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Müllerian Adenosarcoma With Sex-cord Like Differentiation: Report of a Case and Immunohistochemical Study

Sex-kord Benzeri Diferansiyasyon Gösteren Müllerian Adenosarkom: Olgu Sunumu ve İmmün Dokukimyasal Çalışma

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Özet: Çok az görülmesi nedeniyle seks-kord diferansiyasyon gösteren bir müllerian adenosarkom olgusu sunuldu. Tümörün glandüler epitelyal komponentinde atipik hiperplazi ve fokal karsinom gelişimi görüldü. İmmündoku kimyasal boyamada, seks-kord benzeri yapılarda ve bazı alanlarda stroma hücrelerinde düz kas yönünde özellikler görüldü. Seks-kord benzeri yapıların, stroma ile içiçe olması ve benzer immünofenotipik özellikler taşıması, seks-kord benzeri ayrımlaşmanın adenosarkomun stromal elemanlarından geliştiğini düşündürdü. Burada, tümörün histopatolojik özellikleri, ayırıcı tanısı ve histogenezi tartışıldı.

Anahtar Sözcükler: Müllerian adenosarkom, seks-kord benzeri diferansiyasyon, immün dokukimya.

Summary: *An unusual of müllerian adenosarcoma with sex-cord like differentiation is reported. Glandular epithelial component of the tumor showed atypical hyperplasia and focal carcinomatous development. Immunohistochemical staining revealed smooth-muscle feature of sex-cord like structures and in some areas of the stroma. This immunophenotypic similarity and intimate admixture of both of sex-cord like elements and stroma supported that sex-cord like differantiation was arising from stromal cells of adenosarcoma. Herein, histopathological features, differential diagnosis and histogenesis of this rare tumor are discussed.*

Key Words: *Müllerian adenosarcoma, sex-cord like differantiation, immunohistochemistry.*

The spectrum of histopathological findings is rather wide of uterine mesenchymal tumors. Some of uterine neoplasms which are consisting the epithelial and mesenchymal components may cause difficulty in their diagnosis and classification (1-5). In this report, we present a case of mixed epithelial-mesenchymal tumor which had diagnostic difficulty. Tumor was evaluated in müllerian adenofibroma-adenosarcoma spectrum. It had unusual features such as sex-cord like differentiation (SCD) which was assumed arising from the stromal component, and included atypical hyperplasia and focal carcinomatous development. Histopathological and immunohistochemical features, differential diagnosis and histogenesis of the tumor is discussed in a view of the literature.

Case Report

A 42-year-old (G5P3A2) white women presented with abnormal vaginal bleeding for one month. She had irreguler menstruel cycle for two years. She was taking 60 mg medroxiprogesteron acetate (farlutal®) and ethinyl estradiol 0.08 mg + norethisterone acetate 40 mg (östroluton®) at once a day each month. In the examination of curetting material adenomatous endometrial polyp with focal adenocarcinoma was diagnosed. In pelvic ultrasonography; endometrium was 1.7 mm in thickness and it had heterogenity in echo. CA125, Ca19.9, CEA and AFP and AFP values were normal. The general physical examination was unremarkable and routine labarotory studies were within normal limits. Laparotomy disclosed uterine enlargement 6-8 weeks' gestational size. Left ovary was cystic and 6x6 cm in diameter. There was no pathological appearence in the intraabdominal organs. A total abdominal hysterectomy with bilateral salpingooopherectomy, partial omentectomy, bilateral pelvic and paraaortic lymph node dissection were performed. The patient' postoperative course were uneventful. Oncologists thought that a guarded prognosis would be appropriate. She is well and no recurrence developed since two years.

Gross Pathologic Findings: The hysterectomy included a polypoid mass measured 1.5x0.6x0.5 cm involving near cornual region of fundus. Endometrium was unremarkable. Myometrium was 3 cm in thickness and had trabecular appearence. It included a myoma 0.3 mm in diameter. Cystic enlarged left ovary contained greasy material which was composed of sebeum and hair.

