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Correlation between clinical and histopathologic diagnoses of potentially malignant oral lesions

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ABSTRACT

BACKGROUND: *The serious nature of potentially malignant oral lesions (PMOL) demands that the final diagnosis be made on both clinical and histopathologic grounds. The aim of the present study was to determine the correlation between clinical and histopathologic diagnoses of PMOL using a discrepancy index (DI).*

METHODS: *Fifty-one patients with PMOL were examined clinically, and a biopsy was taken from each one. The results of histopathologic diagnosis were compared with the clinical diagnosis. We established that the histopathologic diagnosis was incompatible when the clinical diagnosis was not confirmed. On the basis of the incompatible diagnosis, we calculated a discrepancy index between the clinical and histopathologic diagnosis.*

RESULTS: *Clinically, the homogeneous leukoplakia was the most frequent lesion followed by erosive lichen planus and reticular lichen planus. No cases of erythroplakia were observed. Lesions were most frequently seen at the buccal mucosa, followed by the gingiva (alveolar mucosa) and tongue. The histopathologic diagnosis showed that the majority of the lesions were benign keratoses followed by lichen planus. Three cases of epithelial dysplasia were mild. The DI between clinical and histopathologic diagnosis was 17.6 %. The higher DI was found in erosive lichen planus.*

CONCLUSION: *The obtained findings show that in 90% of leukoplakias, clinical diagnosis was confirmed by histopathologic examination. The discrepancy between clinical and histopathologic diagnoses in 17.6 % of cases suggests that all PMOLs should be submitted to histological analysis.*

KEY WORDS: *Leukoplakia, Oral; Lichen Planus, Oral; Precancerous Conditions; Mouth Disease; Diagnosis, Oral*

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INTRODUCTION

A potentially malignant oral lesion (PMOL) has been defined as a morphologically altered tissue in which cancer is more likely to develop than in its apparently normal counterpart. Leukoplakia is the most common potentially malignant lesion of the oral mucosa (1). It has been suggested that widespread multiple leukoplakias may have a higher potential for developing carcinoma regardless of the grade of epithelial dysplasia (2). Although some previous studies have shown generally poor agreement among pathologists in the histopathologic assessment of oral premalignant lesions (3,4), the taking of a biopsy in leukoplakias should be the standard rule. The problem in such lesions is not so much the histopathologic evaluation of the presence of epithelial dysplasia as it is the possible invasive nature of the lesion (5).

Oral lichen planus (OLP) is one of the most prevalent oral mucosal lesions with an increased potential for malignant development (6). Because of the variations in appearance, the diagnosis of OLP should not be assessed on the histopathologic picture alone, but should also be based on distinct clinical criteria. Histopathologically, typical OLP in a substantial percentage does not correlate with a typical clinical appearance (7).

The management of PMOL is problematical and is largely dependent on the collection of both clinical and histopathologic information.

The aim of the present study was to determine the correlation between clinical and histopathologic diagnoses of PMOL using the discrepancy index.

PATIENTS AND METHODS

The study population comprised 51 patients (31 women and 20 men) aged from 42 to 76 years, who visited the Department of Oral Medicine and Periodontology of the Clinic of Stomatology in Novi Sad, between January 2002 and December 2003. After the patients had provided their consent form, all clinical examinations were performed by one of the authors, with 20-year experience in the diagnostics of oral mucosal lesions. A history was taken from each patient, and the exact location of all lesions were noted down in a case report form, which contained a schematic presentation of the dorsal and ventral view of the mouth, including lips, labial mucosa, gingiva, vestibule, buccal mucosa, floor of mouth, hard palate, soft palate and tongue. The lesions presented clinically as: (i) homogeneous leukoplakia; (ii) non-homogeneous leukoplakia; (iii) erythroplakia; (iv) lichen planus, and (v) actinic cheilitis were determined to be potentially malignant lesions. The clinical diagnosis was reached according to the criteria described in Table 1.

