Adnexa (Core)

The presence or absence of adnexal involvement is a core element. Adnexal involvement has an impact on overall survival rate.[1-3] The presence of adnexal involvement categorises a tumour as Stage IIIA in International Federation of Gynaecology and Obstetrics and pT3a in TNM Staging Systems, respectively.[1-3] Prognosis is worse when ovarian metastases are associated with metastases at other sites.[4] The involved adnexa should also be documented, particularly specifying which ovary and which fallopian tube is involved as well as the location of tubal involvement.

It is important to distinguish between endometrial carcinoma with ovarian metastasis and synchronous primary tumours of the endometrium and the ovary.[5] For high grade tumours, including serous carcinoma, ovarian involvement is almost always categorised as metastatic. However, there is always the possibility of coincidental independent primary serous carcinomas in the endometrium and the tube/ovary, although this situation is exceedingly unusual. Furthermore, metastasis from the adnexa to the endometrium rarely occurs. Ancillary techniques (such as WT1 and p53 staining) and evaluation of the fallopian tube by Sectioning and Extensively Examining the Fimbria (SEE-FIM) protocol may be helpful.[6]

Five percent of endometrioid adenocarcinomas are associated with an endometrioid carcinoma of the ovary. Cases with simultaneous involvement of endometrium and ovary by low grade endometrioid carcinomas are often associated with indolent outcome.

Clinicopathologic criteria can help to distinguish patients with good prognosis (such as those with two independent primary tumours/'low-risk') and patients with bad prognosis (such as those with an endometrial carcinoma with ovarian metastasis/'high-risk'). Distinction between these two prognostic types is based on several criteria including: 1) size of the tumour, 2) histologic type and grade, 3) extent/depth of myometrial invasion, 4) presence of lymphovascular invasion (LVI), 5) tubal invasion, 6) presence of endometrial hyperplasia, 7) presence of ovarian endometriosis, 8) pattern of ovarian invasion, including bilaterality, and 9) presence of additional metastases.

Recent molecular studies have shown that for low grade endometrioid carcinomas, there is a clonal relationship between the endometrial and ovarian tumour in the vast majority of cases, suggesting that the tumour arises in the endometrium, and secondarily extends to the ovary .[7-10] However, this clonal relationship should not be equated with the clinical outcomes expected of metastatic endometrial carcinoma.

In the 2020 edition of the World Health Organization Classification,[11] it is suggested that patients with clonally related low-risk tumours be managed conservatively (as if they were two independent primaries) when the following criteria are met: 1) low grade endometrioid morphology, 2) no more than superficial myometrial invasion, 3) absence of LVI, and 4) absence of additional metastases.[12,13] This is an evolving field, and it is not clear at this time why a subset of metastatic tumours are associated with good prognosis. This phenomenon is also seen in endocervical adenocarcinomas metastatic to the ovaries.[14,15] Potential explanations are: 1) that clonal ovarian metastasis occurs early in the process of endometrial tumour development, thereby allowing tumours in each site to acquire additional, sometimes distinct genetic abnormalities; and 2) tumour cells follow retrograde uterine/transtubal spread, possibly with ovarian implantation, rather than destructive invasion. It is recommended to discuss these cases in multidisciplinary tumour boards.

Although true independent simultaneous endometrial and ovarian carcinomas do exist, they are relatively infrequent, and share characteristics of tumours arising in the setting of Lynch syndrome.[10] In this scenario, endometrioid carcinomas of the endometrium may coexist with ovarian clear cell carcinoma.[16,17]

It is important to remember that the presence of LVI in ovarian hilar or parenchymal vessels or tubal vessels without stromal invasion does not affect stage.

Tumour involvement of the fallopian tube should also be recorded.[4] It is important to stress that the presence of detached aggregates of tumour cells in the tubal lumen, without involvement of the fallopian wall, should not be considered tubal involvement,[18] since this is thought to be an artefact related to the type of surgery performed and/or specimen fixation. However, it has been reported that the presence of serous carcinoma cells in the lumen of the fallopian tube is often associated with peritoneal metastasis.[19] Floating tumour cells in the fallopian tube lumen should not lead to upstaging of the tumour, although this should prompt a careful review of the peritoneal/pelvic washings.

Tubal involvement by endometrial carcinoma in the form of intramucosal spread has controversial prognostic significance. Tubal tumour is generally considered metastatic from the endometrium, but it is sometimes considered to represent a coincidental low-risk 'synchronous' endometrioid carcinoma of the fallopian tube. The approach to distinguishing between low- and high-risk carcinomas could theoretically follow the same paradigm used for tumours involving endometrium and ovary. The prognostic significance of tubal mucosal involvement by endometrioid carcinoma (either low- or high-risk) is unknown.[20]

Tubal involvement by serous carcinoma, with or without stromal invasion is usually a manifestation of metastatic serous carcinoma. Recent studies have shown that endometrial serous carcinoma frequently extends to the fallopian tube, giving rise to a lesion that may be indistinguishable from serous tubal intraepithelial carcinoma (STIC)/STIC-like lesion.[21] There is also the possibility that a bona fide STIC can be the nidus from which serous carcinoma cells detach and implant in the endometrium, simulating a primary endometrial serous carcinoma.[22] Furthermore, there is also the possibility of the coincidental presence of an endometrial serous carcinoma and a primary STIC, but in these cases ancillary techniques are required. Assessment of WT1 expression may be helpful in these scenarios. WT1 immunoreactivity is negative in the majority of primary endometrial carcinomas but positive in almost all carcinomas arising from the ovaries or the fallopian tube.[23]

Endometrial carcinomas metastatic to the fallopian tube wall or its serosa should be interpreted as metastatic unless there is evidence of an origin in endometriosis.

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