6. Neoadjuvant chemotherapy in cervix cancer

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Despite the decrease in the incidence of cervix cancer over the last decade, 13,500 new cases and 4,400 deaths were expected in the United States in 1992 [1]. Accessibility of the cervix for cytologic evaluation via the Pap smear, visual inspection by colposcopy, and histologic evaluation by biopsy have made cervical cancer a preventable and potentially curable disease. Identification and successful treatment of precursor lesions (cervical intraepithelial neoplasia) have accounted for the decreasing incidence. Cervix cancer is prevalent among women of low socioeconomic groups, high sexual promiscuity, and multiparity. It has been found to be associated with human papilloma virus infection; however, the precise role played by viral infections in cervix cancer remains to be defined. However, there is evidence accumulating linking HPV type 16, 18, 31, and 35 infections with lower-genital-tract cancers. This has led investigators to view cervical cancer as a sexually transmitted disease.

In the majority of cases, histologic diagnosis is established by colposcopically directed cervical biopsy, or cervical conization. Squamous cell carcinoma composes approximately 85% of all cervical cancer and adenocarcinoma approximately 15%.

Cervical cancer spreads by three routes: direct extension, lymphatic penetration, and hematogenously spread. Direct extension of the tumor from the cervix can involve any of the adjacent pelvic structures. These include the vagina or the supporting ligaments of the cervix and uterus (parametria) and uterosacral ligaments. The disease may extend anteriorly to the bladder or posteriorly to the rectum. When cervical cancer spreads lymphatically, it does so in a systematic fashion. The primary group of pelvic lymph nodes involved are the paracervical and parametrial nodes, followed by the hypogastric, obturator, and external iliac nodes. The disease then spreads cephalad to the secondary nodes, which are the common iliac and para-aortic groups. If the disease spreads in a caudal fashion, then the inguinal nodes may be affected.

The staging of cervical cancer is performed clinically. Ideally, this is done with the patient under anesthesia to allow precise evaluation of the pelvic structures. The staging, as shown in table 1, is according to the International Federation of Gynecology and Obstetrics (FIGO).

Table 1. International classification of cancer of the cervix

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
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<tbody>
<tr>
<td>O</td>
<td>Carcinoma in situ</td>
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<tr>
<td>I</td>
<td>The carcinoma is strictly confined to the cervix (extension to the corpus should be disregarded).</td>
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<tr>
<td>Ia</td>
<td>Preclinical carcinomas of the cervix, that is, those diagnosed only by microscopy</td>
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<tr>
<td>Ia1</td>
<td>Minimal microscopically evident stromal invasion (&lt;1 mm).</td>
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<tr>
<td>Ia2</td>
<td>Lesions detected microscopically that can be measured. The upper limit of the measurement should not show a depth of invasion of more than 5 mm taken from the base of the epithelium, either surface or glandular, from which it originates, and a second dimension, the horizontal spread, must not exceed 7 mm. Larger lesions should be staged as Ib.</td>
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<tr>
<td>Ib</td>
<td>Lesions of greater dimensions than Stage Ia2, whether seen clinically or not. Preformed space involvement should not alter the staging but should be specifically recorded so as to determine whether it should affect treatment decisions in the future.</td>
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<tr>
<td>II</td>
<td>Involvement of the vagina but not the lower third, or infiltration of the parametria but not out to the sidewall.</td>
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<tr>
<td>IIa</td>
<td>Involvement of the vagina but no evidence of parametrial involvement.</td>
</tr>
<tr>
<td>IIb</td>
<td>Infiltration of the parametria but not out to the sidewall.</td>
</tr>
<tr>
<td>III</td>
<td>Involvement of the lower third of the vagina or extension to the pelvic sidewall.</td>
</tr>
<tr>
<td>IIIa</td>
<td>Involvement of the lower third of the vagina but not out to the pelvic sidewall if the parametria are involved.</td>
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<tr>
<td>IIIb</td>
<td>Involvement of one or both parametria out to the sidewall or obstruction of one or both ureters on intravenous pyelogram without the other criteria for stage III disease.</td>
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<tr>
<td>IV</td>
<td>Extension outside the reproductive tract.</td>
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<tr>
<td>IVa</td>
<td>Involvement of the mucosa of the bladder or rectum.</td>
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<tr>
<td>IVb</td>
<td>Distant metastasis or disease outside the true pelvis.</td>
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</tbody>
</table>

The accepted diagnostic modalities utilized in staging cervical cancer include CXR, IVP, cystoscopy, proctoscopy, sigmoidostomy, and barium enema.

Treatment

Treatment of cervical cancer is governed by the stage of disease. Stage Ib and IIa can be managed by either radical surgery or radiotherapy. The remaining Stages IIb–IVb have traditionally been treated with radiotherapy.

The overall cure rates in Stage I and IIa patients treated with either modality are comparable. The advantages of surgery include precise disease delineation, potential ovarian conservation, and minimal vaginal scarring. The attractiveness of radiotherapy is its applicability to all patients, while its disadvantages include permanent tissue damage.

In advanced disease, stages IIb–IVb, external beam irradiation and intracavity radiation are used. Overall survival rates utilizing this modality are given in table 2.