Mesenchymal Tumors of the Ovary 19

Paul A. Bennett

Abstract

This chapter deals with "pure" mesenchymal tumours of the ovary; a subset of rare ovarian tumours that are composed of mesenchymal tissue without an epithelial, germ cell or sex-cord stromal element. These tumours have an uncertain histogenesis, and the notion of a "pure" ovarian mesenchymal tumour is disputed for many of the entities described in this chapter.

Introduction

The wide variety of pure ovarian mesenchymal lesions reported in the global literature has led to controversy over the histogenesis of these rare lesions, primarily because the ovary bears only a limited amount of normally-occurring mesenchyme from which tumours can develop. For example, whilst it may be speculated that ovarian leiomyomas can arise from vascular or ligamental smooth muscle, the origin of apparently pure ovarian rhabdomyosarcomas is less clear cut given the absence of striated muscle in the normal ovary. Possible origins of mesenchymal lesions therefore include mesenchymal overgrowth of heterologous tumours, overgrowth of the stromal element of an endometriotic deposit, growth within a cyst wall, or origin from mesenchymal tissue within a Sertoli-Leydig cell tumour or a mature or immature teratoma. It therefore follows that each of these theories relies on the obliteration of other tumour components by the proliferating mesenchyme, in order for these lesions to appear purely mesenchymal. These probable pathways of histogenesis are yet to be convincingly proven, however, and the possibility of *de novo* mesenchymal neoplasms arising within the ovarian stroma has not yet been fully excluded.

What follows is a brief discussion of these rare tumours, including clinical presentation, morphological features and prognosis. We have not included pure fibrous tumours of the ovary within this chapter, on account of their presence in the continuum of fibroma-thecoma sex cord-stromal tumours. These entities are instead described in Chap. 15.

P.A. Bennett, BMedSci (Hons), BM BS, FRCPath
Department of Histopathology, St James's University Hospital, Beckett Street, Leeds LS8 1BW, UK
e-mail: drpaulbennett@gmail.com

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Tumors of Smooth Muscle

Leiomyoma

Leiomyomas of the ovary are relatively uncommon, with up to 100 cases described in the worldwide literature [1–52]. An age range of 16–79 years has been reported. Although usually unilateral, bilateral ovarian leiomyomas appear to be more common at the younger end of the spectrum, with cases reported in 16- and 21-year-olds [16, 17, 22]. The most commonly described clinical features are nonspecific and include pain, abdominal swelling, and a palpable mass. Other presenting features include bilateral hydronephrosis [26], pleural effusion [10, 40], ascites [42], and virilization secondary to reactive hyperplasia of the theca interna [7, 13, 25]. Many ovarian leiomyomas were incidental findings, including one discovered during a termination of pregnancy [20]. They have been reported to have an appearance similar to uterine leiomyomas on dynamic-contrast MRI imaging [45].

Grossly, ovarian leiomyomas can vary in size, in keeping with their uterine counterparts. The reported maximum dimensions vary from 3 mm [18] to 250 mm [49]. They are typically solid and well circumscribed with a whorled, gray-white cut surface.

In the majority of reports, these lesions show the characteristic histological features of a leiomyoma: bundles and whorls of eosinophilic spindle cells displaying regular, blunt-ended nuclei. Rarely, they have been reported to show a prominent lipomatous component [9, 15]. Typically, the myocytes display minimal (insignificant) atypia and sparse or absent mitotic activity. As yet, an ovary-specific model of categorizing atypical leiomyomas does not exist due to the relative rarity of these lesions. In cases of increased cellularity and mildly increased mitotic activity, the terms "cellular leiomyoma" and "mitotically active leiomyoma" have been used, in keeping with the terms used for uterine lesions [38]. Similarly, pleomorphic leiomyomas that lack significant mitotic activity have been reported as "symplastic" or "leiomyoma with bizarre nuclei" [8, 38].

Immunohistochemically, ovarian leiomyomas show immunoreactivity for h-caldesmon, desmin, smooth muscle actin, and vimentin.