Light microscopic features: Several fibrous polypoid fragments having focal glandular hyperplasia with atypia and carcinomatous development was observed in the curretting material. In hysterectomy; polypoid mass, its base and adjacent myometrium had a composite tumoral process including neoplastic endometrial glands, stromal component and ovarian SCD (Figure 1-2). Glands were increased in number and their lining epithelium was showing atypia and some of them had carcinomatous appearence in polypoid mass (Figure 3). Some glands were cystically dilated and had polypoid folds projecting into lumen being formed by surrounding stroma (Figure 4). The stroma comprised of spindle cells. It was more cellular and condensed around benign and some atypical glands. Stroma had mitotic figures (MFs) ranging from 0-5 in ten high power fields (mean 1.7; counted with Olympus-CH2, x40 objective), increased cellularity and mild atypia. Sex-cord like elements (SCEs) which comprised of nests, cords, tubular and gland like structures were infiltrating the inner third of myometrium. SCEs were lined by the cells having uniform round, oval, grooved nuclei and clear cytoplasm in two or more cells width. There was no MF in these cells. We observed splitting and gathering of the cells of the stromal component as groups in focal areas (Figure 5). Reticulin staining revealed that fibrils were surrounding SCEs. Masson trichrome staining showed very scanty collagen among the stromal cells. There was PAS positive secretory material in the lumen of the glands.

Immunohistochemistry: Sections were immunostained using the labeled streptavidin-biotin peroxidase complex technique. Immunoreactivity of monoclonal antibodies directed against vimentin (Dako), desmin (Dako), a-smooth muscle actin (Immunon), keratin (wide spectrum, Dako), high molecular weight keratin (34bE12, Dako), epithelial membrane antigen (EMA, Dako) and P53 (DO-7, Dako) were evaluated. Antigen retrieval was carried out in staining procedure. Alpha-smooth muscle actin was positive in the elements showing SCD and in a small number of stromal cells (Figure 6). The other monoclonal antibodies were unreactive with all tumoral components.

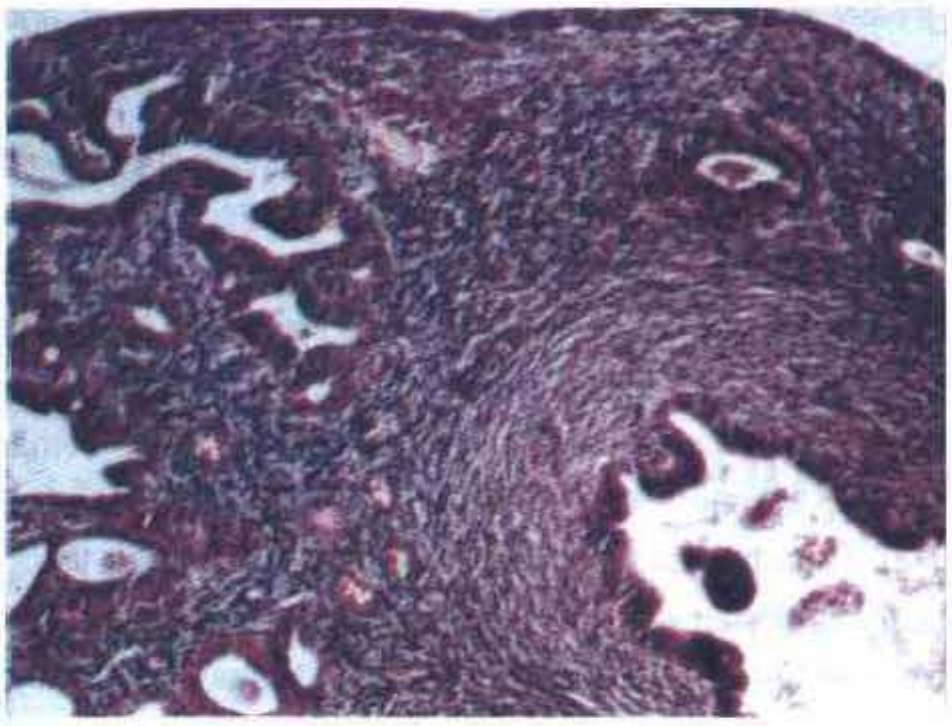

Figure 1. Polypoid mass including atypical glandular hyperplasia and periglandular hypercellularity of the stroma.

