CLINICAL, LABORATORY AND THERAPEUTIC PROFILE OF LICHEN PLANUS

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CLINICAL, LABORATORY AND THERAPEUTIC PROFILE OF LICHEN PLANUS (Abstract): **Aim:** Retrospective study of the clinical manifestations and clinical forms of lichen planus, investigation methods and therapeutic means using data from patients admitted to the Dermatology Clinic of the “Sf. Spiridon” County Clinical Emergency Hospital Iasi, in the interval January 1st-December 30th, 2015; the obtained results were compared with the data in the literature. **Material and methods:** Forty-five patients were included in the study. The data were interpreted by using various statistical notions: arithmetic mean, percentage distribution, standard deviation, coefficient of variation, “t-Student” test. Histopathological examination was performed in most cases to enhance diagnosis certainty. **Results and discussion:** The analysis of the study group (29 women and 16 men) produced many results in agreement with literature data. In 2015 the prevalence of lichen planus in the patients admitted to the Clinic of Dermatology, regardless of clinical form was 4.01% with a female preponderance (female/male ratio 2:1). The mean age of the study patients was 55.31 years and 79.98% of total cases were in the fourth and six decades of life. The main infectious risk factor for the development and progression of lichen planus is hepatitis C virus (13.3%). The most common form of lichen planus (88.8%) was the cutaneous form. **Conclusions:** Lichen planus is a chronic autoimmune disease with undulating course and different clinical subtypes that can affect multiple body regions. **Keywords:** LICHEN PLANUS, PAPULE, AUTOIMMUNE DISEASES, LICHENOID REACTIONS.

Lichen planus is a mucocutaneous inflammatory dermatosis of uncertain etiology, with chronic or subacute course, often self-limited (1). The classic description of lichen planus eruption is given by the 5 Ps: purple, planar, polygonal, pruritic, papules (2).

The estimated prevalence of lichen planus in the general population is in the range of 0.2% to 4%. It occurs more fre-
quently in the fifth or sixth decades of life, predominantly in women. Lichen planus in children is uncommon, but cases with familial aggregation have been reported (3).

The cause of lichen planus is still unknown. The etiologic hypotheses include genetic, infectious, psychological and autoimmune factors (1).

Lichenoid eruptions (LDE—probably a type IV hypersensitivity reaction) are reactive mucocutaneous lesions that are nearly identical clinically and histologically with those in idiopathic lichen planus. Drugs more frequently associated with LDE are the synthetic antimalarials, gold salts, D-penicillamine, methyl dopa, B-blockers, angiotensin-converting enzyme inhibitors, spironolactone, nonsteroidal anti-inflammatory drugs, thiazide, phenothiazine derivatives, allopurinol, tetracycline, sulphonylurea (1).

Notable is the association of lichen planus with such autoimmune diseases as systemic lupus erythematosus, myasthenia gravis, dermatomyositis, ulcerative colitis, chronic active hepatitis, pemphigus vulgaris, dermatitis herpetiformis, bullous pemphigoid, alopecia areata, vitiligo, Sjogren's disease, systemic sclerosis. It supports the immunological hypothesis in the pathogenesis of lichen planus (1).

**MATERIAL AND METHODS**

This open and retrospective study was conducted on a sample of 45 patients admitted with a diagnosis of lichen planus to the Dermatology Clinic of the "Sf. Spiridon" Clinical Emergency Hospital Iasi between January 1st and December 30th, 2015.

Data on clinical manifestations, clinical forms, investigation methods and therapeutic approaches were collected. The obtained data allowed us to classify the patients by gender, age, area of residence, etiology, affected areas, clinical form of lichen planus, association with certain diseases, type of administered treatment and its efficacy, and to compare the obtained results with the literature data. The clinical and histopathological examinations proved to be essential in making the diagnosis. In patients who experienced multiple hospitalizations we focused on the criteria for evaluating treatment efficacy and occurrence of side effects.

