

Chapter 6 ■ Stage IVb disease

Overview

Stage IVb disease can vary greatly, from a solitary metastasis to systemic metastases for which a cure cannot be expected. In the former case, systemic chemotherapy and surgical resection of the metastatic lesion are performed. If these treatments are effective, concurrent chemo radiotherapy (CCRT) is added as local treatment. In the latter case, treatment involves improving quality of life (QOL) by symptomatic relief.

CQ21

What treatments are recommended for stage IVb disease?

Recommendations

- (1) Systemic chemotherapy is recommended for patients with a good performance status and preserved organ function (Grade C).
 - (2) Surgery, radiotherapy (chemoradiotherapy), or a combination of these treatments is selected for patients with distant metastatic lesions such as resectable lung metastases, or with lymph node metastases only (Grade C).
 - (3) If there are severe symptoms accompanying oncological complications, priority is placed on palliative radiotherapy to the causal lesion (Grade B).
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Background and Objectives

There is no consensus on the standard treatment for stage IVb disease with distant metastases. In Japan, different institutions have developed separate treatment strategies. In this section, we will examine appropriate treatment strategies for stage IVb disease, which has a very poor prognosis, based as much as possible on evidence.

Explanations

In Japan, patients with stage IVb disease account for 4.2% of all patients with cervical cancer. These patients are classified as stage IVb according to the International Federation of Gynecology and Obstetrics (FIGO) “Guidelines for the Clinical and Pathological Study of Uterine Cervical Cancer in Japan”.¹ The majority of patients with stage IVb appear to be cases with obvious lung or boney metastases on plain radiography, or with obvious enlargement of superficial lymph nodes and metastasis confirmed by a tissue diagnosis. A study was conducted of cervical cancer patients whose treatment began in 1990, and their 5 year survival rates were stratified by stage. For stage IVb disease, the 5 year survival rate was decidedly poor at 0%.² Aggressive systemic chemotherapy is indicated for patients with stage IVb disease, whose lesions are no longer localized. As is well known in the field of clinical oncology, a radical cure cannot be expected for solid tumors metastasizing to multiple organs, with the exception of some tumors highly sensitive to chemotherapy, such as germ cell tumors and lymphoma.^{3,4} This means that distant metastatic lesions clearly delineated by diagnostic imaging cannot be controlled by local treatments such as surgery or radiotherapy. Systemic treatments, such as chemotherapy, also cannot completely control this type of metastatic lesion. Therefore, treatment strategies for stage IVb cervical cancer are similar to those in recurrent cervical cancer, in which a radical cure cannot be expected. The first goal the treatment is symptomatic relief and improvement of quality of life (QOL). Through such treatment, some prolongation of overall survival (OS) time can also be anticipated.

For patients with stage IVb disease who have a good performance status and preserved organ function, the first choice treatment is generally systemic chemotherapy. However, there have been no trials comparing systemic chemotherapy, with associated toxicity, and best supportive care (BSC). The usefulness of chemotherapy has not yet

been confirmed in a trial.⁵ Logically, such a trial will probably not be performed in the future. Therefore, systemic chemotherapy cannot be said to be the standard treatment for stage IVb. It needs to be explained to patients that the usefulness of systemic chemotherapy has not been established in prolonging the survival time compared to BSC. It should be explained that BSC is also an option, and chemotherapy should be offered to patients who desire it. For chemotherapy regimens, refer to CQ26 for squamous cell carcinoma, and to CQ32 for adenocarcinoma and other non-squamous cell carcinoma.

Better outcomes are reported for solitary lung metastases and solitary (supraclavicular and inguinal) lymph node metastases than for metastases to other organs.^{6,7} If a patient has a resectable distant metastatic lesion confined to the lung or to a lymph node region, long-term survival can be expected with surgery, radiotherapy, chemotherapy, or a combination of these treatments. The treatment can be selected depending on the circumstances of the institution and the patient.

Many patients with grade IVb disease have extensive lesions within the pelvis, and a high incidence of oncological complications. Hydronephrosis and hydroureter accompanying parametrial invasion are particularly common. Precautions need to be taken regarding these complications when using chemotherapy with cisplatin, which can cause renal toxicity. In a patient with bilateral hydronephrosis, life threatening postrenal renal failure can ensue. Preservation of renal function, by emergency ureteral stent placement or nephrostomy, then becomes a priority. If one kidney is unaffected, there may not be any problems clinically if renal function is stabilized. However, if the patient does not respond to chemotherapy, hydronephrosis or hydroureter can eventually affect the hitherto unaffected kidney. A rapid decline in renal function can occur, leading to a reduced ability to excrete drugs, and possibly a decrease in life expectancy. As with bilateral hydronephrosis, the best course is to perform ureteral stent placement or nephrostomy before chemotherapy is commenced.

The following oncological complications are commonly associated with local lesions: abnormal genital bleeding from the cervical region; gastrointestinal hemorrhage from a rectal invasion site; hematuria from a bladder invasion site; edema of the limbs or vulva and lymphangitis from lymph node metastases; cancer pain in the lower abdomen and lower limbs; bone pain and fracture from boney metastases; and raised intracranial pressure from cerebral metastases. When symptoms are severe, commencement of chemotherapy may become problematic due to a decline in performance status (PS), e.g. associated with pain and anemia from ongoing bleeding. In addition, even if chemotherapy is started, the patient may not respond to treatment. Treatment may be discontinued due to persistence or aggravation of symptoms. In such cases, palliative radiotherapy (including brachytherapy), with a highly localized effect, should be performed instead of chemotherapy. After symptomatic relief is achieved, residual lesions should be treated with chemotherapy.^{8,9}

For pain associated with boney metastasis, and symptoms associated with cerebral metastases, radiotherapy is sometimes administered using a relatively large dose per fraction several times.^{10,11} This method of irradiation is also a useful option for controlling lesions other than in the bone or brain, when it is performed as early as possible.

The bone marrow reserve is reduced after radiotherapy to the pelvis. Caution is required, since myelosuppression can be greater than expected from chemotherapy performed following radiotherapy.

There are several approaches to chemotherapy. If a patient responds to systemic chemotherapy, hysterectomy or pelvic radiotherapy can be performed thereafter. Another use of chemotherapy is as part of concurrent chemo radiotherapy (CCRT). When these multidisciplinary treatments are performed in spite of potentially severe toxicity, the treatment goal must be more than symptomatic relief only. Presently, there is insufficient evidence to support the achievement of such a goal, and aggressive application of this type of treatment should be avoided.

【References】

- (1) Gynecologic Oncology Committee Report. *Acta Obstetrica et Gynaecologica Japonica* 2004; 56:7-10. (Level IV) (in Japanese)
- (2) Gynecologic Oncology Committee Report. (38th Annual Treatment Report) *Acta Obstetrica et Gynaecologica Japonica* 2004; 56:751-65. (Level IV) (in Japanese)