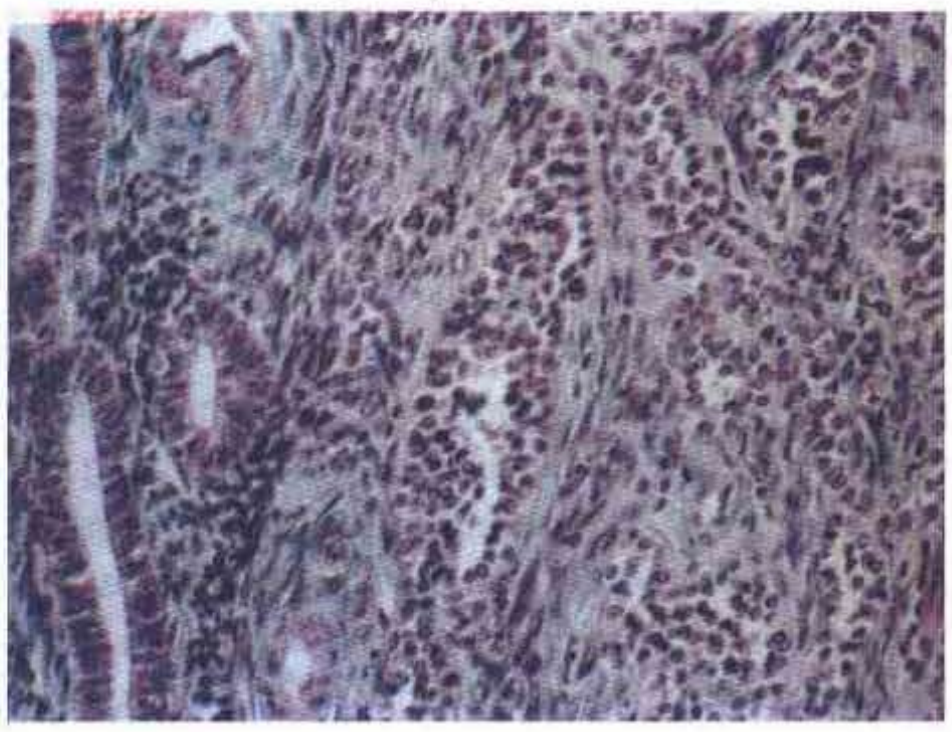

Figure 2. The areas with sex-cord like differantiation extending to myometrium (HEx200).

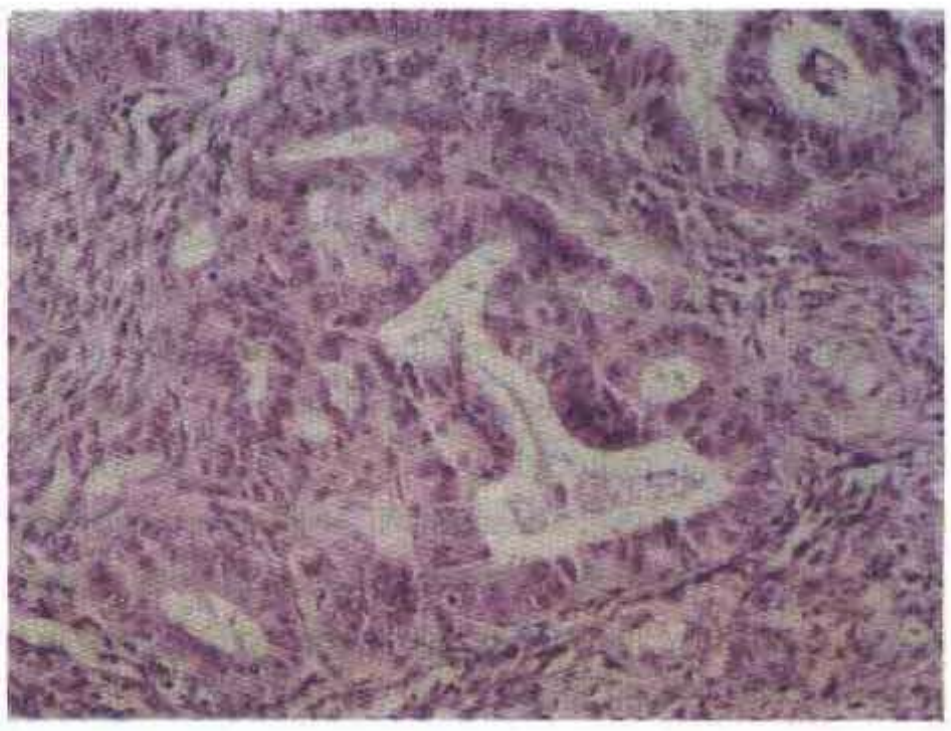

Figure 3. Focal carcinomatous development in glandular elements (HEx200).

