Acta Dermatovenerol Croat 2017;25(4):276-280 CLINICAL ARTICLE

The Value of Etiological Tests and Skin Biopsy in the Management of Prurigo Simplex Subacuta

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Received: February 22, 2016
Accepted: October 1, 2017

ABSTRACT It has been emphasized that prurigo simplex subacuta may be associated with various disorders and may be clinically confused with dermatitis herpetiformis. Aim of the study was to evaluate the value of our set of tests for finding possible associations and for the aforementioned differential diagnosis. Rates of implementations and abnormal results in our set of tests, including skin prick test, skin biopsy, complete blood count, blood chemistry panel, and psychiatric evaluation were analyzed retrospectively between the years of 2010 and 2015 in 130 patients clinically diagnosed with prurigo simplex subacuta. The set of tests was implemented completely in 43.8% patients and with only a single missing test in 31.5% of the patients. The least implemented procedure was psychiatric evaluation (66.9%). The most commonly found issues were psychiatric abnormalities (55.2% of 87 psychiatrically evaluated patients) and atopy (53.8% of 104 skin prick tested patients). The most common finding suggestive of internal diseases was hyperglycemia (25.4% of 130 patients). It was a striking result that hematological malignancies were suspected upon complete blood count and peripheral blood smear and confirmed by further investigations in 4 of 102 patients. Dermatitis herpetiformis was diagnosed in 2 of 120 skin biopsied patients. Because of the substantial rate of implementation, the high frequencies of psychiatric abnormalities and atopy, and detection of hematological malignancies and dermatitis herpetiformis even in just a few patients, we recommend our set of tests for patients clinically diagnosed as prurigo simplex subacuta.

KEY WORDS: prurigo, etiology, association

INTRODUCTION

Prurigo simplex subacuta (PSS), also known as "itchy red bump disease" or "papular dermatitis", is clinically characterized by discrete, pale red papules, which itch intensely, thereafter rapidly evolving into excoriations, and are symmetrically distributed especially on the extensor surfaces of the limbs (1,2). Its associations with atopy and with various internal diseases are well known (3). Moreover, these associations have been emphasized with the use of terms such as prurigo Besnier, prurigo diabetica, prurigo uremica, prurigo hepatica, and prurigo lymphatica. PSS is classified among psychosomatic skin diseases, in which emotional factors play an important role in the etiology (4,5). Although it can be readily distinguished from dermatitis herpetiformis (DH) histopathologically, the clinical differential diagnosis between the two may be difficult (6,7).

In the light of these data, we had previously determined tests necessary in patients with lesions clinically suggestive of PSS. These tests were the skin prick test with common aeroallergens, skin biopsy, fasting blood sugar measurement, kidney, liver, and thyroid

function tests, complete blood count, peripheral blood smear, and clinical evaluation by a psychiatrist. In this study, we reviewed the records of 130 such patients in order to determine the rate of implementation of these tests and more importantly the frequencies of their abnormal results and consequently the level of necessity of each test.

Patients and Methods

We searched for patients clinically diagnosed with PSS in the computerized medical records of our Department between 2010 and 2015. One hundred and thirty such patients were found. Their records were reviewed, especially for data concerning dermatological and systemic clinical findings along with the following tests: (1) skin prick test with common aeroallergens to detect atopy; (2) histopathological examination and direct immunofluorescence test of a skin biopsy specimen to make a differential diagnosis with DH; (3) fasting blood sugar measurement to detect hyperglycemia; (4) blood urea nitrogen and serum creatinine measurements to detect abnormal renal function; (5) serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) measurements to detect abnormal liver function; (6) serum thyroid stimulating hormone (TSH) and free thyroxine-4 measurements to detect abnormal thyroid function; (7) complete blood count and peripheral blood smear hematological malignancies; and (8) clinical evaluation by a psychiatrist.

The rate of implementation of each of these eight tests was calculated. Additionally, the frequencies of abnormal results in these tests were determined. Comparisons between the subgroups of the patients in frequency of abnormal results were statistically analyzed using by the chi-square test. The ethics approval for this study was obtained from the University of Çukurova Research Ethics Board.

