ORIGINAL ARTICLE
UDC: 618.146-006:615-085:616-056

Microinvasive carcinoma of the cervix

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ABSTRACT

BACKGROUND: *Superficially invasive neoplasias of the uterine cervix are a matter of controversy in terms of their definition, prognostic factors and selection of treatment to minimize the risk of recurrences.*

METHODS: *Forty-three women with invasive cervical carcinoma, operated from 1993 to 2003, were postoperatively staged as IA cervical carcinoma. There were 28 patients who were submitted to class III radical hysterectomy, 9 patients to class II hysterectomy, 2 patients to class I hysterectomy, and 2 patients to abdominal trachelectomy and pelvic lymph node dissection. Mean age of patients was 44 years (range, 27-64 years).*

RESULTS: *Twenty-three patients (56.1%) were stage with IA_1 and 18 (43.9%) with stage IA_2 disease according to the 1995 FIGO classification. Tumor histology revealed squamous cell carcinoma in 38 (92.6%) cases, adenocarcinoma in 2 (4.8%) cases and glassy cell carcinoma in 1 (2.4%). The average number of examined lymph nodes was 17.4 (2-53). Lymphovascular space invasion was identified in 3 patients. None of the 41 patients had metastasis to the pelvic lymph nodes or developed recurrence of disease.*

CONCLUSION: *The results suggest that patients with cervical cancer stage IA_1 have an extremely low risk of pelvic lymph node metastasis and an excellent prognosis, so nonradical management that excludes pelvic lymph node dissection could be as effective as radical surgery in these patients. Stage IA_2 invasive squamous carcinoma of the cervix should be treated with radical hysterectomy with lymph node dissection considering the presence of risk factors. The treatment should be individualized and based on an exhaustive pathological evaluation of an adequate cone biopsy specimen.*

KEY WORDS: *Cervical Neoplasms; Neoplasm Staging; Risk Factors; Treatment Outcome*

INTRODUCTION

Cervical carcinoma is the commonest gynecological cancer and is in the second place among women with malignant diseases in Vojvodina (9.4%). Despite the availability of Pap smear screening, almost 324 women in Vojvodina will be diagnosed with invasive cervical cancer each year and nearly 146 women will die of cervical cancer each year (1).

Microinvasive carcinoma of the cervix is an invasive lesion identified only microscopically. All greater tumors even with superficial invasion are stage IB cancers according to 1995 FIGO classification. Mean age of patients is 40 years. The disease is asymptomatic, usually found during investigation for abnormal Pap smear. Cervix often appears normal on routine pelvic exam. The diagnosis can be made only by means of a thoroughly examined conization specimen. With recurrence rates in these two substages, which are no more than 1% to 2%, it has excellent prognosis. Survival of stage IA1 can approach 99% and stage IA2 can approach 97%-98% (2).

PATIENTS AND METHODS

This retrospective study was performed in the Institute of Oncology in Sremska Kamenica between 1993 and 2003. We analyzed the data from patients' histories of 41 women with invasive cervical carcinoma, who underwent to radical hysterectomy and lymphadenectomy and were postoperatively staged as IA cervical carcinoma. Histopatholgical examination of cervical biopsy and/or cervical curettement revealed invasive cervical carcinoma, preoperatively staged as IB1. There were 28 patients who were submitted to class III radical hysterectomy, 9 patients to class II hysterectomy, 2 patients to class I hysterectomy, and 2 patients to abdominal trachelectomy and pelvic lymph node dissection. Mean age of patients was 44 years (range, 27-64 years).

RESULTS

A total of 41 patients were followed from 1 to 10 years with a median follow-up interval of 4.6 years. There were 23 (56.1%) patients with early stromal invasion (IA1) and 18 (43.9%) with microinvasive carcinoma (IA2) according to FIGO criteria (1995). Tumor histology revealed squamous cell carcinoma in 38 (92.6%) cases, adenocarcinoma in 2 (4.8%) cases, and glassy cell carcinoma in 1 (2.4%).

Seven patients were submitted to conization, but for all of them treatment was completed with radical hysterectomy and pelvic lymph node dissection due to diagnosis of stage IA2 invasive cervical carcinoma and/or lymphovascular space invasion. Other 34 patients were

primary radically operated.

The average number of lymph nodes examined was 17.4 (2-53). None of the 41 patients had metastasis to the pelvic lymph nodes. Lymphovascular space invasion was identified in 3 patients. None of 41 patients developed recurrence or died from recurrent disease.

DISCUSSION

The diagnosis and management of microinvasive carcinoma of the cervix are one of the most controversial areas in gynecologic oncology. The staging criteria have changed several times during the past decades. The recommended therapy has also changed, going from radical surgery with any invasion to being more conservative with various depths of invasion.

In 1973, the Society of Gynecologic Oncologists (SGO) defined the microinvasive lesion as one in which neoplastic epithelium invades the stroma in one or more places to the depth of 3 mm or less below the base of the epithelium and in which lymphatic or vascular involvement is not demonstrated. This definition was used as a guide for therapy by many physicians mostly in the United States (2).