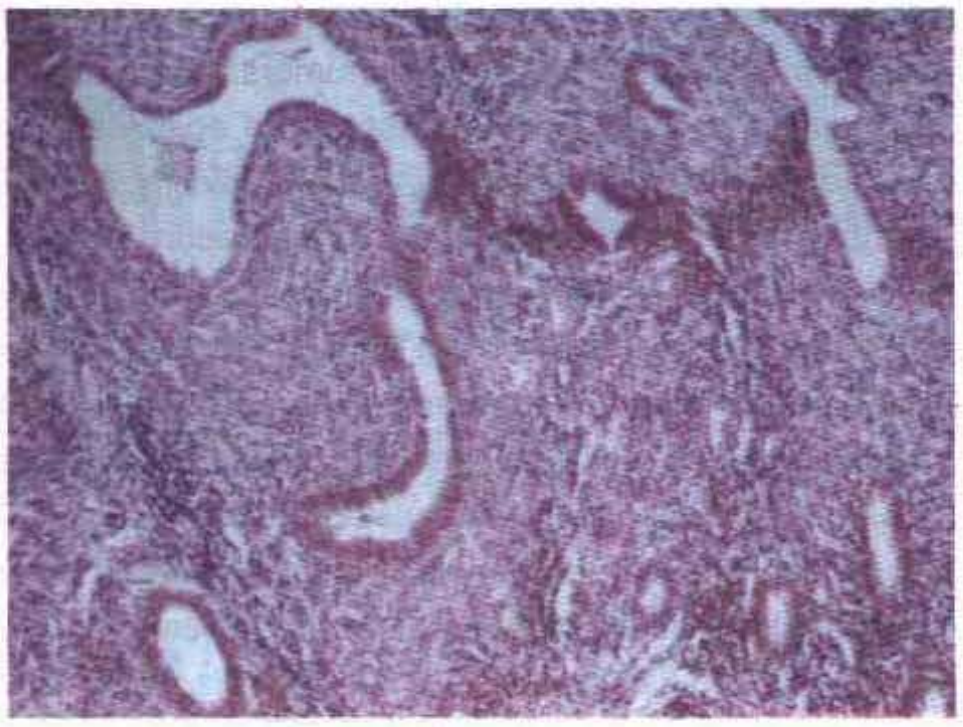

Figure 4. Polypoid folds projecting into lumen of glands (HEx80).