Histopathologic examination of all lesions was performed. If the lesions were small, an excisional biopsy was usually performed. For the large lesions, an incisional biopsy was performed and multiple specimens from different areas were taken. The biopsy specimens

Table 1. The criteria for clinical diagnosis of potentially malignant oral lesions

Diagnosis	Criteria
Homogeneous leukoplakia	a predominantly white lesion of uniform flat, thin appearance that may exhibit shallow cracks and smooth, wrinkled or corrugated surface with a constant texture throughout
Non-homogeneous leukoplakia	a predominantly white or white-and-red lesion that may be irregularly flat, nodular or exophytic
Erythroplakia	a bright red velvety lesion that could not be diagnosed as any other lesion
Reticular lichen planus	a predominantly white bilateral, more or less symmetrical lesion with raised lines or striae forming a lace-like network
Erosive lichen planus	a predominantly red, irregular, erosive or ulcerated lesion associated with the reticular form in the peripheral region or elsewhere in the oral mucosa
Actinic cheilitis	fine or desquamating mucosa lip vermillion with ill-defined margins and with a history of regular and prolonged exposure to sunlight

were fixed in 10% formalin, embedded in paraffin, cut, and stained with hematoxylin-eosin by the standard laboratory procedure. The lesions were histopathologically diagnosed as: benign keratosis, epithelial dysplasia, lichen planus, and actinic cheilitis (8). The histopathologic diagnoses were made by an experienced pathologist using the criteria described in Table 2. In the case of multiple biopsies, the severest histopathologic diagnosis was considered as the final result.

Table 2. The criteria for histopathologic diagnosis of potentially malignant oral lesions

Diagnosis	Criteria
Benign keratosis	no specific changes, hyper- or parakeratosis of epithelium, acanthosis, inflammatory infiltrate in lamina propria
Epithelial dysplasia	cytological epithelial dysplastic changes
Lichen planus	hyper/parakeratosis, basal cell destruction, saw-tooth rete ridges, lichenoid T-lymphocytic inflammatory infiltrate
Actinic cheilitis	hyper- and parakeratosis, acanthosis or epithelial atrophy, changed shape of rete ridges, possible epithelial dysplasia, suprabasal acantholysis, solar change (actinic elastosis) in lamina propria

The histopathologic diagnosis was compared with clinical diagnosis. The histopathologic diagnosis was considered incompatible with the clinical diagnosis when the clinical diagnosis was not confirmed. We calculated a discrepancy index (DI): (the number of incompatible diagnosis/the number of total sample) x 100 (9).

RESULTS

Clinically, leukoplakia (homogeneous and nonhomogeneous) was the most frequent lesion followed by erosive and reticular lichen planus. The majority of the patients presented multiple lesions in oral mucosa. Among 26 homogeneous leukoplakias, gingiva (n=15) and buccal mucosa (n=10) were the major affected sites, whereas buccal mucosa (n=3), gingiva (n=2), and palate (n=2) were predominantly affected with nonhomogeneous leukoplakias (Table 3). No cases of erythroplakia were observed.

Table 3. Distribution of patients with PMOLs by clinical diagnosis, sex and anatomical location

Clinical diagnosis	Patients n (L) %	Sex M/F	Anatomical location: Buccal mucosa	Gingiva (alveolar mucosa)	Vermillion	Palate	Mouth floor	Tongue
Homogeneous leukoplakia	26 (30) 51.0	17/9	10	15	3	1	0	1
Non-homogeneous leukoplakia	4 (9) 7.8	2/2	3	2	0	2	1	1
Reticular lichen planus	5 (8) 9.8	0/5	5	1	0	0	1	2
Erosive lichen planus	15 (24) 29.4	3/12	15	2	2	0	0	5
Actinic cheilitis	1 (1) 2.0	0/1	0	0	1	0	0	0
Total	51 (72) 100.0	22/29	33	20	6	3	2	9

(L) number of lesions

The histopathologic examination indicated that the majority of the lesions were benign keratoses. Three cases of epithelial dysplasia were mild. In 5 cases of lichen planus, clinical diagnosis was not confirmed by the histopathologic examination. In one case with clinical characteristics of erosive lichen planus, the histopathologic diagnosis was cheilitis solaris (Table 4). The DI between clinical and histopathologic diagnoses was 17.6%. The higher DI was found in the group of lesions clinically defined as erosive lichen planus.

Table 4. Distribution of PMOLs according to histopathologic and clinical diagnoses

Clinical diagnosis	Patients n (L) %	Sex M/F	Anatomical location: Buccal mucosa	Gingiva (alveolar mucosa)	Vermillion	Palate	Mouth floor	Tongue
Homogeneous leukoplakia	26 (30) 51.0	17/9	10	15	3	1	0	1
Non-homogeneous leukoplakia	4 (9) 7.8	2/2	3	2	0	2	1	1
Reticular lichen planus	5 (8) 9.8	0/5	5	1	0	0	1	2
Erosive lichen planus	15 (24) 29.4	3/12	15	2	2	0	0	5
Actinic cheilitis	1 (1) 2.0	0/1	0	0	1	0	0	0
Total	51 (72) 100.0	22/29	33	20	6	3	2	9

(L) number of lesions

DISCUSSION

In the present study, the most common clinically found PMOL was leukoplakia, (58.9% of the sample analyzed). This finding is in agreement with those from previous reports (9,10,11). The most frequent location of leukoplakia was gingiva (alveolar mucosa), followed by buccal mucosa and lip vermilion. The manifestations of OLP were by far the most prevalent in buccal mucosa, followed by tongue and gingiva (alveolar mucosa). Our previous study showed the same frequencies of the affected locations among individuals with oral lichen planus (12), which is in accord with other studies (13-16).