The differential diagnosis of leiomyomas includes fibro-thecomatous lesions, on account of their bland, fascicular, spindled morphology. However, these lesions lack the cigar-shaped nuclei of leiomyoma and often show more prominent extracellular collagen deposition. While they may show smooth muscle actin-positive immunoreactivity, fibro-thecomatous lesions are negative for desmin and h-caldesmon. Differentiation from leiomyosarcoma is discussed below. Finally, ovarian involvement by leiomyomatosis peritonealis disseminata and intravenous leiomyomatosis should be ruled out.

Surgical excision is recommended, with some authors advising preoperative frozen section and ovary-preserving surgery in reproductive age women [51, 52]. Limited evidence is available regarding prognosis, although no cases of recurrent ovarian leiomyoma have yet been reported, including in the mitotically active variants.

Leiomyosarcoma

Primary ovarian leiomyosarcoma is rare, with less than 30 individual case studies documented in the global literature [53–79], together with a larger series of 26 cases [38]. The tumors most commonly occur in postmenopausal women, though have been reported to occur in patients as young as 20 [74]. Common presenting symptoms are pain, abdominal swelling, and a palpable abdominal mass. They have been discovered in conjunction with ovarian leiomyomas, suggesting malignant transformation of these lesions [67].

Grossly, ovarian leiomyosarcomas tend to be large, solid masses that can measure up to 250 mm maximally [79]. They typically have a more variegated appearance than benign tumors,

showing areas of necrosis and hemorrhage. Microscopically, ovarian leiomyosarcomas are composed of interlacing bundles of plump spindle cells, as expected of smooth muscle tumors. A minority have been reported to be myxoid [64, 78] or epithelioid [75], in keeping with uterine leiomyosarcomas. Compared to leiomyomas, ovarian leiomyosarcomas show prominent nuclear pleomorphism and hyperchromaticity, together with prominently increased mitotic activity including atypical mitoses. Coagulative tumor cell necrosis is also sometimes encountered (Fig. 19.1). While the criteria for defining smooth muscle malignancy in the ovary are not widely defined, Lerwill et al. proposed that at least two of the following features should be present to secure a diagnosis of malignancy: moderate or severe diffuse cytological atypia, a mitotic count $\geq$10 figures/10 high power fields, or tumor cell necrosis [38]. However, it should be noted that the authors in this series warned that nuclear atypia and a lower mitotic count were sufficient for clinically malignant behavior in a minority of cases. As for uterine lesions, it is perhaps reasonable to use the term "smooth muscle tumor of uncertain malignant potential" in the small number of cases where the distinction of a benign from a malignant neoplasm cannot be made reliably on the presently available criteria.

Immunohistochemically, ovarian leiomyosarcomas typically show positive immunoreactivity for h-caldesmon, desmin, smooth muscle actin, and vimentin. Some studies report bcl-2 immunoreactivity in these lesions [72, 78], the significance of which is uncertain.

The main differential diagnosis for these lesions is metastatic leiomyosarcoma from elsewhere, particularly the uterus. This should be supported by a previous history, in particular of a sarcoma at another site or the presence of a uterine mass. These cases must be discussed at the gynecological oncology multidisciplinary meeting and, depending on local protocol, also at the sarcoma multidisciplinary meeting. Secondary involvement by gastrointestinal stromal tumors should also be considered. These are often less pleomorphic and less mitotically active than the usual leiomyosarcomas and show positive immunoreactivity for CD117 (c-kit) and CD34.

The recommended treatment of ovarian leiomyosarcoma is surgical debulking and a full staging laparotomy. There are few studies into the efficacy of chemoradiotherapy, although most reports suggest it is of unproven benefit [69, 71]. Follow-up of many of the above case reports is incomplete, but the overall prognosis for these lesions is bleak. Lerwill et al. reported a mortality rate of 62 % at a mean of 24 months for the cases in their study [38]. A similarly high mortality rate is reported for many of the other case reports in the literature.

