Pathology of uncommon ovarian cancers

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Introduction

Within the group of malignant ovarian tumours, there are approximately 100 different entities that can be subdivided based on pathological features [1–3]. Many of these ovarian malignancies are uncommon. The importance to recognizing the different malignant ovarian tumours is twofold: First, many of these entities have a distinct clinical course and require specific treatment. Second, some of the more uncommon ovarian malignancies mimic the common forms of ovarian cancers, which may lead to misdiagnosis and inappropriate treatment.

In this chapter, an overview is given of the various types of ovarian malignancies with an emphasis on recognizing the relatively uncommon forms of ovarian cancer.

Mucinous tumours, sex cord tumours of the ovary and small cell cancers of the ovary are categories of uncommon ovarian malignancies that are discussed separately in further chapters.

General principals of subdividing ovarian tumours

In general, ovarian malignancies, like other malignancies, are subdivided based upon histogenesis. The classification put forward in 1999 by the World Heath Organization (WHO) and the International Society of Gynecological Pathologists is most commonly used [3].

Tumours of the ovary may arise from three ovarian components, leading to a classification of three types:

(1) surface epithelial tumours, derived from the surface epithelium and the underlying stroma (in embryology giving rise to the müllerian ducts);
(2) sex-cord stroma tumours, derived from the specialized ovarian stroma (including the sex cords and precursors of the endocrine cells of the postnatal ovary);
(3) germ cell tumours, derived from germ cells (which migrated to the ovary from the yolk sac).

These three categories are discussed in the following sections. It should be kept in mind that metastases from tumours elsewhere in the body other than to the ovary can mimic many of the primary ovarian tumours discussed below; however, it is beyond the scope of this chapter to discuss those as well.

Surface epithelial tumours

Surface epithelial tumours are considered to arise from the surface epithelium of the ovaries. The tumours can be subclassified based on two grounds: the type of epithelium of which the tumour consists:

(2) mucinous
(3) serous
(4) endometrioid
(5) clear cell
(6) urothelium (Brenner tumours)

The tumours can also be subdivided based on their expected behavior:

(1) benign
(2) borderline (or a typically proliferating; low malignant potential)
(3) malignant

The histological features that are used to subdivide in the categories benign, borderline or malignant differ with respect to the histological type of epithelium. Therefore, the differential diagnosis between benign, borderline or malignant should be considered for each of these tumour types separately.

Serous tumours

Malignant tumours

Serous carcinoma is the most common malignancy of the ovary. 70% of serous carcinomas present with stage II to IV disease. These tumours do not fall in the category of uncommon ovarian tumours and are therefore not discussed in detail.

Serous borderline tumours

Serous borderline tumours are relatively uncommon [4]. The importance of understanding the histopathological and clinical features of these tumours lies in the fact that they should be distinguished from serous carcinoma. The obvious reason for this is that serous carcinoma usually requires aggressive treatment, including chemotherapy. For serous borderline tumours, completely different treatment strategies should be followed. Serous borderline tumours have a very distinct morphology: at surgery they are usually composed of one or more cysts that are lined by polypoid excrescences and finer papillae. The cysts may contain a thick mucinous fluid; this should, however, not be confused with evidence of a mucinous tumour. Many serous borderline tumours also contain solid components; these are termed serous borderline cystadenofibromas. At microscopical examination, the tumours are characterized by polypoid structures and papillae; these papillae are arborizing and form secondary and tertiary papillae. The lining consists of cuboidal to columnar epithelial cells; often these cells are ciliated. The cells may also contain more abundant cytoplasm. By definition, there is an absence of frank stromal invasion in these tumours.

In 30% of patients with a serous borderline tumour, both ovaries are affected. In about 30–40% of the cases, tumour cells are also found outside the ovary. The most common site outside the ovary is the peritoneum, where peritoneal implants are found [5]. These peritoneal implants are usually smaller than 1 cm; however, in rare cases, larger implants can also be identified. These implants are subdivided in three categories:

(1) non invasive epithelial implants
(2) non invasive desmoplastic implants
(3) invasive implants

The invasive implants account for less than 10% of the peritoneal implants found in association with serous borderline tumours.

Implants of serous borderline tumours can also be identified in the lymph nodes of the abdomen; and in rare cases, in lymph nodes above the diaphragm.

The clinical course for the majority of patients with serous borderline tumours, even in the presence of peritoneal implants or lymph node implants is usually that of a benign tumour with excellent survival. In a small proportion of patients, however, a more malignant course is apparent when progressing. In many of the patients with progressive disease, the development of low grade invasive carcinoma is observed. Abundant research in serous borderline tumours has been dedicated to the identification of factors that can predict malignant behavior. At present, the most important features associated with malignant behavior are:

(1) invasive implants (on this there is general agreement)
(2) so called micro papillary growth pattern of the primary tumour. However, this areas contains more controversy.

