Management of Recurrent Gynaecological Malignancies

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1. Introduction

Women diagnosed with recurrent gynaecological cancer form a heterogeneous group. Management of the different clinical presentations obviously necessitates a variety of treatment plans and the clinical outcomes will be different. The initial site, tumour type and disease stage best predicts the prognosis together with time from diagnosis. On the other hand the site and size of recurrence as well as previous treatment(s) will determine the treatment possibilities.

Generally it makes sense to use a different treatment modality from the one that failed, i.e. surgery after radiation failure and radiation after surgical failure.

This article will not aim to present a comprehensive discussion per tumour type. Rather it will present generalized comments on the management of some common patterns of disease recurrence. The discussion will therefore be according to previous treatment and anatomical location of the recurrent tumour.

2. Definitions

2.1 Local Recurrence

Cancer recurrence after primary treatment limited to the site (although not the organ) of primary disease.

2.2 Loco-Regional Recurrence

Cancer recurrence after primary treatment limited to the site of primary disease, as well as in the area around the original organs, often involving the first lymph node station (pelvic or inguinal).

2.3 Systemic Recurrence / Metastatic Disease

Cancer recurrence after primary treatment located in more than the above location. This category includes all recurrences with tumour in more than one area. For the purposes of this discussion, ovarian cancer confined to the abdominal cavity but outside the pelvis will be considered as systemic disease.

3. Local and Loco-Regional Pelvic Recurrence

Localised tumour is usually amenable to surgical removal or radiation treatment, while metastatic or non-localised disease relies on systemic treatments, usually chemotherapy. Even high dose pelvic radiation is usually well tolerated and many gynaecological malignancies are very radiosensitive.

Combining treatment modalities can improve cure rates, salvage rates and tumour control but will almost always increase treatment complications.

3.1 Central Pelvic Recurrence

The most common example of this disease pattern is vault and above-vault cancer recurrences seen after surgical treatment of endometrial cancer. This disease pattern also occurs after surgical and radiation treatment of early stage cervical cancer.

Generally it makes sense to use a different treatment modality from the one that failed, i.e. surgery after radiation failure and radiation after surgical failure. This is an over-simplification and treatment needs to be carefully individualised.

3.1.1 No previous radiation

Tumour recurrences of up to 5cm in diameter located centrally in the pelvis are often treated successfully and often cured by pelvic radiation. Although larger tumors are seldom cured by radiation or chemo-radiation, this will still be the modality of first choice for many of these patients as the treatment complications are generally lower. Effective surgery would imply a free margin around the tumour implicating radical surgery if the recurrence is bulky (>4cm).

Most ovarian cancer recurrences involve the pelvis. If disease is confined to the pelvis, it is usually resectable and this is often beneficial. The level of benefit is mostly determined by the absence or not of extra-pelvic diease.

3.1.2 After previous radiation

In this group of patients repeat radiation is usually not an option nor is it expected to have a huge effect. Because of, among other factors, poor perfusion, cancer recurrence in previously irradiated areas are typically chemo- and radiation resistant.

Central pelvic recurrence after previous radiation is the classical indication for pelvic exenteration. This group therefore contains those women who can be salvaged by surgery.

Success of the surgical effort will be determined by the following factors:

a.) Anatomical position of the tumour

Better outcome is predicted if:

- The tumour is central
- No vital organs are involved
- Complete removal is technically possible
- The tumour size is smaller than 5cm
- Removal is radical with a tumour free margin

b.) Biological behaviour of the tumour

Aggressive and metastatic behaviour predicts a poor outcome and is indirectly measured by:

- Time to recurrence

- Histological tumour grade
- Histological tumour type
- Growth rate as measured clinically and on imaging
- Initial stage

c.) Presence or absence of metastatic tumour deposits:

In spite of very strict criteria, many patients with local and loco-regional recurrence will succumb from extra-pelvic tumour metastases diagnosed in the years and sometimes even months after successful treatment of the local disease.

On the other hand increasing the criteria or the imaging used to diagnose micro-metastases often detects unrelated disease and postpones treatment. Over-investigating will thus deprive some patients the opportunity to have salvage treatment.

3.2 Pelvic Sidewall Recurrence

In gynaecologial cancer, two disease scenarios typically explain sidewall recurrence. The first is tumour that initially stretched onto the sidewall by direct spread and now recurs in the same position. The typical patient had an initial stage 3B cervical cancer and now presents again with local tumour stretching via the uterine ligaments to the sidewall.

The second scenario will be a patient with undiagnosed or unremoved (micro- or macroscopic) pelvic nodal disease at the time of initial treatment. The primary tumour could be cervical, uterine or ovarian in origin. Nodal disease often persists as the node forms a chemo-sanctuary and the cancer presents once again as a pelvic wall tumour.