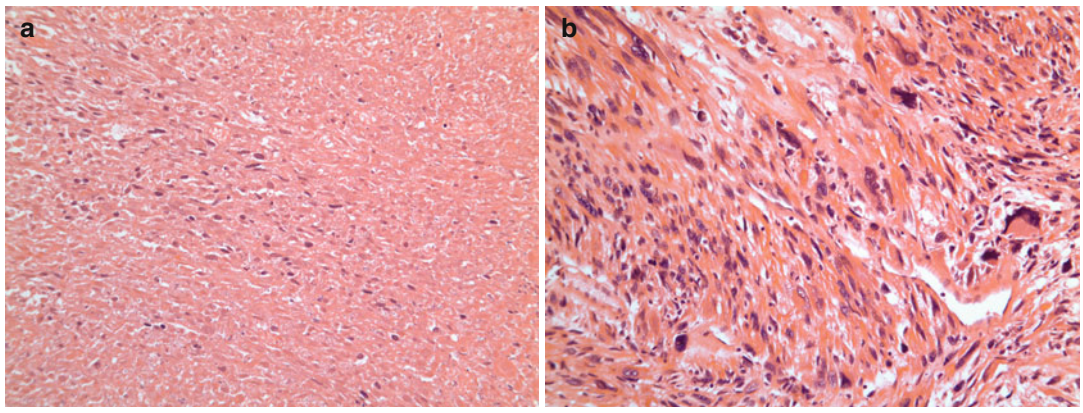

Fig. 19.1 (**a**) The typical pattern of coagulative necrosis seen in leiomyosarcoma, with admixed cytologically atypical myocytes. (**b**) Ovarian leiomyosarcomas show diffuse cytological atypia and increased mitotic activity, as seen here

Tumors of Striated Muscle

Rhabdomyoma

A single case of ovarian rhabdomyoma has been recorded in the literature. Rather than being a "pure" neoplasm, this case comprised small nodules of rhabdomyoma within the wall of a serous cystadenoma [80].

Rhabdomyosarcoma

Pure primary rhabdomyosarcomas of the ovary are rare, with less than 20 recorded examples [81–91] and a small series of 13 cases [92]. They have been reported between the ages of 4 and 79 years. Common presenting symptoms are abdominal pain and swelling, with many having evidence of metastatic disease at presentation. One case presented with such extensive bone marrow involvement, together with atypical cells in the blood, that it was initially diagnosed as an acute lymphoblastic leukemia [85].

Grossly, these lesions are unilateral and can measure up to 195 mm maximally. The cut surface varies from gray to yellow, with areas of hemorrhage and necrosis. Microscopically, the majority of the documented cases are of the embryonal subtype, which are typically composed of variably cellular sheets of small round blue tumor cells with little cytoplasm. These cells often show brisk mitotic activity. A clue to diagnosis is the presence of rhabdomyoblasts, which are typically larger with prominent eosinophilic cytoplasm. Less commonly seen are alveolar rhabdomyosarcomas, which form irregular nests of eosinophilic cells with round nuclei and prominent nucleoli.

Immunohistochemically, the tumor cells show strong positive immunoreactivity for myoglobin, myo-D1, myogenin, desmin, and smooth muscle actin. Electron microscopy may reveal Z-bands and myofilaments.

The differential diagnosis of embryonal rhabdomyosarcoma must include other small round blue cell tumors, especially in cases presenting in children. Lymphoma, leukemia, neuroblastoma, primitive neuroectodermal tumor, and small cell carcinoma of pulmonary or hypercalcemic type should all be considered. These may all present as primary or secondary lesions in the ovary. Alveolar rhabdomyosarcomas may need to be differentiated from metastatic epithelioid neoplasms, such as carcinomas and melanomas. The use of immunohistochemistry should render the diagnosis straightforward in most cases.

Most patients are treated with a full staging laparotomy including salpingo-oophorectomy and adjuvant chemotherapy. Ovarian rhabdomyosarcoma is an aggressive tumor with a poor prognosis, based on the limited prognostic data available. In the case series by Nielsen et al. [92], 8 of the 13 patients had extra-ovarian disease at presentation, and a total of 7 patients had died within 26 months. However, a recent case series showed a good initial response to vincristine, doxorubicin, and cyclophosphamide in children treated for both the embryonal and alveolar subtypes [89].

Tumors of Cartilage

Chondroma

While benign cartilaginous tissue is commonly found as a component of other ovarian tumors, pure chondromas are exceedingly rare. A single well-documented case exists, in which a 39-year-old woman presented with an ovarian tumor entirely composed of benign mature cartilage [93].

