ABSTRACT

Carcinoma of the vulva is at the fourth place by its incidence out of all malignant diseases of female genital organs. It is considered that it represents 3% to 5% of all genital malignancies. Although it appears most commonly between 65 and 75 years of age, the incidence of vulvar carcinoma in younger age groups has been on the constant increase. The reported patient with a previous history of HPV infection was presented with carcinoma of the vulva before the age of 50, which gave metastases into inguinofemoral lymph glands. In spite of the administered radical hysterectomy associated with bilateral lymphadenectomy and the subsequent radiation therapy, the patient developed local and regional recurrences 19 months following the surgery, with the final systemic spread of the disease. The treatment of advanced stages of carcinoma of the vulva, in spite of the administration of combined radical procedures (operation, irradiation), does not give adequate results -izlečenjem pacijentkinje. I pored toga naš zadatak je da im koliko god je to moguće produžimo i olakšamo život. Therefore, our aim is to alleviate and prolong the life span of these patients as much as possible.

Key words: vulvar cancer, diagnosis, staging, treatment

INTRODUCTION

The incidence of pre-invasive disease of the vulva has almost doubled over the past decade, resulting in an increase of incidence of invasive carcinoma of the vulva (1). Cancer of the vulva is the fourth most common malignancy of the female genital tract. By recent reports, it accounts for approximately 3–5% of all genital cancers (2).

There are two peaks of incidence of this disease. In older women, between 65 and 75 years of age, the etiology of the carcinoma is attributed to chronic irritation or other poorly understood cofactors (3). Development of pre-malignant vulvar disease and vulvar carcinoma in situ in younger women (less than 50 years of age) is probably associated with human papillomavirus (HPV) infection. In 1997, Jones RW reported that the incidence of vulvar carcinoma increased from 2 to 21 % in the period of 20 years (4). However, association of the genesis of malignant disease of the vulva with HPV infection is not as strong as it is for cervical cancer. Women with history of genital warts or other HPV-related diseases have a relative risk for carcinoma in situ of 18.5, i.e. 14.5 for invasive carcinoma of the vulva. Estimates indicate that women who smoke have a four- to fivefold increase in the incidence of carcinoma in situ of the vulva and a 20% increase in vulvar carcinoma. This incidence is also increased in women with multiple sexual partners (5).

Early stages of vulvar cancer are usually asymptomatic and they are recognized only by careful inspection of the vulva. The advanced stages of vulvar cancer are manifested with bleeding, pain, or discharge. However, some patients do not visit their doctors although the previously mentioned symptomatology had been present even for a longer period of time (2, 6).

Diagnostics includes sampling of the tissue obtained from any visible lesion of the vulva, even in asymptomatic patients. The lesions may appear as thickenings, ulcerations, leukoplakia and warts. The use of either a colposcope or Collins’ test is a benefit to a correct localization of these lesions, particularly if they are of small size. The squamous cell carcinoma of the vulva is the most frequent histopathological finding (85%) but some other types can also occur such as: malignant melanoma (5%), basocellular carcinoma, adenocarcinoma of the Bartholin’s gland, verrucous carcinoma, Paget’s disease, sarcoma etc. The squamous cell carcinoma usually occurs on the labia majora being of unifocal character. Approximately 5% of lesions are of multifocal character being localized on the labia minora, clitoris and perineum (1).

CASE REPORT

A 45 year old patient was reported to the Department of Obstetrics and Gynecology in Novi Sad at the end of 1998, complaining of pruritus, sore and whitish patches on external genitals. Otherwise the patient was healthy except that she occasionally used different preparations to treat pruritus in the period of the last 10 years, such as: Dienoestrol unguent, Oestradiol cream, Fluocinolonacetonidum and Gentamycin unguent. This therapy did not result in any improvement, whereas in the last 3 months the patient recognized white lesions on the vulva. Gynecological examination revealed disturbed architecture of...
the entire vulva associated with „erasure“ of the clitoris and labia minora presented with white plaques, which could correspond to dystrophy of the vulva. A hyperkeratotic node was noted in the region of the posterior commissure, of a firm consistence and indurated surface similar to the „kissing“ ulcer. Biopsy of the vulva was made with complete resection of the lesion in the region of the posterior commissure, and histologic examination confirmed the presence of acanthotic flat cell layer epithelium with characteristics of squamous hyperplasia in some regions and dysplastic lesions of the second degree (VIN 2) with koilocytosis. Dense inflammatory infiltration was recorded in the stroma. The patient was dismissed following the biopsy but did not go for the control check-up for the next 3 years.