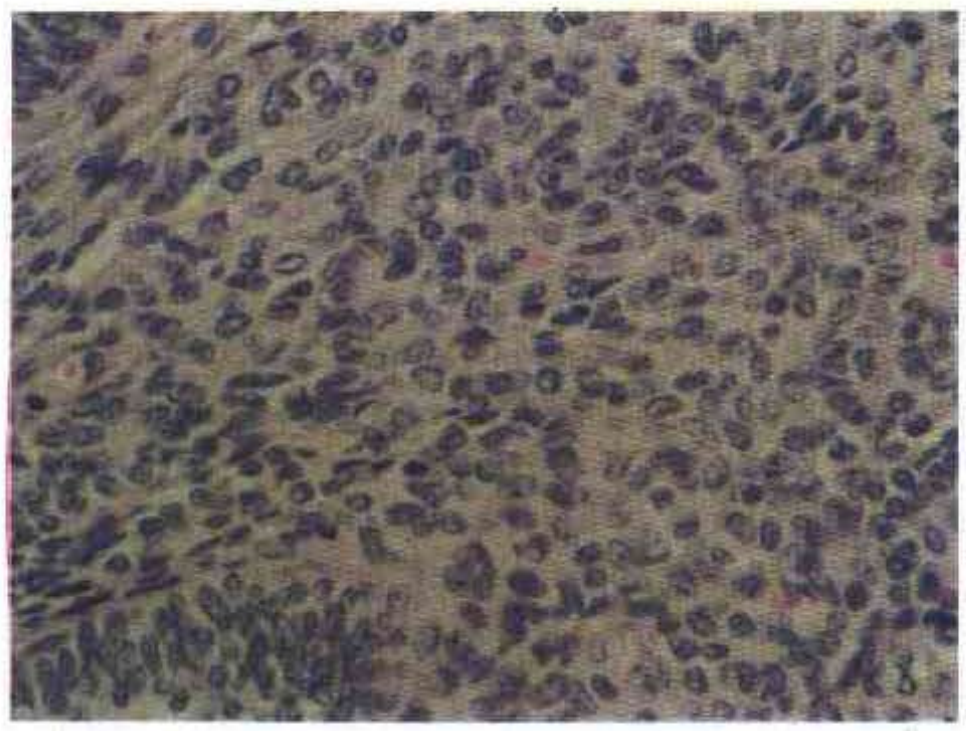

Figure 5. Splitting and gathering into groups of stromal cells (HEx400).

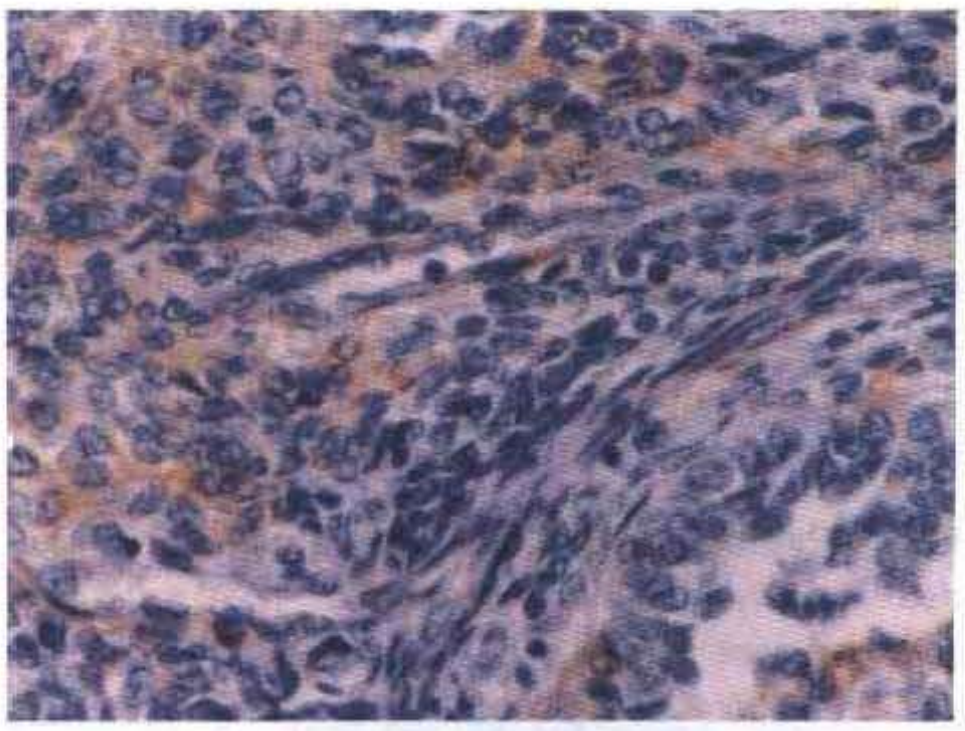

Figure 6. A-smooth muscle actin positivity in stromal cells and in SCE (Immunoperoxidasex400).

Discussion

Müllerian adenofibroma and müllerian adenosarcoma are respectively benign and low-grade variants of mixed epithelial-mesenchymal tumors. Difficulty may be encountered in differential diagnosis between these two tumors in some cases because of there is no sharp line separating them (5-9). Both tumors have benign glandular elements which are admitted generally as active participiants in the neoplastic process, but some authors believe in that they are entrapped glands in the neoplastic stroma (1,4,5,10,11). In adenofibroma and adenosarcoma may be seen very rarely carcinomatous development in glandular component or adenocarcinomas in uninvolved endometrium (4,6). Diagnostic problem between adenofibroma and adenosarcoma arises from the features of the stromal component. Recently, it has been proposed that if a tumor has one or more following features such as; two or more MFs/10 HPF or marked cellularity or more than mild degrees atypia in stromal cells, it should be diagnosed as adenosarcoma (6).