Chondrosarcoma

Primary chondrosarcomas of the ovary are also very rare, with only a single case report in the literature [94]. This was in a 61-year-old woman who presented with an abdominal mass. In this case, the chondrosarcoma appeared well differentiated and was successfully excised. There was no evidence of recurrence 4 years later.

Typically, chondrosarcomas have a blue-gray cut surface. Microscopically, the chondrocytes are more numerous, more pleomorphic, and more mitotically active than those seen in benign cartilaginous lesions. Immunohistochemistry is of little use.

The main differential diagnoses are between malignant cartilage in a carcinosarcoma with heterologous elements and metastatic chondrosarcoma from elsewhere. Thorough sampling of the lesion to look for epithelial elements, together with a good clinical history, is essential.

Tumors of Bone

Osteoma

There are no convincing examples of pure osteomas in the literature. Osseous metaplasia is a fairly common component of leiomyomas and fibromas, and osseous tissue is commonly seen in teratomas.

Osteosarcomas

Pure ovarian osteosarcomas are extremely rare, and only seven cases have been reported so far [95–101]. These are in the age range of 43–75 years and all presented with an abdominal mass and/or abdominal pain. A calcified mass is sometimes visible on abdominal X-ray [97, 98].

Grossly, these tumors usually measure over 100 mm in maximum diameter. The cut surface is solid and hemorrhagic, with focal areas of cystic change and necrosis also reported. Calcified areas may also be present, as described above. Microscopically, these tumors show the typical features of osteosarcomas seen elsewhere in the body: highly pleomorphic spindle cells with numerous mitotic figures arranged in sheets and bundles, associated with focal osteoid deposition.

Due to the typical appearance of osteosarcoma, the main differential diagnoses include metastasis from elsewhere and origin in a heterologous tumor. A careful history and extensive sampling should provide clues to the origin of this tumor.

As with other ovarian mesenchymal tumors, the limited data on pure ovarian osteosarcomas means that prognostic information is lacking. However, the studies quoted above suggest that these lesions are very aggressive, with most patients dying within 8 months. Hines et al. [97] report that their patient was disease-free following 8 courses of cisplatin-doxorubicin chemotherapy, but this is not reflected in any other studies.

Tumors of Neural Tissue

Neurofibroma

Pure neurofibromas of the ovary are extremely rare, and only two cases have been reported [102, 103]. Each of these was in a patient with known type 1 neurofibromatosis. One case presented as a pelvic mass, simulating a malignant neoplasm, while the other presented as chronic pelvic pain.

Like typical neurofibromas elsewhere, ovarian lesions are usually solid and well circumscribed. Microscopically, they are poorly defined and are composed of fascicles of elongated, tapering spindle cells with inconspicuous mitotic activity. The stroma may be focally myxoid and may also show scattered mast cells. The spindle cells are focally positive for S100, aiding in the main differential diagnosis with fibromas, which are S100 negative. The prognosis appears to be excellent, with no recurrence reported after 3 years in one of the above cases [103].

Schwannoma

Schwannomas of the ovary have been described [104] but are again extremely rare. They apparently resemble schwannomas seen elsewhere. In contrast to neurofibromas, they show a more varied hyper- and hypocellular sheetlike appearance (the so-called Antoni A and Antoni B areas) and are more diffusely and strongly S100 positive.

Ganglioneuroma

A single case of pure ovarian ganglioneuroma has been reported [105]. This tumor arose in a 4-year-old girl who presented with a swollen abdomen. Upon excision, the ovary was entirely replaced by ganglion cells, which typically show pale eosinophilic cytoplasm, round nuclei, and prominent nucleoli.

Malignant Peripheral Nerve Sheath Tumor

A well-described case of ovarian malignant nerve sheath tumor is reported in the literature [106]. This was diagnosed in a 71-year-old woman who presented with abdominal pain and swelling. A 15 cm smooth lesion was excised from the left ovary. Histologically, this tumor was extremely cellular, being composed of short fascicles of spindle cells with tapered nuclei and varying amounts of lightly eosinophilic cytoplasm. The mitotic count was 4 per 10 high power fields. S100 was negative, a reported feature in some malignant peripheral nerve sheath tumors [107]. This patient did not respond to doxorubicin and cyclophosphamide and died less than 5 months following diagnosis.