For data interpretation, we used various statistic notions: arithmetic mean, percentage distribution, standard deviation (to highlight dispersion of data around the calculated value), coefficient of variation (which is an index of dispersion used to compare statistical series), student’s t test (indicating the presence or absence of a significant difference between the two means and between two statistical series that could be correlated with the intervention of objective factors).

**RESULTS AND DISCUSSION**

In 2015 the prevalence of lichen planus in the patients admitted to the Clinic of Dermatology, regardless of clinical form was 4.01%. Per the literature data, the estimated prevalence of lichen planus in the general population is in the range of 0.2% to 4% (3), with geographic area variations.

Among the study patients the urban/rural ratio was 1:1.5. This difference could be related to prolonged occupational sun exposure (farming), multiple studies suggesting a relationship between exposure to ultraviolet (UV) light and disease severity, while improvement in lesions is obtained using UV protection (4).

There was a female preponderance in our study (female/male ratio 2:1) (fig. 1), result in accordance with the literature data (5).
The mean age of the study patients was 55.31 years (range 9 to 87 years). The data are consistent with the literature data, per which lichen planus may occur at any age, with a peak incidence in the third to the sixth decades of life (5). In this study, 79.98% of total cases were in the fourth and six decades of life (fig. 2). A case of childhood lichen planus was recorded in a 9-year-old girl, accounting for 2.22% of all cases, but without familial aggregation of lichen planus (6).

As for the clinical manifestations of lichen planus, the study protocol aimed to analyze the following: disease history, general and local physical examination, association with other diseases. The onset was insidious in most cases, with a progressive development of symptoms and lesions.

Of the medications administered prior to the occurrence of the disease the most common were the drugs for cardiovascular diseases (66.66%) and non-steroidal anti-inflammatory drugs (15.6%), drug classes known as having an important role in the onset or further progression of lichen planus.

Another factor responsible for the development and progression of lichen planus is the infectious one, hepatitis C virus being the most studied agent. Laboratory investigations revealed that 6 (13.3%) of the study patients had chronic hepatitis C, a high percentage considering that the seroprevalence of hepatitis C virus in the general population is about 5% (7). These patients presented mucocutaneous involvement. Other viral infections incriminated are those with herpes family of viruses: herpes simplex, Epstein-Barr, cytomegalovirus and herpesvirus 6. Helicobacter pylori infection (8) was detected in 3 patients.
Local physical examination is useful for the classification of lichen planus cases based on clinical form, lesion morphology and anatomical region.

Of the 45 patients, 40 (88.8%) had cutaneous LP, 5 presented only mucosal involvement (11.1%), and 15 patients both cutaneous and mucosal involvement, accounting for 33.3% of all cases (per the literature data, 30-70% have lichen planus with mucosal involvement (5)).

In the 40 cases of lichen planus with cutaneous involvement, the most common morphological subtype was represented by the classic form (18 cases, 45%) (fig. 3).

The second most common subtype was the atrophic form. Long-term use of potent and super potent topical corticosteroids may lead to the development of this form of lichen planus. In the present study, only 2 of the 7 patients with atrophic lichen planus were known to have lichen planus and were on treatment, the remaining 5 being at their first hospital admission.

Other common subtypes were the hypertrophic subtype, 5 patients (fig. 4), and follicular subtype, 5 patients (fig. 5), 4 of them women presenting alopecia plaques on the scalp and one male patient with lesions on the chest.

Of the 45 patients included in this study 20 (44.4%) presented mucosal involvement. Oral lesions were the most common, and most patients were females (tab. 1).

Of the 13 patients with oral involvement 7 presented the reticular form, which is the most common form. Five patients had the erosive form, the symptoms consisting of pain, burning sensation, sometimes dysphagia. One of these 7 patients,
an 87-year-old male, presented atrophic-erosive lichen planus lesions (fig. 6).

