older than 65 years. Pruritus is the most common dermatological complaint in people over the age of 65 years, and according to the older inadequate terminology their pruritus could be defined as "senile pruritus" (23). This term may hint at degenerative changes in the skin or along the neuronal pathway of itch transmission. Only four of the 25 patients older than 65 years had dementia, which excludes central nervous changes in the perception of itch as a main cause and suggests degenerative changes in the skin to be of greater importance. Often there were no signs of primary dermatitis, but dry skin and secondary reactive conditions were found in elderly patients.

Dry skin, reduced sweating, decreased production of sebum, thicker stratum corneum, impaired skin barrier, reduced reaction to histamine or a sub-clinical eczema have been suggested as causes of itch in elderly people (24). While dry skin responds to emollients, subclinical eczema and reactive skin lesions may respond to topical treatment with moderate potency topical steroids or with tacrolimus. Our findings support the hypothesis of a subclinical eczema, as the majority of patients had no inflammation in the skin, but a subpopulation of these patients (34 patients) improved with low or moderate potency topical steroids (23). Even if such therapy is not normally practised on non-inflamed skin, the results suggest that there is potential for anti-inflammatory therapy in the skin of elderly people. Sedating antihistamines that are the first-line treatment of generalized itch may result in impaired memory or psychomotor function in elderly people. Many of our elderly patients had fatigue when undergoing such therapy. Non-sedating antihistamines were tried in 70 patients; 34 benefited from the medication, while 17 did not respond and 19 were not followed up.

Thirty patients in whom several therapeutic options were ineffective were treated with narrowband UVB, all but one with good effects. This therapy, which offers short exposure time in the booth, may be considered as a treatment of choice. UV exposure should, however, be administered with caution as sunburn reactions evolve more slowly in ageing skin.

We conclude that the most severe and long-lasting itch was found in patients with multiple systemic diseases and in patients with PUO. It also appears that investigation of patients with chronic pruritus seldom reveals a previously unknown systemic disease that is responsible for causing pruritus. Pruritus of the scalp and face was most common in psychogenic pruritus. Even if sedating antihistamines are the first-line treatment, caution should be exercised when treating elderly patients for whom non-sedating antihistamines, topical steroids at most itchy locations and phototherapy may be recommended.

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REFERENCES

1. Dalgard F, Lien L, Dalen I. Itch in the community: associations with psychosocial factors among adults. *J Eur Acad Dermatol Venereol* 2007; 21: 1215–1219.
2. Rea JN, Newhouse ML, Halil T. Skin disease in Lambeth. A community study of prevalence and use of medical care. *Br J Prev Soc Med* 1976; 30: 107–114.
3. Kiellberg Larsen H, Sand C. Referral pattern of skin diseases in an acute outpatient dermatological clinic in Copenhagen. *Acta Derm Venereol* 2005; 85: 509–511.
4. Ständer S, Weisshaar E, Mettang T, Szepietowski JC, Carstens E, Ikoma A, et al. Clinical classification of itch: a position paper of the International Forum for the Study of Itch. *Acta Derm Venereol* 2007; 87: 291–294.
5. Sommer F, Hensen P, Böckenholt B, Metzke D, Luger TA, Ständer S. Underlying diseases and co-factors in patients with severe chronic pruritus: a 3-year retrospective study. *Acta Derm Venereol* 2007; 87: 510–516.
6. Weisshaar E, Apfelbacher C, Jäger G, Zimmermann E, Bruckner T, Diepgen TL, et al. Pruritus as a leading symptom: clinical characteristics and quality of life in German and Ugandan patients. *Br J Dermatol* 2006; 155: 957–964.
7. Polat M, Oztas P, Ilhan MN, Yalçın B, Alli N. Generalized pruritus: a prospective study concerning etiology. *Am J Clin Dermatol* 2008; 9: 39–44.
8. Kantor GR, Lookingbill DP. Generalized pruritus and systemic diseases. *J Am Acad Dermatol* 1983; 9: 375–382.
9. Beare JM. Generalized pruritus. A study of 43 cases. *Clin Exp Dermatol* 1976; 1: 343–352.
10. Rajka G. Investigation of patients suffering from generalized pruritus with special references to systemic diseases. *Acta Dermatol Venereol* 1966; 46: 375–382.
11. Lyell A. The itching patient: a review of the causes of pruritus. *Scot Med J* 1972; 17: 334–347.
12. Zirwas MJ, Seraly MP. Pruritus of unknown origin: a retrospective study. *J Am Acad Dermatol* 2001; 45: 892–896.
13. Afifi Y, Aubin F, Puzinat E, Degouy A, Aubrion D, Hassam B, et al. Pruritus sine materia: a prospective study of 95 patients. *Rev Med Interne* 2004; 25: 490–493.
14. Schneider G, Driesch G, Heuft G, Evers S, Luger TA, Ständer S. Psychosomatic cofactors and psychiatric comorbidity in patients with chronic itch. *Clin Exp Dermatol* 2006; 31: 762–767.

15. Misery L, Wallengren DJ, Weisshaar E, Zalewska A; French Psychodermatology Group. Validation of diagnosis criteria of functional itch disorder or psychogenic pruritus. *Acta Derm Venereol* 2008; 88: 503–504.
16. Gupta MA, Gupta AK. Medically unexplained cutaneous sensory symptoms may represent somatoform dissociation: an empirical study. *J Psychosom Res* 2006; 60: 131–136.
17. Greaves MW. Itch in systemic disease: therapeutic options. *Dermatol Ther* 2005; 18: 323–327.
18. Haroon TS. Diabetes and skin – a review. *Scott Med J* 1974; 19: 257–267.
19. Yosipovitch G, Yarnitsky D, Mermelstein V, Sprecher E, Reiss J, Witenberg C, et al. Paradoxical heat sensation in uremic polyneuropathy. *Muscle Nerve* 1995; 18: 768–771.
20. Abeles AM, Pillinger MH, Solitar BM, Abeles M. Narrative review: the pathophysiology of fibromyalgia. *Ann Intern Med* 2007; 146: 726–734.
21. Shaw RJ, Dayal S, Good J, Bruckner AL, Joshi SV. Psychiatric medications for the treatment of pruritus. *Psychosom Med* 2007; 69: 970–978.
22. Mazeh D, Melamed Y, Cholostoy A, Aharonovitch V, Weizman A, Yosipovitch G. Itching in the psychiatric ward. *Acta Derm Venereol* 2008; 88: 128–131.
23. Kretzmer GE, Gelkopf M, Kretzmer G, Melamed Y. Idiopathic pruritus in psychiatric inpatients: an explorative study. *Gen Hosp Psychiatry* 2008; 30: 344–348.
24. Ward JR, Bernhard JD. Willan's itch and other causes of pruritus in the elderly. *Int J Dermatol* 2005; 44: 267–273.
25. Hoss D, Segal S. Scalp dysesthesia. *Arch Dermatol* 1998; 134: 327–330.