Paraganglioma

Paragangliomas of the ovary are rare. A recent small case series [108] included three patients of ages 22, 58, and 68 years. The ovaries were grossly solid, with tumor sizes ranging from 80 to 220 mm. The microscopic appearance was typical of paraganglioma, with each case showing a nested ("Zellballen-like") tumor of granular epithelioid cells set within a vascular stroma. The tumor cells stained positively for neuroendocrine markers, and one case showed the classical appearance of peripheral S100-positive sustentacular cells around the nests. The presence of focal inhibin positivity was raised as a potential pitfall in these lesions, particularly when considering sex-cord stromal tumors as a differential diagnosis. The typical features of paraganglioma are demonstrated in Fig. 19.2.

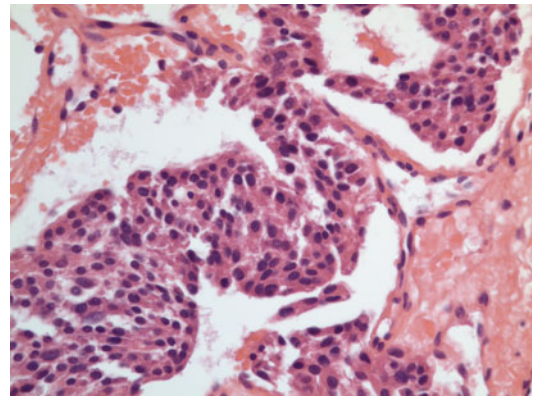

Fig. 19.2 Ovarian paragangliomas often form small nests, or "Zellballen," as seen here. A rim of sustentacular cells is visible surrounding the nested cells

Tumors of Vascular and Lymphatic Tissue

Hemangioma

The ovary has a rich vascular supply, and it is therefore unusual that ovarian hemangiomas are so rare, with only approximately 40 well-recorded cases in the literature [109–139]. These occurred between the age ranges of 11 and 81 years. Most presented with an abdominal mass or were discovered incidentally during surgery. Other means of presentation included ascites [126, 129, 136], acute abdominal pain [123], an elevated serum CA125 [129, 132, 136], and pleural effusion [132]. Most hemangiomas show a characteristic vascular pattern on ultrasonography, although markedly calcified hemangiomas have also been detected on preoperative imaging [138]. Bilateral lesions have occasionally been reported [119].

Grossly, hemangiomas are usually only 10–20 mm in maximum diameter. However, larger lesions of over 100 mm have been reported [127]. The cut surface is typically spongy and hemorrhagic. Microscopically, the diagnosis is usually straightforward. Most hemangiomas are of the cavernous type, showing variably sized

blood-filled spaces lined by a single layer of endothelial cells. Intravascular thromboses may be present. Adjacent stromal luteinization has been reported in a small number of cases [125, 126, 130]. Immunohistochemically, these lesions stain positively for CD31, CD34, and factor VIII-related antigen.

As always, the ovary should be extensively sampled to exclude a hemangiomatous component of a teratoma. Otherwise, the principal differential diagnosis lies between hemangioma and the small hilar capillary proliferations that are commonly seen in the normal ovary. This distinction can be difficult in smaller lesions, but the presence of a well-defined mass should secure the diagnosis of hemangioma. The absence of erythrocytes in the dilated spaces should raise the possibility of lymphangioma, which, unlike hemangioma, will show positive immunoreactivity for D2-40.

Ovarian hemangioma should be managed by simple oophorectomy.

Angiosarcoma

Pure angiosarcomas of the ovary are vanishingly rare, and around 20 well-reported cases are present in the literature [140–152]. Most arise in premenopausal women but have been described in patients as old as 81 years [151]. The most common presenting symptom is abdominal pain and swelling, although anemia associated with hematoperitoneum has also been reported [150].

Grossly, angiosarcomas can vary in size. A small series by Nucci et al. showed a range of 35–140 mm [144]. They are typically brown, hemorrhagic, and friable. Microscopically, they are composed of variably sized, proliferating vascular channels lined by markedly pleomorphic cells with brisk mitotic activity. There may be areas of solid growth and necrosis. Occasionally, a spindled morphology may predominate. Immunohistochemical reactivity for CD31, CD34, factor VIII-related antigen, and smooth muscle actin is typically encountered. Cytokeratins may be positive in epithelioid angiosarcomas.