The histopathologic diagnosis showed that benign keratosis was the most frequent PMOL. In 92.3% of leukoplakias, clinical diagnosis was confirmed by the histopathologic examination. The histopathologic analysis showed that three cases clinically diagnosed as leukoplakias were, in fact, OLP. In these cases, OLP appeared as a white plaque unilaterally located, without a reticular pattern, and therefore diagnosed as leukoplakia. Although these three cases contributed to the increase in the DI, no histologic examination might lead to misdiagnosis and therapeutic errors. This finding leads to a conclusion that a biopsy should always be taken from a plaque lesion. In addition, the differential diagnosis between plaque-like OLP and leukoplakia can be obtained by histopathologic analysis since these two conditions are clinically similar (7). In five cases with a clinical diagnosis of erosive lichen planus, the histopathologic diagnosis revealed non-specific chronic inflammatory process. In all these cases, the surface erosion existed, with the destruction of the epithelium, leaving only the fibrin-covered granulation tissue at the floor of the lesion. In the present study, the correlation between the clinical and histological diagnoses of OLP was missing in 5 cases, which contributed to the higher DI. This finding suggests that in the diagnosing of OLP we cannot rely on a clinical or histological diagnosis alone. Also, we think that the clinical diagnosis was not confirmed in these cases because the biopsy specimens were inadequate, exhibiting only an ulcerated surface. The biopsy of lesioned tissue, particularly if OLP is of an erosive form, can be challenging. A biopsy specimen of predominantly erythematous and ulcerated mucosal lesions should be taken few millimeters away from an ulcer so that the specimen's epithelium and connective tissue remains intact (17). It has been suggested that punch biopsies provide greater interobserver reliability than wedge biopsies in the histopathologic diagnostics of PMOL (18).

In one case with a clinical diagnosis of erosive lichen planus, the histopathologic diagnosis was cheilitis solaris. In this case, clinically considered, the lesion presented an erythematous surface with an eroded vermilion, from which part of the biopsy was taken, and also a bilateral reticular pattern on buccal mucosa. The difference in the clinical and histopathologic diagnoses might be partly caused by the fact that the clinical information did not accompany the biopsy specimen and the pathologist was not aware of the clinical presentation and exact location of the lesion. In a somewhat similar study regarding the presence and degree of epithelial dysplasia, the inclusion of clinical information did not improve the interobserver agreement rate in the diagnosis of oral epithelial dysplasia (19). In addition, Fischer and coworkers (18) reported the least agreement on histopathologic diagnosis for lip and labial mucosa lesions compared with other mucosa sites. Moreover, van der Meij and co-workers (20,21) reported that interobserver agreement in the clinical and the histological assessments of OLP, defined by kappa, varied from poor to moderate and from moderate to substantial, respectively. The intraobserver agreement appeared to be significantly higher in both studies.

In our study the DI was 17.6%. The discrepancy between the clinical and the histopathologic diagnoses of erosive OLP significantly contributed to the increase in the DI. However, Onofre and coworkers (9) found a DI of 24.4%, and the higher DI was detected among the homogeneous and non-homogeneous leukoplakias although they investigated a smaller number of cases with leukoplakia than the present study. Recently, the lack of the clinicohistopathologic correlation in the diagnosing of OLP was found and therefore a set of revised diagnostic criteria for oral OLP was proposed, based on the WHO definition of OLP, including clinical as well as histopathologic aspects (7). Several studies have used biologic markers to identify the molecular genetic differences among PMOLs (22-24). Thus, the use of the molecular markers may lead to a more accurate histopathologic diagnosis of PMOL and may, in the future, become the indicators of an adequate treatment.

In conclusion, the obtained results show that in 90% of leukoplakias, the clinical diagnosis was confirmed by the histopathologic examination. The discrepancy between the clinical and histopathologic diagnoses in 17.6% of cases suggests that all PMOLs should be submitted to a histopathologic analysis.