In 1979, The Japanese Society of Obstetrics and Gynecology adopted the SGO definition except patients with confluent patterns of invasion who were excluded and were considered to belong to stage IB1.

In 1995 The Cancer Committee of the International Federation of Obstetrics and Gynecology (FIGO) subdivided stage I cervical cancer into stage IA_1, IA_2, IB_1, and IB_2 (Table 1). Stage IA1 carcinoma of the cervix is a lesion which invades the cervical stroma to a depth of 3.0 mm or less bellow the base of the epithelium, and no more than 7.0 mm wide. In stage IA_2 invasion is limited to measured stromal invasion with maximum depth of 5 mm and not wider than 7 mm. FIGO classification is made for comparison purposes and not as the guide for therapy (3).

Table 1. FIGO classification of an early stage cervical carcinoma

STAGE I - The carcinoma is strictly confined to the cervix.	
IA	Invasive cancer identified only microscopically, measured stromal invasion is < 5.0 mm deep and < 7.0 mm wide.
IA_1	Measured invasion of stroma < 3.0 mm in depth and < 7.0 mm wide.
IA_2	Measured invasion of stroma < 5.0 mm in depth and < 7.0 mm wide.
IB	All greater lesions, even with superfitial invasion, are stage IB cancers.

Lymphatic vascular space involvement would not exclude a patient from FIGO definition of stage IA cervical carcinoma. However, there are many reports about significant prognostic factors that predict lymph node metastases and survival. Depth of invasion and lymphatic vascular space invasion are the most important prognostic parameters for lymph node involvement and the risk of recurrence (4) (Table 2). Incidence of lymphatic vascular space invasion in stage IA_1 and IA_2 is 5% and 25% (5).

Table 2. Prognostic factors for stage IA cervical carcinoma

1.	Depth of invasion
2.	Superficial spread of lesion
3.	Lymphovascular space infiltration
4.	Confluent pattern of invasion
5.	Lymph node involvement
6.	Positive cone margins

Patients with cervical cancer stage IA_1 have an extremely low risk of pelvic lymph node metastases (less than 0.5%) (6). In a group of 180 patients Copeland et al. demonstrated a 0.3% risk of pelvic node metastases in patients without lymphovascular space involvement whose lesions invaded 3 mm or less. The presence of lymphovascular space involvement increased the risk of nodal metastases to 2.6% and of recurrence to 4% (7).

In 82 patients with 3 mm or less depth of invasion Takeshima found the incidence of lymph node metastasis in 1.2%. The incidence of lymph node metastasis was 3.4% in patients with 3 to 5 mm depth of invasion. None of the patients in this series had metastasis to the parametrial tissues (8).

Patients with carcinoma where depth of invasion extends to 5 mm have increased risk of lymphovascular space involvement and metastatic disease. The pelvic node metastasis rates lie between 3 and 5% (2). In Burghardt's review of 409 patients with microinvasive carcinoma 7 (1.7%) patients developed fatal recurrences (9).

So, the therapy of microinvasive cervical cancer (stage IA_1 and IA_2) depends on the presence of significant prognostic factors and must be individualized. It depends on depth of invasion, superficial spread of lesion, lymphovascular space infiltration, poor differentiation, confluent pattern of invasion, lymph node involvement and positive cone margins (10). Exact work-up of the cone is the basis for successful treatment.

Patients with cervical cancer stage IA_1 have an extremely low risk of pelvic lymph node metastases and they can be treated safely with cervical conization, or simple hysterectomy (11). Every histologic criteria of this definition must be met and all conization margins must be free of dysplasia or invasive disease. Patients must be reliable so that they can be followed closely with periodic Pap smears to detect recurrent cervical neoplasia.

Patients with FIGO stage IA_1 cervical cancer and lymph vascular space invasion or positive cone margins should be treated by class II radical hysterectomy and pelvic lymph node dissection.

Patients with stage IA_2 cervical cancer have a significant risk for lymph nodal metastases, and should be treated with radical surgery - class III radical hysterectomy with pelvic node dissection. Considering the risk of recurrence is not very high, lower than 5%, some other risk factors of recurrence have to be taken into account in modifying management, like lymphovascular space involvement, confluent growth pattern and poor differentiation.

Young patients, who desire to preserve childbearing function, can be treated with radical trachelectomy and pelvic lymphadenectomy.

CONCLUSION

Superficially invasive neoplasias of the uterine cervix are a matter of controversy in terms of their definition, prognostic factors and selection of treatment to minimize the risk of recurrences. With increased experience, more conservative therapy was found to be just as efficacious as radical therapy. Conservative therapy for stage IA_2 carcinoma of the cervix does not seem unreasonable. These questions will be resolved in the future as more data is accumulated.

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ORIGINAL ARTICLE
UDC: 616..31-001:616-091.8:616.071

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