Angiosarcoma may occur as part of a carcinosarcoma or an adenosarcoma, so an epithelial element should be searched for. In pure tumors, the main differential diagnoses lie between other malignant sarcomatous tumors, such as leiomyosarcoma, and metastases from elsewhere. Immunohistochemical immunoreactivity and a comprehensive discussion at the relevant multidisciplinary meetings will make the diagnosis clear.

These lesions are commonly treated with radical surgery and chemotherapy. Based on the limited examples available, the prognosis for angiosarcoma is poor, with many patients presenting with late-stage disease and dying within a year. However, a remission of 6 years has been recorded following treatment with doxorubicin and ifosfamide [148], and a case of apparent remission in a late-stage (FIGO IIIC) angiosarcoma has also recently been described following a six-cycle epirubicin and ifosfamide regimen.

Lymphangioma

Pure ovarian lymphangioma is very rare, and only a small number of cases have been reported [153–157]. They appear to arise in peri- and postmenopausal women, although one example was reported in a 19 year old following radiotherapy for Wilms' tumor [155]. The presenting symptom is usually an adnexal mass, although one case presented with chylous ascites [154].

Lymphangiomas can occur bilaterally [156]. Grossly, they display a honeycombed, spongy cut surface. Microscopically, thin-walled channels of varying sizes are seen, some of which may contain lymphocytes. The endothelial lining is flat and regular. Immunohistochemical reactivity for CD34, CD31, and D2-40 is usually seen.

The differential diagnosis lies between hemangioma and adenomatoid tumor. Distinction from hemangioma is discussed above. Adenomatoid tumors tend to contain solid cords of cells among their dilated channels and lack the typical immunohistochemical profile of lymphangioma. Instead, they show positive reactivity for mesothelial markers including calretinin and cytokeratins.

Tumors of Adipose Tissue

Lipoma

While fat is a common component of mixed tumors and teratomas, pure fatty lesions are extremely rare. An apparently pure lipoma was reported recently in a 66-year-old woman [158]. It was composed of sheets of benign fat, without any other tissue component.

Liposarcoma

A single case of pure ovarian liposarcoma has been reported [159]. It was diagnosed in a 13-year-old girl who presented with pelvic pain and a right ovarian mass. Histologically, the lesion was diffusely myxoid and contained a chicken-wire vascular morphology. The diagnosis of a myxoid liposarcoma was made. This was supported by demonstration of TLS-CHOP fusion by fluorescent in situ hybridization, which occurs as a result of the characteristic t(12;16) translocation associated with these lesions.

Miscellaneous Mesenchymal Tumors of the Ovary

Endometrioid Stromal Sarcoma

Primary ovarian endometrioid stromal sarcoma is again another rare tumor. Approximately 20 well-documented cases are described [160–165]. These arose in women between the ages of 20 and 76 years, who presented with symptoms of pain and abdominal swelling.

Grossly, the tumors measure an average of 110 mm [161]. Bilateral involvement is common. They are often solid and yellow-brown but may show areas of cystic change. Histologically, the appearance is comparable to endometrioid stromal sarcoma in the uterus. The typical pattern is sheetlike growth of oval and spindle-shaped cells with hyperchromatic nuclei and scant cytoplasm. Mitoses are generally inconspicuous. Small arterioles are commonly seen, around which the tumor may grow in a whorled pattern (Fig. 19.3). Areas of sex-cord stromal differentiation, smooth muscle differentiation, and myxoid change may occur. In contrast to uterine endometrioid stromal sarcoma, ovarian lesions tend to show a more nodular growth pattern and commonly lack the classical tonguelike growth pattern seen so often in the uterus. Endometriosis may be seen alongside these lesions and they may even originate within the stroma of an endometriotic cyst.

Immunohistochemically, ovarian endometrioid stromal sarcomas show positive reactivity for CD10, vimentin, and smooth muscle actin. Areas of smooth muscle differentiation may show positive reactivity for desmin and areas of sex-cord-like differentiation for inhibin.

