observed. The apical expression pattern of the normal epithelium was changed to an all-around" pattern. Northern blot analysis also showed a loss of mRNA expression in tumor samples and HEC-1 B endometrial adenocarcinoma cells. Loss of protein expression in the tumor samples was further observed by Western blot. In conclusion, CD66a protein expression is deregulated in endometrial carcinomas, showing reduction or loss of expression with increased malignancy grade and a change from the apical to a pencellular, membranous localization (10).

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Aggressive forms of endometrial carcinoma

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Clear cell carcinoma

Freouencv

Clear cell carcinoma accounts for 1-5% of all endometrial carcinomas.

Histovathology

Clear cell carcinoma consists of cells with clear, vacuolated cytoplasm due to the presence of glycogen, hobnail cells or flattened or cuboidal cells. In the latter cell types, the clear cytoplasm is inconspicuous and in the hobnail cells the nuclei protrude to the surface of the cells. The nuclei generally are pleomorphic with marked atypia. This tumor exhibits a variety of growth patterns, including papillary, solid, tubular and cystic. Usually, there is a mixture of the different growth patterns. About 15% of the cases are mixed with other subtypes of endometrial carcinoma, including serous papillary carcinoma.

Differential diagnosis

Differential diagnosis is with serous papillary carcinoma and secretory carcinoma.

Prognosis

Patients with clear cell carcinoma of the endometrium have an overall death rate significantly higher than that of patients with ordinary carcinoma and clear cell carcinoma tends to occur in older patients (mean age 66 years). In stage I disease, survival is related to the extent of myometrial infiltration, age and nonsolid type. Two-thirds of the patients relapse outside the pelvis (upper abdomen, lungs and liver).

Serous panillary carcinoma

Freouencv

The frequency of serous papillary carcinoma is 1-10% 01 all endometrial carcinomas.

Histovathology

The tumor grows in complex papillary fronds with central fibrovascular connective tissue cores identical to those seen in ovarian serous carcinoma or is composed of glands. The lumens have an irregular gaping appearance. Necrosis is common and psammoma bodies are present in about one-third of the cases. The tumor cells are smaller than the endometrioid cells, cuboidal or hobnail shaped with a greater nuclear/cytoplasmic ratio, marked nuclear pleomorphism and eosinophilic cytoplasm. Invasive foci of serous carcinoma often show small glands and cysts with intraluminal papillary projections. These tumors often invade the myometrium deeply and also invade the vessels. Endometrial serous intraepithelial carcinoma is seen in a number of cases and is the only lesion from which serous carcinoma is thought to arise. The surrounding nonneoplastic endometrium is usually atrophic and the transition between atrophic and neoplastic endometrium is abrupt.

Since these tumors are almost always composed of high-grade nuclei, nuclear grading is not necessary. The diagnosis of serous papillary carcinoma itself establishes the presence of a highly malignant endometrial carcinoma.

Differential diagnosis

A differential diagnosis may have to be made with villoglandular! papillary endometriold adenocarcinoma, clear cell carcinoma of the papillary type, spread from ovarian serous papillary carcinoma.

Prognosis

Serous carcinoma is a highly malignant tumor, even when superficial or confined to an endometrial polyp or in the early stages. It occurs in older women, with a mean age of about 70 years. The metastatic pattern is similar to that of its ovarian counterpart.

Small cell carcinoma

Frequency

The frequency of small cell carcinoma is <1%.

Histovathology

Small cell carcinoma of the endometrium has features resembling small cell carcinoma of the lung. The growth pattern is usually diffuse with extensive necrosis. The cells are small or of intermediate size with hyperchromatic nuclei, numerous mitotic figures and scanty cytoplasm. Immunohistochemical evidence of neuroendocrine differentiation is demonstrated in most tumors (neuron-specific enolase, chromogranin, synaptophysin, leu-7). Some tumors show an admixture with ordinary adenocarcinoma or squamous cell differentiation.

Prognosis

In contrast to the common types of endometrial carcinoma, most patients with small cell carcinoma present with advanced stage and die of widespread disease within a year. In the Norwegian series, the 5-year survival was 64%. This is probably due to a better stage distribution compared to other published series with this disease. The mean age is about 58 years.

Differential diagnosis

The differential diagnosis is with malignant lymphoma, leukemia, stromal sarcoma, embryonal rhabdomyosarcoma, primitive neuroectodermal tumors and malignant mixed mOllerian tumor.

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Mesenchymal tumors of the uterus

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This paper confines itself to discussing recent changes in opinion or understanding of uterine pure mesenchymal tumors.

Smooth muscle tumors

Mitotically active leigmyomas

It has become clearer in the past 5 years what the relative value of mitotic counts in uterine smooth muscle tumors (SMTs) is. Previous recommendations regarding mitotic counts and outcome are now known to have been too dogmatic. Leiomyomata without significant cytological atypia (none or only mild atypia) may have mitotic counts up to 20 per 10 high power field (HPF) and still pursue a benign course. Such tumors tend to occur in reproductive life and to be seen especially in the secretory phase of the cycle. Mitotically active leiomyomata should not show abnormal mitoses or coagulative necrosis. Cytologically bland tumors with more than 20 mitoses per 10 HPF are not yet sufficiently well understood for definite comment.

Lelomyomas with bizarre nuclei

When lelomyomas with bizarre nuclei show focal atypia without coagulative necrosis or abnormal mitoses, they may behave as benign tumors even with mitotic counts above 10 per HPF. In the series of Bell *etal.,* diffuse atypia and a mitotic count above 10 per 10 HPF was associated with malignant behavior. A more recent paper suggests that half of bizarre leiomyomas" show diffuse atypia and confirms that maximum mitotic rates of up to 7 per 10 HPF may be seen without malignant behavior.

Eoithelioid smooth muscle tumors

Well-defined margins, a clear cell pattern, hyalinization and the absence of necrosis are good prognostic features in epithelioid SMTs. Mitoses may be low, however, even in frank epithelloid leiomyosarcomas, with some having mitotic rates as low as 3-4 per 10 HPF. Most, but not all, malignant examples show pleomorphism, necrosis and hypercellularity and caution is required in the diagnosis of these tumors.

Myxoid smooth muscle tumors

Myxoid SMTs are uncommon but increased mitotic rates and plecmorphism etc. may be absent even in highly aggressive examples. The presence of an infiltrative margin and a size greater than 4.0 cm are indications of malignancy and all myxoid SMTs must be treated with caution. They should be differentiated from leiomyomas with hydropic degeneration and "perinodular hydropic leiomyomas.

Cellular smooth muscle tumors

Cellularity *per* se is not a worrying feature in SMTs unless accompanied by pleomorphism etc.. Cellular SMTs may, however, be very difficult to distinguish from stromal tumors. Unlike stromal tumors they tend to merge with the myometrium at their periphery and have large, thick walled blood vessels in contrast to the small arterioles typical of stromal tumors. Cellular lelomyomas may also show cleft-like spaces. Immunohistochemistry is of limited value.

Hemorrhagic cellular (aooolectic.l leiomvomas

Pregnancy, progesterone therapy and gonadotropin-releasing hormone analog therapy may all produce worrying changes in benign SMTs, including pleomorphism, infarction, increased mitoses and hemorrhage. The keys to the correct interpretation of these benign, but worrying, changes are the clinical history, lack of coagulative necrosis, well-defined tumor margins and occurrence of the changes in several tumors.

Stromal tumors

The classical differentiation of stromal tumors into stromal nodules, low-grade stromal sarcomas and high-grade stromal sarcomas has