**TABLE I**

**Distribution of mucosal lesions by anatomical areas**

<table>
<thead>
<tr>
<th>Affected mucosal region</th>
<th>Number of patients</th>
<th>Total</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Males</td>
<td>Females</td>
<td></td>
</tr>
<tr>
<td>Oral cavity</td>
<td>4</td>
<td>9</td>
<td>13</td>
</tr>
<tr>
<td>Genital mucosa</td>
<td>3</td>
<td>7</td>
<td>10</td>
</tr>
<tr>
<td>Total</td>
<td>7</td>
<td>16</td>
<td>23*</td>
</tr>
</tbody>
</table>

*the total corresponds to 23 patients as some of them presented both oral and genital involvement

In this study, the diseases most frequently associated with lichen planus were hypertension, diabetes mellitus and chronic venous insufficiency.

A number of autoimmune diseases have been found to be associated with lichen planus: alopecia areata (2 cases, 4.44%), autoimmune thyroiditis/Graves' disease (6 cases, 13.3%), systemic lupus erythematosus (3 cases, 6.66%), vitiligo (3 cases, 6.66%), vasculitis (1 case, 2.22%), plaque morphea (1 case, 2.22%), scleroderma (1 case, 2.22%), pemphigus vulgaris (2 cases, 4.44%), psoriasis (2 cases, 4.44%), making a total of 21 patients, representing 46.6% of the study group. Also, the association with hypersensitivity reactions is mentioned in numerous studies (9): arthritis (3 cases, 6.66%), allergies to various compounds (8 cases, 17.7%), asthma (1 case, 2.22%), gastritis (2 cases, 4.44%), atopic dermatitis (1 case, 2.22%), making a total of 15 patients (33.33%). The results are consistent with the data in the literature and support the autoimmune theory (1).

The triad of oral lichen planus, diabetes mellitus and hypertension, association known as Grüenspan’s syndrome was found in two patients (4.44% share).

The results of laboratory investigations are nonspecific, excluding direct and indirect immunofluorescence, immunohistochemistry and histopathology.

Histopathological examination was performed in most cases to enhance diagnostic certainty, in agreement with the data in the literature (10). The most common changes are the orthokeratotic hyperkeratosis, hypergranulosis, acanthosis, tapered rete ridges, band-like lymphoplasmocytic inflammatory infiltrate at the dermo-epidermal junction the presence of Civatte bodies (apoptotic keratinocytes). These are exemplified in the following iconography,
with images of biopsies collected from our patients (fig. 7, 8, 9, 10).

**Fig. 7.** Hyperkeratosis, hypergranulosis, acanthosis – Classic lichen planis. HE 4x

**Fig. 8.** Spongiosis with exocytosis, Civatte bodies – Lichenoid eruption. HE 10x

**Fig. 9.** Submucosal bullae – Oral lichen planus. HE 4x

**Fig. 10.** Discrete perifollicular inflammatory infiltrate – Follicular lichen planus. HE 4x

Regarding the treatment of lichen planus, the following ones were mainly administered: topical (88.88%), systemic (17.7%) and intralesional corticosteroid therapy (2.2%), therapy with immunosuppressive agents (2.2%), PUVA therapy (2.2%), anti-histamines (93.3%), vitamin C (88.8%) and calcium gluconate (82.2%) (as adjuvants to the main therapy). The main treatment option was topical corticosteroids and in 6 cases (13.3%) was also associated systemic therapy. Systemic corticosteroid therapy was used in 8 cases (17.7%) of lichen planus with severe multiple of both the skin and mucous membranes. Thus, 4 of these cases (8.8%) had rash extended and oral lesions insufficiently responsive to topical treatment, and 3 cases (6.6%) with rash, erosive oral and genital, only one case of lichen planus eruptive generalized unresponsive to topical therapy. Individualized treatment regimens were tailored for each patient, their efficacy, occurrence of possible side-effects and the interaction with the medication used to treat the associated diseases associated being closely monitored.