The main differential diagnosis of ovarian endometrioid stroma sarcoma is a metastasis from the uterus. The absence of a uterine mass and the presence of endometriosis in the ovary are supportive of a primary ovarian lesion. Other possibilities include sex-cord stromal tumors and fibro-thecomas. In these instances, extensive sampling should identify at least some areas of more typical endometrial stromal differentiation. Furthermore, fibromas lack the typical vasculature of endometrioid stromal sarcoma. Care should be taken with immunohistochemistry for the reasons noted above and because some sex-cord stromal tumors also stain for CD10 [166].

Treatment is usually surgical, with some cases receiving chemotherapy and/or radiotherapy. The apparently successful use of hormone therapy has also been documented [164]. Overall, however, the outcome is unpredictable. The only large case series in the literature showed a correlation with tumor mitotic count. Of the 14 patients in this study with primary ovarian disease, 11 were still alive at the time of write-up. Those that died all had more than 10 mitotic figures per 10 high power fields [161].

Myxoma

Less than 20 ovarian myxomas have been reported [167–173]. The patients ranged in age from 12 to 46 years old and presented with abdominal or adnexal masses.

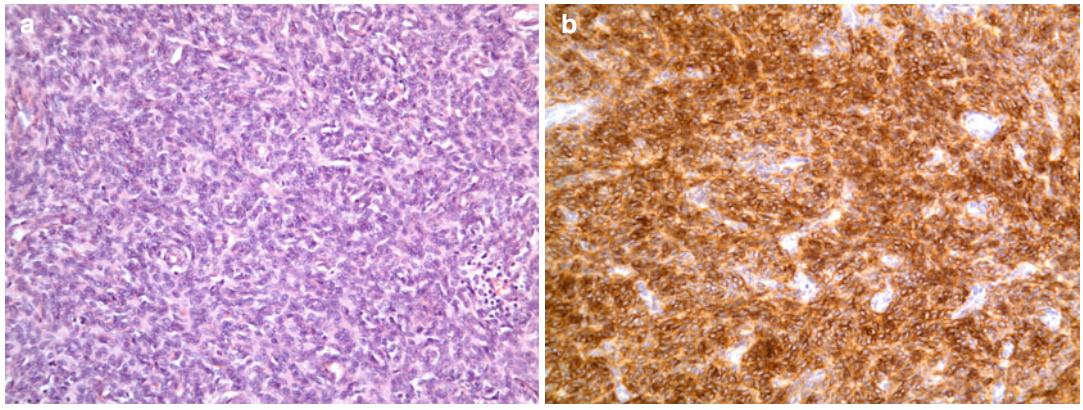

Fig. 19.3 (**a**) Endometrioid stromal sarcomas arising in the ovary are identical to their uterine counterparts, showing hyperchromatic cells arranged in a whorled pattern around small blood vessels. (**b**) CD10 positivity in endometrioid stromal sarcoma arising in the ovary

Macroscopically, these tumors ranged in size from 50 to 220 mm. Most appeared solid and gelatinous on cut surface, although some showed focal cystic change [169] and others had focal hemorrhagic features [171]. Microscopically, these lesions are composed of bland, variably hyperchromatic spindle and stellate cells with inconspicuous mitotic figures. These cells are dispersed within a loose myxoid stroma containing varying amounts of intervening capillary channels. Foci of fibrosis are occasionally seen (Fig. 19.4).

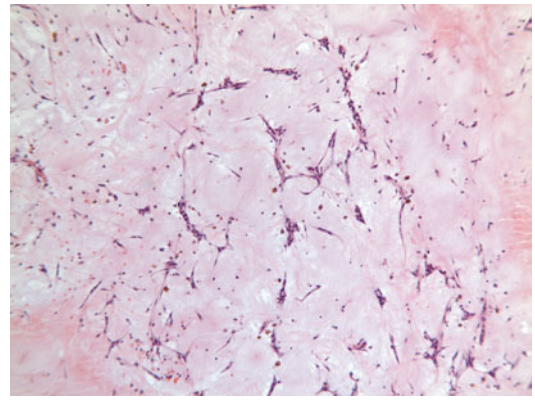

Fig. 19.4 The typical appearance of ovarian myxoma: spindle and stellate cells scattered in a loose myxoid stroma, together with intervening capillary channels

Myxomas have a nonspecific immunohistochemical appearance and typically show positive reactivity for vimentin and smooth muscle actin [169]. S100, cytokeratins, and vascular markers are negative. Desmin is usually negative, although focal positivity has been reported [170]. Staining for alcian blue is usually strongly positive, on account of the large amount of hyaluronic acid within the stroma of these lesions.