RESULTS

Of 130 patients with PSS, 85 (65.4%) were women and 45 (34.6%) men. Their minimum, maximum, average, and median ages were 17, 88, 51.8 (Standard Deviation (SD) ± 5.7), and 51.5 years, respectively. The duration of their diseases were between 1 month and 30 years, with a median of 15 months. All patients had been treated with antiscabietics, but their itchy papules persisted. Moreover, there was no sign suggestive of insect bites in their recent medical histories and physical examinations or any specific drug history that could have provoked PSS.

A skin prick test was performed in 104 patients (80%); skin biopsy in 120 (92.3%); fasting blood sugar measurement in 130 (100%); renal function tests in 130 (100%); liver function tests in 130 (100%); thyroid function tests in 120 (92.3%); screening tests for hematological malignancies in 102 (78.5%); and psychiatric evaluation in 87 (66.9%). Among these 8 tests, all 8 were performed in 57 (43.8%) patients, 7 in 41 (31.5%), 6 in 21 (16.2%), 5 in 10 (7.7%), and 4 in 1 (0.8%) patient.

Atopy, i.e. skin prick test positivity, was found in 53.8% (56/104) of patients. Histopathological examination showed only postinflammatory hyperpigmentation in 1 patient and only crust formation in 2 patients. Histopathological findings were consistent with PSS in 115 patients. In the remaining 2 patients, histopathological and immunopathological findings were consistent with DH. The common clinical finding of these two patients was that intact vesicles were found among excoriated papules, even if few in number. Hyperglycemia was found in 25.4% (33/130) of patients. Abnormal renal, liver, and thyroid function tests were observed in 5.4% (7/130), 2.3% (3/130), and 8.3% (10/120) of patients, respectively. Hematological malignancies were suspected upon complete blood count and peripheral blood smear and confirmed by further tests in 3.9% (4/102) of patients. They were myelodysplastic syndrome in 2, hairy cell leukemia in 1, and chronic lymphocytic leukemia in 1 patient. Of 87 patients in whom a clinical evaluation by a psychiatrist was performed, 48 (55.2%) had psychiatric abnormalities. Anxiety disorder was found in 22, depressive disorder in 17, somatoform disorder in 3, and other psychiatric disorders in 6 patients.

Briefly, the most common issues found in our tests for PSS were atopy and psychiatric abnormalities. The frequency of atopy was not significantly different between male and female patients (24/37 versus 32/67), between patients aged up to 51.5 years, which was the median age of our patients, and older patients (30/56 versus 26/48), and between patients having the disease for up to 15 months and patients with a more prolonged disease (30/56 versus 26/48). This was also valid for psychiatric abnormalities (male versus female patients: 12/27 versus 36/60; younger versus older patients: 22/41 *versus* 26/46; patients with a shorter disease duration versus a longer disease duration: 23/45 versus 25/42).

DISCUSSION

With decreasing order of frequency, the issues which were found in this study by our seven tests were psychiatric abnormalities (55.2%), atopy (53.8%), hyperglycemia (25.4%), abnormal thyroid function tests (8.3%), abnormal renal function tests (5.4%),

findings suggestive of hematological malignancies (3.9%), and abnormal liver function tests (2.3%). As the eighth test, histopathological and immunopathological examination resulted in findings consistent with DH in 2 (1.7%) of the 120 patients, in whom a skin biopsy was taken.

Although the main purpose of this study was to determine the levels of necessity of tests which were done in our patients with PSS depending on the frequencies of their abnormal results, such a determination also requires some evaluation other than examining these frequencies. First of all, they should be compared with the frequencies of abnormal results of the same tests in the general population.

In 2013, the Health Ministry of Turkey published a report about the prevalence of chronic diseases in Turkey (8). According to this report, the standardized rate of mental health problems was 11.3%. This rate was different for men and women, 7.1% and 15.5%, respectively. These rates were even somewhat lower in the Mediterranean region where our city is located, 6.5% and 15.2%, respectively. Thus, it was very obvious that, in our patients, PSS was associated with a markedly increased prevalence of psychiatric abnormalities. Therefore, clinical evaluation by a psychiatrist was a very necessary procedure for these patients.