She was again admitted in January 2002; the changes on the external genitals still persisting but now more intensive and associated with pain increasing while walking. On examination, almost complete left side of labium minoris turned into the tumorous mass 5x7cm of size, firm in consistence, of uneven surface, standing free from the base. Inguinal lymph nodes were not enlarged at palpation. Surgical treatment was indicated. In the course of preoperative treatment, all laboratory findings were within the limits of referent values, such as the findings of the internist and anesthesiologist. Ultrasonography recorded normal finding on the genital organs. The ex-tempore biopsy of the specimen obtained from the left-side labium lesion confirmed the suspicion of malignancy, and the histologic diagnosis of the „carcinoma planocellulare keratodes gradus I infiltrativum“ of the vulva was made with the following radical vulvectomy and bilateral inguinal lymphadenectomy.

The procedure of extirpation of inguinal lymph nodes included two separate „S“ incisions on the skin, from the spina iliaceae anteriores superior towards the region beneath and laterally to the symphysis. Following the exploration of inguinal and oval pouches and extirpation of the fat tissue together with lymph nodes, the ligation of the v. saphene magna was performed twice on both sides with the subsequent bilateral drainage of the inguinal region by vacuum drains. Definite histologic finding confirmed the ex-tempore diagnosis with the spread of metastases of the planocellular carcinoma of the vulva into two lymph nodes of the left groin. The operation and postoperative course were regular with the per-primam healing of the wounds on both groins and the vulva. Following the operation, the patient was directed to the Oncologic Commission and underwent the subsequent complete radiotherapy (TCT). The following year she went twice for the control check-ups. On the first control, the CT and abdominal ultrasonography were normal. Leucopenia was recorded within the complete blood count testing. The examination revealed the presence of leukoplakia on the posterior commissure. Other findings were normal. On the second control, nine months later, the NMR of the small pelvis and the complete blood count findings were normal, whereas the gynecological finding was unchanged.

Nineteen months upon radical vulvectomy and radiotherapy, at the end of 2003, the patient was presented with erithematous clearly limited change on the skin of the perineum towards the anus, associated with pruritus. The tissue sample was obtained and sent to histologic examination – Dg: Inflammation chronic. The tissue of previously diagnosed carcinoma was not found in the examined specimen.

At the beginning of 2005, the patient was again admitted to the Department of Obstetrics and Gynecology due to the recurrence of vulvar carcinoma, three years following the radical vulvectomy and complete radiotherapy. Gynecological examination: a bilateral induration of elevated ridges was present at the site of previously removed labia, located more on the right side, with the signs of necrosis spreading towards the anus and urethra. A complete laboratory testing was done, the urine culture, wound smear and histologic examination of the biopsy material obtained from the lesion in the perineal region. The culture of the urine sample was negative. The wound smear revealed Proteus mirabilis and Escherichia coli so that the antibiotic therapy was administered: Amikacin 500 IM q12h, Metronidazole 400 mg PO q8h together with a daily toilet of the region of the vulva and perineum. The obtained histologic finding of the biopsy material confirmed the recurrence of the vulvar carcinoma – Dg: Carcinoma planocellulare keratodes. Malignant cells were in vascular spaces. The examinations also included the rectosigmoidoscopy. An induration with elevated edges and necrosis in the middle and around the whole anal orifice were present in the perineal region. The anal canal was narrowed, almost obstructed – for a small finger, the infiltrative process involved the whole circumference. The rectum was of normal size and shiny mucosa was with the patches of hyperemia. The sigma: haustral, regular diameter of the lumen with smooth and shiny mucosa. The sigma was examined for 60 cm in length. Dg: Infiltratio ani stenosans, maligna susp. Colitis chr. Non specifica. CT examination of the small pelvis: (contrast per os et iv.): Dg: Infiltratio vaginae, regiae analis, rectalis et cervicis susp. The urologist made an effort to perform the cystoscopy but without success due to the impossibility of identification of the external urethral ostium. The consulted team including the plastic surgeon, urologist and specialist in general surgery suggested the patient to be transferred to the Institute of Surgery for further surgical procedure. The mentioned team of specialists performed the following operation: Op. Lap med. inf. sec Milles. Resection vaginae et hysterectomy totalis cum adnexectomy bilateralis. Lymphadenectomy fossae obturatoriae bil. Resectio uretrae. Drainage. Plastica sec Thiersch. Suturae directae (Figure 1, 2, 3, 4).
On the fourth postoperative day the patient became febrile - up to 38°C. The samples of the urine culture were obtained on the fifth and fourteenth postoperative day and the findings were normal. The nasogastric probe was removed on the third postoperative day and the patient was given the peroral nutrition on the sixth postoperative day. On the sixteenth postoperative day, the patient was transferred back to the Department of Obstetrics and Gynecology. Following the admittance, the patient was febrile up to 38°C, subjectively feeling well. The wound smear was obtained and sent to microbiological examination; the following microorganisms were isolated: Klebsiella pneumoniae, Citrobacter freundii and Escherichia coli; the following 10-day therapy was administered: Imipenem 500 mg IV q8h, together with a daily treatment and toilet of the wound; the urine culture – negative. The repeated analyses of the wound smear pointed to the presence of highly resistant mixed bacterial flora: first Acinetobacter species sensitive only to Imipenem, and then Proteus mirabilis. During the whole period, there were no problems with functioning of the intestines across the preternatural anus. The patient had the Foley catheter for the whole course of the disease changed on each three weeks, along with permanent control of the urine. During the hospitalization, analgetics were also administered to the patient. From the fortieth postoperative day on, the patient became highly febrile again. The skin grafts only partially attached, whereas the rejection occurred in the region of the perineum. The decision to repeat administration of Imipenem was made, based on wound smear culture findings.