The differential diagnosis of ovarian myxomas includes massive edema of the ovary, which can be identified by the presence of normal ovarian structures within the stroma. The presence of prominent areas of fibrosis may point to an ovarian fibroma with myxoid change. Most importantly, myxomas must be differentiated from myxoid sarcoma, namely, liposarcomas or rhabdomyosarcomas. Extensive sampling of these cases should reveal some of the more typical features of these lesions, as described earlier in this chapter. Finally, epithelioid tumor cells within a myxoid stroma may point to a primary or metastatic mucinous carcinoma, which should also be excluded.

The treatment of ovarian myxoma is surgical excision. The prognosis is good, and all 13 patients in a small case series were tumor-free after 1–13 years [169]. A single case of recurrent disease is documented in a 65-year-old woman, 19 years after surgery [170]. This tumor had an aneuploid cell population and may have therefore represented a low-grade sarcoma as opposed to a typical myxoma.

PEComa

Perivascular epithelioid cell tumors (PEComas) have been the subject of much discussion in the 20 years since they were first identified as a unique group of tumors by Bonetti et al. [174]. The distinctive cells present in these tumors were named "perivascular epithelioid cells," a cell type which has no normal tissue counterpart. It was discovered that tumors of this cell type share common histological and immunohistochemical features, as described later. The PEC tumor group brought together angiomyolipomas of the kidney, clear cell ("sugar") tumors of the lung, and lymphangioleiomyomatosis. Since their initial description PEComas have been described in many different organs and tissues, including the ovary, despite some ongoing controversy over their histogenesis and nomenclature.

PEComas of the ovary are extremely rare, with only five cases reported in the literature. These include a 33-year-old woman with pulmonary and extrapulmonary lymphangioleiomyomatosis, the latter involving the ovary [175], and an epithelioid angiomyolipoma of the ovary associated with a separate renal angiomyolipoma in a 39-year-old woman [176]. Also described are a 41-year-old woman with cervical PEComa and intra-abdominal PEComatosis that involved the ovarian hilum [177] and a 59-year-old woman with malignant uterine PEComa and lymphangioleiomyomatosis affecting multiple sites, including the ovary [178]. Finally, the most recent example is of a 33-year-old woman with no significant history, who presented with an isolated ovarian PEComa [179]. Three of the above cases were in patients with known tuberous sclerosis [176–178].

Grossly, ovarian PEComas are reported to range from less than a millimeter in size (the so-called "PEComatosis," associated with larger lesions elsewhere) to up to 45 mm. The gross appearance was of a solid and/or cystic mass. Histologically, PEComas are typically composed of a mixture of spindle and epithelioid cells that display granular to clear cytoplasm and well-defined cell membranes. Nuclei are often regular, but bizarre forms have been reported [176]. Occasional nucleoli may be seen and mitotic figures are typically scanty. A perivascular distribution may be evident. Angiomyolipomas contain smooth muscle, prominent vessels, and admixed fat, along with the epithelioid cells mentioned above.

PEComas share a common immunohistochemical feature, in that the epithelioid cells are typically immunoreactive for melanocytic markers such as Melan-A and HMB45. Smooth muscle actin and vimentin are also commonly positive. Cytokeratins and desmin are negative.

The differential diagnosis of PEComas is relatively wide, and these lesions are often only considered following exclusion of other tumors. Their epithelioid and spindled morphology should necessitate exclusion of carcinomas and sarcomas. Recognition of some of the common morphological features of PEComa in the absence of a clear diagnosis should prompt the pathologist to request the appropriate immunohistochemical marker study, as described above.

Ovarian PEComas have all been treated with surgical excision. While most appear to behave in a benign fashion, it is difficult to speculate on the prognosis of these lesions, given the limited data available. A patient with widespread PEComatosis with ovarian involvement was disease-free 29 months following surgery [177]. It has been suggested that PEComas behave more aggressively if focally necrotic and of a large size. Whether or not this rule can be applied to ovarian PEComas remains to be seen. It is extremely likely that the coming years will produce more reports of this unique tumor type within the ovary.

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