Our case had both of epithelial and mesenchymal components. Because of epithelial component comprised of benign, hyperplatic, atypical and a few carcinomatous glands, they were accepted as neoplastic. Stromal component had 1.7 MFs/10 high power fields in most active areas, increased cellularity and mild cellular atypia. The splitting and gathering into groups in the cells of the some areas of stroma made an impression as if SCEs were being formed by tumoral stromal cells. These elements were showing infltrative growth pattern into the inner one third of adjacent myometrium. Although mitotic count was lower than two, with the other features described above, stromal component was evaluated in favour of low grade sarcomatous and consequently tumor diagnosed as müllerian adenosarcoma with SCD. There are only nine case of adenosarcoma having SCD in the literature (2,12). Our case has similar features to the case 6 reported by Clement and Scully (2).

In the differential diagnosis of the presented case were included low grade endometrial stromal sarcoma (LGESS), uterine tumor resembling ovarian sex-cord tumor (UTROSCT), stromomyoma, carcinofibroma and carcinosarcoma.

LGESSs are monophasic neoplasms, however, very rarely in these tumors may be seen benign, atypical and carcinomatous glands sparcely or in large numbers. Clement and Scully reported three cases of LGESSs with extensive endometrioid glandular differentiation creating diagnostic and nosological problems (3). Rosai and et al think that müllerian adenosarcoma might be variant of endometrial stromal sarcoma (ESS) inducing the formation and/or proliferation of glands. They suggest that the development of SCD (a well known feature of ESS) in adenosarcoma as well support their sight (13).

Immunohistochemically, ESS generally shows vimentin expression. In some studies smooth muscle actin, desmin and cytokeratin positivity (typically in the epithelial-like structures) was demontrated in these tumors (14-16). Binder and et al suggested that ESSs coexpressing vimentin and keratin should be classified as epithelial and/or mesenchymal neoplasms (17).

In our case immunohistochemical staining disclosed smooth-muscle features in some of sex-cord like structures and stromal cells. This immunophonetypic similarity seen in both of stroma and SCEs support that SCD might be arising from mesenchymal component (which is predicted to derive from endometrial stroma) of the tumor. Large areas of stroma had features of nonspecific mesenchyme. This is the first case report diagnosed as a Müllerian adenosarcoma with SCD examined immunohistohemically in the literature.

In adenosarcoma with SCD, SCEs may account 5-50% of the tumor (13). UTROSCT which is probably a variant of endometrial stromal tumor contains extensive SCD scattered within typical endometrial stromal cells (10). Light and electron microscopic examination of these tumors revealed that SCEs had features of epithelial differentiation (10,17). There is only one case of UTROSCT studied with immunohistochemical staining in literature, and it showed keratin positivity in SCEs (17). In our case, the areas showing SCD constituted 50% of the tumor and these elements was predominantly were taking place in myometrium. Also in our case, keratin positivity were not determined in SCEs.

We eliminated combined smooth muscle-stromal tumor (stromomyoma), because in our case myogenic differentiation was not extensive and there was no nested smooth muscle and stromal areas.

Carcinofibroma includes extensive carcinoma and abundant fibrous stroma. Our case showed focal carcino-

matous development and stromal component wasn't fibrous. For that reason, we did not diagnose as carcinofibroma.

Carcinosarcoma composes of uniformly distributed carcinomatous glands throughout in a high grade sarcomatous component. In our case stromal areas showed low grade sarcomatous features and carcinomatous glands were focal and a few.

In soma cases of adenosarcoma, there is a history of chronic estrogenic stimulus and radiation exposure. Our patient was taking estrogen and progesteron inappropriately during the last two years. We thought that these drugs may have a role in tumoral development and its growth rate.

A discussed above there is a heterogenity of histopathological and immunohistochemical findings of uterine tumors including mesenchymal and epithelial elements. In these tumors, diversity of the findings may be a reflection of the variable differentiation capacity of a heterogen tumoral cell population or totipotentiality of the progenitor primitive mesenchymal cells from which was supposed to uterine mesenchymal tumors develop. We thought that intimacy of the histopathological findings of müllerian adenosarcoma and ESS in the literature might be suggesting a possible histogenetic relationship between them. Increasing numbers of case reports would be helpful to document the morphological and immunohistocheical spectrum of these tumors and to make the classification related to their histogenesis.

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