3.2.1 Central tumour stretching to the sidewall

When malignancy originating from a central organ recurs with sidewall involvement, the recurrence will almost invariably be non-salvageable and not suitable for a surgical attempt. Some success has been documented with pelvic exenteration. It is not offered to patients recurring with a tumour size of more than 5cm, bilateral involvement or central as well as sidewall disease. This pattern suggests a very large tumour volume and disease resistant to initial treatment, usually radiation.

The ideal imaging modality to confirm the margins of disease is currently MRI paying notice to interrupted tissue layers and hydro-ureter. Clinical evaluation of the extent of disease can be difficult, but impaired kidney function, severe pain and venous obstruction are clinical signs of pelvic sidewall involvement. Pelvic examination is often difficult after radiation when all tissues appear fused.

In most cases management should be supportive and palliative, although treatment can involve known or novel chemotherapeutic agents as well as limited repeat radiation.

3.2.2 Single pelvic nodal recurrence

When the primary tumour is controlled and the recurrence is isolated, the treatment intent should be radical or curative rather than palliative.

With a single large recurrence involving the pelvic sidewall, surgical removal can be feasible in some patients. Involvement of vital organs determines whether the tumour is resectable.

As the surgery is risky and not always successful, radiation naïve patients usually would receive pelvic radiotherapy first.

4. Local and Loco-Regional Vulvo-Vaginal Recurrence

4.1 Local Recurrence

4.1.1 No previous radiation

Treatment of cancer of the female external genitalia after previous surgery is by radiation or chemo-radiation. However, many small recurrences are truly localized and easily excised, while some large recurrences are better treated by a combination of surgery and radiation treatment. Tumour recurrence in the vagina only is rare and management follows the same principles.

The ideal treatment should be determined by a team containing an expert gynaecological oncology surgeon and a radiation oncologist and must be individualised.

Tumour recurrences of up to 5cm in diameter located centrally in the pelvis are often treated successfully and often cured by pelvic radiation.

4.1.2 Previous radiation

Recurrence after previous radiation will usually not be amenable to further radiation, although recurrence after radiation can sometimes be cured by surgery in both vulval and vaginal cancer.

After radiation, reconstruction is usually by vascularised flap. Care should be taken to rule out direct peri-osteal or bone infiltration during the metastatic work-up.

If complete surgical removal is judged to be feasible and the tumour is proven beyond reasonable doubt to be confined to the vulva area, this will be the only hope to obtain local tumour control and hopefully cure and surgery should therefore be offered. Such surgery will influence bladder, vaginal or lower bowel function and patients need extensive pre-operative surgical planning and counselling.

4.2 Vulvo-vaginal cancer recurrence with inguinal node involvement (loco-regional recurrence)

4.2.1 Isolated inguinal nodal recurrence

Only unilateral single nodal groin recurrence with controlled or controllable primary tumour should be considered for treatment with curative intent. Generally such inguinal node recurrence follows the principles of isolated single pelvic nodal disease as discussed under 3.2.2. Again this disease pattern is amenable to radiation treatment in the radiation naïve and surgery should be offered after previous radiotherapy. Attention should be paid to pelvic nodal status and local control.

The outcome of the group of patients with this clinical picture is not favourable and this is a true salvage situation. Some patients with large nodes may benefit from a combined approach with both surgery and radiation.

4.2.2 Extensive loco-regional recurrence

This is vulvo-vaginal cancer recurrence involving more than one area, i.e. uncontrolled local vulva disease with nodal recurrence as well as disease involving more than one node or bilateral nodal disease. This disease pattern is not salvageable with current treatment modalities and supportive care should be offered, including possibly palliative radiation and sometimes also systemic treatment.

5. Systemic or Metastatic Disease

5.1 Isolated systemic recurrence or metastasis

When an isolated recurrence occurs outside the site of primary disease, the fear always exists that other systemic metastases are subclinically present. In certain special situations such metastases can be treated radically with either surgery or radiation. The best result that can be reasonably expected is an improved tumour free survival or overall survival but generally not cure. This is also true for isolated intra-abdominal recurrence of ovarian cancer.

The factors that would plead for a more radical approach would be a favourable anatomical position, factors that point towards favourable biological behaviour (listed under 3.1.2) and special tumour types like granulosa cell tumours. Young and healthy patients can tolerate more aggressive and combined treatment approaches.

5.2 Multiple metastases

Like many patients with isolated systemic recurrence, those with multiple metastases would qualify for systemic approaches including biological, chemotherapeutic and hormonal treatment. Toxicity, previous treatment and tumour type will determine the choice of modality.

6. Conclusion

While recurrent ovarian cancer is considered incurable, many other locally recurrent cancers are potentially curable. Locally recurrent ovarian cancer also qualifies for secondary surgical removal if the prerequisites are met. For this reason women with localised recurrences after initial treatment always warrant and deserve referral for expert evaluation regarding their suitability for salvage treatment.

Salvage treatment with a curative intent will usually be radical or ultra-radical surgery or radical radiotherapy in radiation naïve patients. Even if cure is not a reality, patients can benefit greatly from optimal treatment of recurrent disease, whether this involves resection or not.

References on request