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Correlation between prostate-specific antigen and histopathological difference of prostate carcinoma

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ABSTRACT

BACKGROUND: *Adenocarcinoma of prostate (ACP) is one of the most frequent tumors in men older than 50. Prostate specific antigen (PSA) is the most reliable serum marker in the diagnostics and following of prostate carcinoma, and Gleason's system of estimation of tumor differentiation, as well as classical estimation of tumor differentiation from 1 to 3, are generally accepted systems of prostate carcinoma evaluation.*

METHODS: *Forty examined individuals with verified ACP and compared values of PSA and tumor differentiation as well as estimated comparability of these two systems are reported.*

RESULTS: *Highly positive correlation between the values of PSA in serum and the degree of tumor differentiation determined by Gleason's system, as well as the low correlation between PSA and histological differentiation estimated using classical system from 1 to 3 were found.*

CONCLUSION: *It could be concluded that Gleason's system for tumor differentiation determination is more superior system of histological grade determination than the other systems.*

KEY WORDS: *Prostatic Neoplasms; Adenocarcinoma; Prostate-Specific Antigen; Neoplasm Staging; Cytodiagnosis; Sensistivity and Specificity*

INTRODUCTION

Prostate-specific antigen (PSA) is the most useful tumor marker in the diagnostics of prostate carcinoma (1). PSA is serin protease produced by ductal and acinal epithelial cells of normal, hyperplastic, and malignant tissue of the prostate. By the influence of pathological processes the cell integrity is destroyed leading to release of PSA into circulation, i.e. the processes inside prostate, such as hyperplasia, inflammation, tumors, lead to the increase of serum PSA value the most frequently (2-4). The investigations have revealed that every gram of cancer prostate tissue increases the value of serum PSA for 2.3 ng/ml in average, while every gram of hyperplastic tissue increases the same parameter 10 times less compared to cancer tissue (5,6). The PSA value increase is determined by histological characteristics of epithelial cells. In neoplastic processes the increase of serum PSA depends on differentiation of tumor cells. The less differentiated prostate tumors can cause lower PSA concentrations in comparison to those well differentiated (7). In prostate carcinoma (PC) evaluation there are few systems used for estimation of tumor cells differentiation i.e. histological grade of tumor. In literature the grade systems suggested by Mostofi, Broders, and Gleason are the most cited. Classical determination of histological grade according to Mostofi is based on criteria of nuclear anaplasia and formation of gland structures. According to this system prostate carcinoma could exert three histological grades: grade 1 (well differentiated), grade 2 (moderately differentiated), and grade 3 (poorly differentiated) (8).

Meanwhile, Gleason's system (GGS) is nowadays one of the most used grade systems in PC (9). The base of GGS is represented by five histological figures, which, using small microscopic magnification, encompass analysis of gland architectonics, the degree of glandular differentiation as well as stromal invasion, but not the degree of nuclear anaplasia (10,11). The aim of the work is to determine the relation between serum PSA and differentiation of prostate carcinoma using Gleason's system and classical determination of histological grade from 1 to 3, as well as to estimate comparability of these two systems.

MATERIALS AND METHODS

The investigation included 40 individuals in age from 60 to 79 years (average age, 69.9 years), who had the clinical symptoms of prostatism at digitorectal examination (DRE), established enlargement of prostate suspected to malignant process or benign prostate enlargement accompanied with PSA values above 4ng/ml. The investigation was carried out at Urology Section and Section for Pathology at the Military Hospital in Niš, at the Clinic for Urology and Institute for Pathology of Clinical Center Niš, and in the radioisotopic laboratory "Pharmacia Diagnostica" in Niö in the period from January 2002 to January 2003. Beside the basic disease the examined individuals didn't have any other health disorder which could significantly influence the function of urinary tract. All patients have been taken a standard urological examination according to modified protocol in keeping with diagnostic protocol for prostate carcinoma (12) (Table 1).

Table 1. Modified diagnostic protocol for prostate carcinoma

PSA (ng/ml)	DRE	Diagnostic protocol
≤ 4 ng/ml	Negative	Following by PSA and DRE
> 4 ng/ml	Negative	Ultrasonography and biopsy of suspected lesions
>10 ng/ml or any other values	Positive	Biopsy of palpable and ultrasonographycally suspected lesions

DRE – digitorectal examination

Using this protocol the standard diagnostic methods have been applied: DRE, transabdominal ultrasonography of prostate, determination of serum PSA, biopsy of prostate.