The course and prognosis are generally favorable, most patients (73.3%) showing...
complete or partial remission of the lesions on treatment. In the patients (26.6%) with persistent lesions the treatment was reconsidered. Clinical forms with negative evolution or absence of remission were the mucosal lichen planus cases, both the oral and genital mucosa. 6 patients (13.3%) had various complications. Thus, three of them (6.6%) suffered diffuse or localized cicatricial alopecia, one man (2.2%) with erosive lichen planus genital complicates with phimosis, and two females (4.4%) develop agglutination of labia minora. Given the risk of complications, sometimes debilitating in lichen planopilaris and mucosal lichen planus, and of malignant transformation of the erosive mucosal forms, patients were informed about these risks and periodic clinical, biological and therapy reassessment visits were recommended.

CONCLUSIONS
The profile of the patients enrolled in this study is consistent with the data in the literature. Thus, our findings emphasize frequently with the association between liver damage and lichen planus, especially HCV infection (6 patients, 13.3%) and cirrhosis (3 cases, 6.6%). In our study, dyslipidemia was found in 48.88% of cases with lichen planus, the most frequent association was made with the cutaneous form (35.5%) followed by the oral (22.2%) and genital form (8.88%). In 2016, Lai YC et al (12) published similar results regarding the association between lichen planus and dyslipidemia. Although, palm-plantar lichen is very rare (1-2% according the literature), in our study it was present in 10% of cases, being characterized by multiple, bilateral lesions associated with severe pruritus. Forward studies will explain this statistics results.

Lichen planus may have a psychosocial impact affecting the quality of life of patients, our study revealing that 8.8% of cases were diagnosed with depression. Giving attention to pathogenesis, clinical picture and an early diagnosis are essential for selecting the most appropriate treatment. Our data referring to the therapeutic options have been aligned with European standards of treatment. Given the undulating nature of the disease, periodic monitoring of disease course and therapeutic efficacy are required.

REFERENCES

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CDH17 IS A MORE SENSITIVE MARKER FOR GASTRIC ADENOCARCINOMA THAN CK20 AND CDX2

Metastatic cancers can be difficult to diagnose in a clinical setting with most being carcinomas. In the past, a panel consisting of cytokeratin (CK) 7, CK20, and CDX2 antibodies has been used to assess gastrointestinal (GI) tumors of unknown primary. Expression of CK7 is observed in a wide variety of carcinomas, thus, it is an important marker in diagnosis. CK20 expression is specific to certain types of cancer and is typically used in combination with CK7 to distinguish different types of tumors. CDX2 is a homeobox gene that encodes an intestine-specific transcription factor and is expressed in the nuclei of epithelial cells throughout the GI tract. Immunohistochemical expression of CDX2 protein in primary and metastatic colorectal carcinomas has been previously documented. CK7 along with CK20 or CDX2 markers constitute an important panel for the diagnosis of GI tumors versus tumors of unknown origin. However, in difficult cases, expression patterns may vary and the presence or absence of these markers may not lead to a definitive diagnosis. Cadherin 17 (CDH17), also called liver-intestine cadherin, is a cell-adhesion protein that is transcriptionally regulated by CDX2, and is involved in tumor invasion and metastasis. CDH17 is a novel diagnostic marker for GI tract carcinoma with greater sensitivity than CDX2 in colon cancers. Recently, a mouse monoclonal CDH17 (clone IH3) antibody has been developed to aid pathologists in interpreting GI adenocarcinomas, especially in cases of unknown primary origin. There have been conflicting results with CDH17 antibodies, even when using the same designated clone as presented in this study. This study will present an immunohistochemical evaluation in a side by-side comparison with antibodies CDH17, CK20, and CDX2 in various neoplastic tissues, with emphasis on GI adenocarcinomas. CDH17 may also be helpful in cases that are negative for CK7, CDX2, and CK20. The study results confirm that CDH17 expression analysis may be of significant value in the diagnosis of GI tumors and those of unknown origin (Altree-Tacha D, Tyrrell J, Haas T. CDH17 Is a More Sensitive Marker for Gastric Adenocarcinoma Than CK20 and CDX2. *Arch Pathol Lab Med* 2017; 141: 144-150).

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