We could not find any data from our city, Adana, on the prevalence of atopy in the general population. In a population-based epidemiological study from Ankara, the capital city of Turkey, skin prick tests were found to be positive for at least one aeroallergen in 25% of the participants (9). In a similar study from Antalya, a city located in the Mediterranean region, this figure was 31.1% (10). A similar study was also done in city nearer to ours, namely Gaziantep. In this study, the sample was chosen from the general population of the city center. However, skin prick-tested subjects were not randomly chosen from the sample, but where rather subjects who had allergy or respiratory complaints in the past year, and constituted the risk group. The frequency of positive skin prick tests in these subjects was almost 44% for adults (11). The frequency in our patients with PSS was higher (53.6%) even than that of this risk group. Moreover, our frequency was not far from the rate of 61.8%, which was obtained in patients with atopic dermatitis in a study done in Dörtyol, a town very close to our city (12). Therefore, it is most likely that PSS in our patients was associated with an increased prevalence of atopy. The skin prick test was thus a necessary test in these patients.

In a report by the Health Ministry of Turkey, the rate of subjects with impaired fasting plasma glucose or with diabetes mellitus was 26.9% in the general population (8). The rate of hyperglycemia in our patients with PSS was not higher; on the contrary, it was slightly lower. In a study performed on 512 Turkish adults, the prevalence of hypothyroidism was found to be 4.4% and that of hyperthyroidism was 4.7%, according to TSH levels (13). Our rate of abnormal thyroid function tests was not higher than the sum of these rates but was, again, slightly lower. Thus, at first glance, one might say that measurements of fasting blood sugar, serum TSH, and free thyroxine-4 are not necessary tests in PSS. However, the association of this disease with diabetes mellitus and thyroid diseases have been emphasized some texts dealing with its etiology (3,14-16). Moreover, these measurements are inexpensive, at least in our country. On the other hand, as mentioned above, this disease is associated with psychiatric abnormalities in over half of the patients (4,5). However, as seen in our data, the implementation rate of clinical evaluation by a psychiatrist is low, at least in our country, partly because of patient resistance. Using simple tests showing a patient that there is no internal cause for their itching may reassure them, thus breaking their resistance to a psychiatric evaluation.

In a population-based survey of chronic renal disease in Turkey, which was performed on over 10000 subjects, the prevalence of chronic renal disease (CRD) was found to be 15.7% according to micro- or macro-albuminuria and glomerular filtration rate (17). Our rate of abnormal renal function tests was markedly lower than this rate. However, it is well known that serum creatinine levels do not increase until a moderate to severe reduction in glomerular filtration rate occurs (18). Thus, our rate corresponds to that of at least CRD Stage 3. The sum of rates for CRD Stage 3, 4, and 5 (5.2%) in that study was almost equal to our rate (5.8%). In a study from the Northern Turkey, the prevalence of elevated serum ALT and/or AST was found to be 13.3% (19). Our rate of abnormal liver function tests was markedly lower than this rate. This might be explained by regional differences, since our city is located in Southern Turkey. Based on these findings one might also say that testing blood urea nitrogen, serum creatinine, ALT, and AST are not necessary tests in PSS. However, the association of this disease with chronic kidney and liver failure has been emphasized in almost all texts dealing with its etiology (3,14-16). Therefore, as with the measurements discussed above, renal and liver function tests should also be performed in all patients with PSS.

We could not find any suitable data for comparison of the rate of hematological malignancies found in our study. However, we believe that such a

comparison is not obligatory to evaluate the place of complete blood count and peripheral blood smear as tests in PSS, since they are of great value in detecting hematological malignancy even in only a single malignancy can be detected using these readily available screening tests.

We could not find any general population-based data from Turkey to compare it to the rate of DH observed in our study. This rate (1.7%), however, was much higher than the prevalence of DH reported from various other countries (20-22). More importantly, DH does not usually improve significantly with nonspecific antipruritic remedies, topical corticosteroids, which are the main agents in the symptomatic treatment of PSS, and requires a specific drug, namely dapsone. It was thus of great value to establish the correct diagnosis via skin biopsy even in only a single case among patients having lesions suggestive of PSS. Skin biopsy should therefore be performed at least in patients with intact vesicles among excoriated papules, and in those who do not improve with treatment based on the results of other tests and with nonspecific antipruritic remedies and topical corticosteroids.

CONCLUSION

We recommend these eight tests in cases PSS for the following reasons: atopy and psychiatric abnormalities may be found in the majority of the patients; they have great value in detecting hematological malignancies and establishing a diagnosis of DH even if the number of detected cases is low; the exclusion of internal diseases may reassure the patients; and finally the rate of implementation of these eight tests is high.

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