Mucinous tumours

These tumours are discussed in a separate chapter.

Endometrioid tumours

The most common malignant epithelial ovarian tumours are serous carcinoma and endometrioid carcinoma. However, discussion of endometrioid carcinoma is outside the scope of this chapter.

Benign endometrioid tumours, usually adenofibromas, account for less than 1% of benign ovarian tumours. Endometrioid borderline tumours are extremely rare and account for approximately 2% of all borderline ovarian tumours [6]. As endometrioid borderline tumours are a rare entity that can give rise to confusion with endometrioid carcinoma, this tumour is discussed in some more detail below. In addition to endometrioid tumours, endometriosis is a relatively common finding; the major theory on how endometrioid tumours of the ovary arise assumes that these tumours arise from endometriosis.

Endometrioid borderline tumours

Most endometrioid borderline tumours of the ovary are adenofibromatous. The tumour consists of glands, lined with endometrioid type epithelium with features that are similar to complex hyperplasia of the endometrium with atypia, but with the absence of invasive growth [6].

As the glands can be complex and in close proximity to each other, there may be some confusion with an endometrioid carcinoma. To make the distinction between the two tumour types is important, because the rare cases of endometrioid borderline tumours have not been associated with progressive disease or metastasis. These tumours can therefore be managed conservatively.

As in the endometrium, the frank malignant endometrioid tumours of the ovary can also present in the form of a malignant mixed Mullerian tumour. In these cases, it may be difficult to differentiate between either the tumour from sarcomas or other tumours with a sarcomatous component.

Sex cord-stromal and steroid cell tumours

Sex cord stromal tumours include all ovarian tumours that contain granulose cells, theca cells, Sertoli cells, Leydig cells and/or gonadal stromal fibroblasts. Tumours can contain various combinations of these sex cord cells of stromal cells but are rare and often accompanied by hormonal changes.

Further discussion on these tumours are presented in a separate chapter.

Germ cell tumours of the ovary

Germ cell tumours arise from primordial germ cells in the ovary. Several subtypes are recognized:

Mature teratoma

The most frequently encountered germ cell tumour is mature teratoma, often described as dermoid cyst. This is the most common type of ovarian germ cell neoplasm, accounting for 20% of ovarian neoplasms overall. These tumours may become very large (the largest tumour described in the literature was close to 200 kg). The tumour is composed of cells that are produced by each of the three germ layers: ectoderm, mesoderm and endoderm.

Immature teratoma

This tumour comprises less than 1% of the teratomas of the ovary; this tumour usually arises in the first two decades of life and contains immature tissues derived from one or more of the three germ layers [7]. In view of the differential diagnosis between mature teratoma and immature teratoma, the resection specimens of teratomas should always be well sampled, certainly in younger patients.

Dysgerminoma

The most common malignant germ cell tumour is dysgerminoma, accounting for approximately 1% of all malignant ovarian tumours. Most dysgerminomas arise in patients between 5 and 50 years of age. The tumours are solid and have the same microscopic appearance as testicular seminomas in males. Like seminomas, dysgerminomas are associated with excellent prognosis [8].

Yolk sac tumour

This tumour, also referred to as endodermal sinus tumour, is the second most common malignant germ cell tumour. These tumours arise in patients with a median age of 18 years and are usually solid with cystic areas. At microscopy, the tumours are characterized by a growth of epithelioid cells with a papillary and sometimes glandular growth pattern, often forming the typical "Schiller-Duval" bodies. The growth pattern of these tumours can show marked heterogeneity, giving rise to confusion with other ovarian tumours, including carcinoma [9]. The tumours are sensitive to chemotherapy, leading to 40% survival rates in patients with high stage disease.

Choriocarcinoma

In its "pure" form, this tumour is exceedingly rare [10]; more frequently it is observed as a component of a mixed germ cell tumour. The histology of these tumours is similar to the gestational form of choriocarcinoma encountered in the uterus.

Embryonal carcinoma

This type of tumour is extremely rare and easily confused with yolk sac tumour, it resembles the embryonal carcinomas observed in the male testis. Patients with embryonal carcinoma are very young (median age 12 years).

Gonadoblastoma

This extremely rare tumour occurs almost exclusively in dysgenetic gonads (almost always on the basis of 46XY pure gonadal dysgenesis) [11]. The tumours are usually smaller than 10 cm and composed of immature germ cells and sex cord-stromal cells. The tumours are benign, but there is a risk of developing malignant germ cell tumours from one of the benign components.

Conflict of interest statement

None declared.

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