The repeated CT of the small pelvis administered in the middle of May 2005, revealed local recurrences with infiltrations of the pelvic floor, urinary bladder, parametrium, presacral region together with bilateral hydronephroses and multiple meta changes on the liver. The skin above the anterior superior iliac spine (the right side), the thighs and the back were also presented with meta changes (histologically verified). The patient was dismissed on personal request at the end of April and she died soon.

**DISCUSSION**

The primary therapy of vulvar carcinoma requires operative approach for the first three stages of the disease.
Surgical procedure includes excision of the total tumorous mass up to the adjacent healthy tissue. The second and advanced stages of the disease require the additional bilateral inguinofemoral lymphadenectomy. The Gynecology-Oncology group recommends inguinofemoral lymphadenectomy in each patient with the invasion depth of more than 1 mm (7). Several studies published in the last decades of the last century confirmed that vulvar carcinoma metastasized first into inguinofemoral lymph nodes and then into the small pelvis lymph nodes (8). The lowest of the lymph nodes in the range of deep femoral lymph nodes was named after their authors – Cloquet’s or Rosenmuller’s node being located immediately below the Poupart’s ligament. First, the aim of lymphadenectomy is to investigate the presence of metastases in inguinofemoral lymph glands and in this way to decide for the additional radiation therapy. Second, the removal of the lymph glands into which the cancer primarily metastasizes, prevents the lymphogenic spread of the disease. Also, the absence of metastases in the Rosenmüller’s lymph gland is a good prognostic sign suggesting that the disease had not spread into lymph nodes of the small pelvis (9, 10).

When there are two or more than two positive lymph glands, the radiation therapy should be administered. From the review of reported studies, the risk that the tumors smaller than 2 cm of size will metastasize into lymph glands is 20%, but if the primary tumor is larger, the risk is double (11). The „S“ incision on the skin of the inguinal, introduced to our Department by Segedi D. in 1994 (after German surgical school), proved to be the best for the present, in relation to postoperative healing (there were no wound dehiscences) and it has a beneficial cosmetic effect.

The risk of recurrences increases with an increase of the number of positive lymph glands. The patient with three or more than three present positive lymph glands has a great possibility for local or regional recurrences as well as for a systemic spread of the disease (12). The local recurrence can be managed by surgical treatment. Radiation therapy and surgical treatment is recommended in case of recurrent metastases within lymph glands, whereas the chemotherapy is recommended in the systemic metastases. The effect of chemotherapy is poor, almost none in the recurrent disease (10, 12).

The treatment of advanced stages of vulvar carcinomas, beside combined radical procedures (operation, irradiation) does not give adequate results – the cure. Therefore, our aim should be alleviation and prolongation of the patient’s life as much as possible. There is a wrong attitude present particularly in people who do not deal with surgery, that these patients should not be operated. The aim of surgical treatment is a decrease of tumorous masses up to the adjacent healthy tissue. The second, the removal of the lymph glands into which the cancer primarily metastasizes, prevents the lymphogenic spread of the disease. Also, the absence of metastases in the Rosenmüller’s lymph gland is a good prognostic sign suggesting that the disease had not spread into lymph nodes of the small pelvis (9, 10).

The five-year survival rate in the patients with advanced stages of carcinoma of the vulva associated with positive lymph glands is 52.4% (13). There are no strict data for our country but we suppose that the rate is much smaller because the control of the patients operated due to malignancies has been relatively poor. The patients have not been followed long enough and they do not regularly go for the control check-ups. In our opinion, the situation could be significantly improved if the patients with malignant diseases could be operated in specialized institutions (2–3 are optimal for the whole Serbia) and if they regularly went for the control check-ups.

REFERENCES: