DOWNLOAD PDF CYTOPATHOLOGY OF ENDOMETRIAL HYPERPLASIAS

Chapter 1 : Pathology Outlines - Endometroid intraepithelial neoplasia (EIN) / Atypical endometrial hyperpl

Endometrial Hyperplasias A multicentric European study testing the reproducibility of the WHO classification of endometrial hyperplasia with a proposal of a.

Volume 4, Issue 4, July , Pages: Manoli To cite this article: February 18, ; Accepted: March 21, ; Published: June 13, Abstract: Abnormal uterine bleeding AUB is a commonly encountered complaint in gynecology department. Endometrial cancer is the fourth most common malignancy in women and the most frequent gynecological cancer in developed countries. With 5,28, new cases every year, cervical cancer is the fourth most common cancer affecting women worldwide, after breast, colorectal, and lung cancers. Manual Liquid Based Cytology MLBC is a cost effective technique that enables cells to be suspended in a monolayer and thus improve detection of precursor lesions and specimen adequacy. The residual sample can be used for other tests like Cell block and immunocytochemistry. To study a cost effective method of studying both endometrial and cervical cancer with help of ancillary techniques like cellblock, immunocytochemistry 3To compare the findings between conventional pap smear CPS and MLBC in detection of gynecological conditions of endometrium and cervix. Samples were collected using Ayres spatula by split sample technique from transformation zone of cervix which included outpatients of gynecology dept. The women were aged between years, 82 cases with bleeding history were taken to study endometrial pathology, while cases of white discharge per vagina were selected to study the cervix. Histopathological correlation was done for cases wherever possible. MLBC is a cost effective method for detections of cancerous lesions of endometruim and cervix. Morphological Distribution of Histopathological Examination 3. Comparison of Cell Block Diagnosis with Histopathology 3. Uses of Cell Block Are 6. The incidence of EC increased from The main risk factors for EC are obesity, diabetes, estrogen use, tamoxifen treatment polycystic ovarian syndrome PCOS , a history of infertility, alcohol abuse and antidepressant agents [8 , 9 , 10 , 11]. Many of these factors are tightly linked to current lifestyles in developed countries. It is also the fourth most common cause of cancer death deaths in in women worldwide. Graph showing the incidence of endometrial carcinoma with age and ethnicity. Worldwide incidence of cervical cancer. The main focus is on the secondary prevention of cervical cancer through early detection, a focus point of National Cancer Control Programme revised in [13]. Though the cytological examination has been the mainstay for early detection of cervical cancer, its widespread use has not been possible in the developing countries due to paucity of resources, man power and other facilities. Use of these technologies however are quite resource intensive and therefore not feasible in the setup of developing countries. On the other hand, Manual Liquid Based Cytology MLBC is a technique that enables cells to be suspended in a monolayer and thus improves detection of precursor lesions and improvement of specimen adequacy. MLBC has been reported to improve the effectiveness of cervical cancer screening in a population by increasing the detection of histologically confirmed neoplastic and preneoplastic disease while simultaneously decreasing over diagnosis of benign processes [17]. There are studies [15 , 18] which have dealt with liquid based cytology and have found its diagnostic accuracy comparable with conventional Pap smears. MLBC method however is specific to the laboratory, available equipments, fixatives and polymer solutions, etc. Specific objectives of the study were: As MLBC can be used for ancillary studies like cell block study, immunocytochemistry and HPV testing, one of the ancillary techniques which we studied is cell blocks prepared from residual tissue fluids and fine-needle aspirations which can be useful adjuncts to smears for establishing a more definitive cytopathologic diagnosis. Samples were collected using the split-smear technique from 82 patients sample size in the age group of 20 to 60 years attending the gynecology out-patient clinic at JSS Hospital, Mysore, prospectively from July to July for a period of two years. All the patients were clinically examined in detail according to the proforma and relevant radiological findings were collected. Material collected was stained by Pap stain. It was immediately put into a vial containing the fixative solution. The fixative contained 0. The sample was collected and mixed with equal parts of fixative. It was centrifuged at rpm for 5 minutes. The supernatant was decanted and excess fixative was blotted ml of polymer solution containing 2 gm of agarose, 10 ml of polyethylene glycol, 2 ml of poly-L-lysine and 88 ml of distilled water

was added to the deposit. It was again centrifuged at rpm for 5 minutes. The deposit was pipetted in a circular motion on to a glass slide. Stained with the Conventional Pap stain. After fixation, smears were stained using conventional Pap stain. Both smears were screened and results were compared. Cyto-histologic correlation was done. The Bethesda system was used for reporting cervical cytology for both groups. Detailed gross examination was done and bits were given. Paraffin embedded H and E stained sections were obtained and studied under light microscopy. Similarly another study on cervical pathology was conducted Samples were collected using the split-smear technique from patients sample size in the age group of 20 to 80 years attending the gynaecology out-patient clinic at JSS Hospital, Mysore. All the patients were clinically examined in detail according to the proforma and details of other relevant laboratory investigations were collected only if necessary. The cases collected were patients with clinical suspicion of cervical pathology. The processing of the samples was done as in the study on Endometrial pathology. Cyto-histologic correlation was done in those cases in which a colposcopic biopsy was also done. Whenever possible, ancillary techniques were applied for preparations of cell blocks and HPV- DNA testing from the residual cytocentrifuged sample. To extend our work on ancillary techniques we took the study further, to work on cell block as ancillary technique with IHC on cell blocks whenever necessary. The cell blocks studied were lesser than the liquid based cytology cases. The study was undertaken to prepare the cell blocks from samples of manual liquid based cytology MLBC and to compare it with conventional pap smears and liquid based smears and correlate with histopathology wherever possible. In the present study KI 67 and p16 markers were done on cell block preparation. Results In the present study, 82 cervical smears prepared by conventional pap and MLBC were studied, out of which 52 cases Out of 46 cases of endometrial cells- 35 were benign and 11 were atypical cells in conventional pap smear, while in manual liquid based cytology 28 were benign and 10 were atypical endometrial cells out of 38 cases. Table 1 Table 1.

Chapter 2 : Cytopathology and More | Endometrial cells in Pap testsâ€”when are they significant? â€“ CAP

For endometrial hyperplasias, the sensitivity of the Papanicolaou test was even lower (39 of tests; %), but BAEMC represented the majority of endometrial-type cells reported (36 of 39 tests). CONCLUSIONS.

On cutting open, most of the cancers are focally or diffusely exophytic, even when deeply invasive. In cases of serous adenocarcinomas, the uterus is relatively small and atrophic and reveals papillary excrescences on the cut surface. MMMTs are invariably polypoid and extensively fill the endometrial cavity Figs. Microscopy showed a well differentiated endometrioid adenocarcinoma FIGO grade I arising on a background of complex atypical endometrial hyperplasia Fig. Gross appearance of an endometrioid carcinoma fixed specimen. Anteriorly cut open total abdominal hysterectomy specimen with bilateral adnexae displaying polypoid tumor in the endometrial cavity. Histopathology revealed well differentiated endometrioid adenocarcinoma Microscopic examination of endometrioid adenocarcinomas is based upon incorporation of architectural patterns and severity of nuclear atypia. In the case of lower architectural grade and higher nuclear grade, the overall grade is escalated. On immunohistochemistry, most well to moderate endometrioid adenocarcinomas display positive estrogen receptor ER and progesterone receptor PR staining Figs. At times, endometrioid adenocarcinomas display squamous differentiation that is a metaplastic change Fig. Tumor cells exhibit mild nuclear atypia. Tumor seems to retain glandular pattern, but nuclear atypia is moderate. Glandular differentiation is lacking. Interspersed are few benign endometrial glands arrow and interspersed stromal cells displaying positive immunostaining, acting as internal positive control. Unlike endometrioid adenocarcinomas, in such cases, history of estrogen replacement therapy is less likely than abnormal cervical cytology. As aforementioned, the uterus in such cases is small and atrophic. Microscopically, this tumor is characterized by an array of patterns, although papillary pattern is more common. Besides, glandular and solid patterns are also noted. These are associated with intraepithelial carcinoma along with atrophied endometrium. On immunohistochemistry IHC , these tumors exhibit diffuse p53 and p16 immunostaining Fig. Cells exhibit marked pleomorphism, conspicuous hobnail arrangement, variably eosinophilic to clear cytoplasm, and prominent eosinophilic nucleoli in several cells. Stroma is hyalinized leading to formations of eosinophilic bodies. Deep purple psammoma bodies may be identified. The differential diagnoses include Arias-Stella reaction, serous adenocarcinoma, secretory type of endometrioid carcinoma, and yolk sac tumor. Only gold members can continue reading. Log In or Register to continue Share this:

Chapter 3 : Hyperplasia - Wikipedia

The endometrium (lining of the uterus) may develop endometrial hyperplasia, which include precancerous (intraepithelial) neoplasms (atypical complex hyperplasia) and nonneoplastic entities (simple and many complex hyperplasias without atypia); these are characterized by a proliferation of endometrial glands of irregular size and shape.

Cytopathology and More Endometrial cells in Pap testsâ€”when are they significant? The Bethesda system recommends reporting normal endometrial cells in women 40 years or older and any atypical endometrial cells under the atypical glandular cells category. Unlike AEMCs and EMCCs, NEMCs are reported only in women 40 years and older based on the Bethesda system , because age is more consistently available than menopausal status or clinical symptoms and the incidence of significant endometrial pathology in women under 40 years is extremely low. We try to address some of the questions in this field: Normal endometrial cells The Bethesda system suggests reporting the presence of normal exfoliated endometrial glandular cells only in women 40 years of age and older regardless of the date of the last menstrual period, for the reasons stated previously. NEMCs are more likely to be identified in the first half of the menstrual cycle 21 to 24 percent than in the second half of the cycle two percent 13,14, and more commonly in premenopausal than in postmenopausal women. This finding might be explained by more consistent use of sampling instruments for liquid-based cytology with better access to the endocervical canal. For women of childbearing age, the presence of endometrial cells on a Pap test is closely related to menstrual cycle phase. The endometrial cells are expelled from the endometrial cavity during menstrual bleeding and a few additional days up to the 12th day of the cycle. The presence of endometrial cells on a Pap test after the 12th day of the cycle is considered abnormal. NEMCs are usually packed together like a ball or three-dimensional clusters with no well-defined cell borders. The nuclei of NEMCs are usually round or bean-shaped and small, similar to the nuclei of intermediate cells. The nucleoli are inconspicuous and the chromatin pattern is difficult to discern owing to cell clustering and darkness. The cytoplasm is scant, basophilic, and occasionally vacuolated. The background is often bloody in conventional Pap tests, and it is usually cleaner with less blood and more single cells in liquid-based preparations. Histiocytes and endometrial stromal cells are occasionally present as well. During the mid-cycle of the menstrual period, NEMCs appear as less compacted clusters of loosely attached endometrial glandular cells without stromal cells, even with detached single endometrial cells. They have a basophilic cytoplasm with occasional vacuoles, spherical nuclei with inconspicuous nucleoli, and a size no larger than the size of the nuclei of intermediate or parabasal squamous cells. The differential diagnosis of NEMCs from Pap tests includes endocervical cells, inflammatory cells such as macrophages and lymphocytes, and histiocytes and parabasal cells. Endocervical cells ECCs are usually arranged in flat sheets or strips of parallel cells, not in three-dimensional clusters. More cuboidal configuration may also occur. Lymphocytes have a distinct coarse chromatin pattern unlike endometrial cells. Macrophages rarely form clusters. Histiocytes vary in size and number of nuclei and occur as individual cells or loose clusters, and have bean-shaped nuclei. Parabasal cells have nuclei resembling other squamous nuclei and more distinct and dense cytoplasm. Parabasal cells are usually present in sheets or small clusters instead of balls. NEMCs on Pap tests are mostly associated with normal endometrium, such as proliferating endometrium and atrophic endometrium. However, it has been shown that they are also associated with pathologic conditions, including polyps, hyperplasia with and without atypia, low- and high-grade adenocarcinomas, leiomyoma, immediate postpartum state, abortion, acute endometritis, and cervical and vaginal endometriosis. Normal endometrial cells on Pap tests are rarely associated with significant pathology in premenopausal women without abnormal bleeding. Anderson Cancer Center, found that about 2. Symptoms such as abnormal uterine bleeding are significant indicators for endometrial carcinoma. In followed-up women with NEMCs, most endometrial pathology has been found to be accompanied by symptoms. Therefore, symptomatic women with NEMCs on Pap test should undergo endometrial sampling regardless of menopausal status. Postmenopausal women with NEMCs may be at higher risk of endometrial lesions, too. One report showed that only those menopausal women with symptoms mainly bleeding had significant pathology, but none of the asymptomatic menopausal women were found to have

hyperplasia or carcinoma. Therefore, endometrial assessment is recommended for all postmenopausal women with NEMCs regardless of symptoms. Although menstrual and symptomatic statuses are very important in evaluating the significance of normal endometrial cells on Pap test, the information is not always available to the pathologist and clinician. This is the reason why the Bethesda system suggested NEMCs be reported only in women 40 years and older, because age is more consistently available than menopausal status or clinical symptoms. Our recent study demonstrated that significant lesions were present in women 50 years and older with NEMCs found after day 12 of the menstrual cycle or who are postmenopausal 5. AEMCs commonly appear as small three-dimensional clusters of five to 20 cells. The cells are small to moderate in size with scant to moderate cytoplasm. The nuclei are mildly to moderately enlarged and slightly hyperchromatic with or without small nucleoli. But the nuclei are smaller than atypical endocervical cells and adenocarcinoma cells. Cell borders are usually poorly defined, and cytoplasm may be vacuolated18,19 Figs. One report examined morphologic features of endometrial cancer in ThinPrep tests and suggested that enlarged nuclei and the presence of nucleoli in endometrial cells were the most reliable indicators of atypical endometrial cells or endometrial cancer. Sometimes it is difficult to differentiate benign and atypical endometrial processes, especially when cells show degenerative changes. Atypical endocervical cells are also in the differential diagnosis of atypical endometrial cells, although atypical endocervical cells usually are larger, have abundant cytoplasm, and are flat sheet in arrangement. It is sometimes impossible to tell these two entities apart. Under this circumstance, atypical glandular cells NOS would be appropriate. Adenocarcinoma cells either endometrial or endocervical usually show prominent pleomorphism with enlarged nuclei, irregular nuclear membrane, and prominent nucleoli. Background of necrotic debris might be present. High-grade squamous cervical lesions or squamous carcinomas in women may in rare instances be difficult to differentiate from atypical endometrial cells. Significant pathology and management. The presence of atypia significantly increases the risk of an underlying endometrial pathology hyperplasia or carcinoma. Postmenopausal women with AEMCs on Pap test have a risk for endometrial carcinoma of nine to 50 percent. Endometrial carcinoma cells Compared with AEMCs and NEMCs, endometrial carcinoma cells are more likely to have large and hyperchromatic nuclei with chromatin clearing, prominent nucleoli, and tumor diathesis. Cytoplasm is usually cyanophilic and vacuolation may be present. Neutrophils are usually present18,19 Figs. Endometrial carcinoma has a spectrum of morphology depending on grade and subtype. Well-differentiated endometrioid adenocarcinoma generally shows slight nuclear enlargement and atypia, which are difficult to differentiate from benign endometrial cells. Higher grade and serous carcinoma show significantly pleomorphic nuclear features, which are easily differentiated from benign-appearing endometrial cells. Endometrial carcinoma cells on Pap tests have a significant pathologic meaningfulness, and patients with EMCCs need to be evaluated immediately. Our recent study shows that all patients with EMCCs on Pap tests 21 cases had malignant lesions upon histological followup. Summary Normal exfoliated endometrial cells in both the first half and second half of the menstrual cycle in asymptomatic menstruating women are unlikely to be associated with significant endometrial pathology and need not be evaluated unless otherwise clinically indicated. Significant endometrial pathology occurs in symptomatic women with normal endometrial cells on cytology, in postmenopausal women, or in any age group of women with atypical endometrial cells on Pap tests and needs to be evaluated. Clinicians should provide the best demographic and clinical information to the pathologist, so that more specific recommendations can be rendered. If clinical information, such as symptoms and menstrual status, is not available, age might be used to stratify the risk of endometrial pathology. CA Cancer J Clin. The Bethesda System: The cellular detection of endometrial carcinoma and its precursors. Inadequacy of papanicolaou smears in the detection of endometrial cancer. N Engl J Med. Significance of endometrial cells in the detection of endometrial carcinoma and its precursors. Gondos B, King EB. Significance of endometrial cells in cervicovaginal smears. Ann Clin Lab Sci. Gusberg SB, Milano C. Detection of endometrial cancer and its precursors. Who is teaching teens about HPV? Incidence and clinical significance of morphologically benign-appearing endometrial cells in patients age 40 years or older: The presence of endometrial cells in cervical smears in relation to the day of the menstrual cycle and the method of contraception. Normal exfoliation of endometrial cells in premenopausal women. The significance of benign endometrial cells in

cervicovaginal smears. Normal endometrial cells in cervical cytology: The Bethesda System recommendation for reporting of benign appearing endometrial cells in Pap tests of women age 40 years and older leads to unwarranted surveillance when followed without clinical qualifiers. Diagnostic Principles and Clinical Correlates. The precursors of endometrial cancer: Endometrial cells in cervical cytology: J Low Genit Tract Dis. Reporting endometrial cells in women 40 years and older: Am J Clin Pathol. Clinical relevance of benign endometrial cells in postmenopausal women. Cytologically benign endometrial cells in the papanicolaou smears of postmenopausal women. Am J Obstet Gynecol. Routine endometrial sampling of asymptomatic premenopausal women shedding normal endometrial cells in Papanicolaou tests is not cost effective. Normal endometrial cells in liquid-based cervical cytology specimens in women aged 40 or older. Normal appearing endometrial cells in cervical smears of asymptomatic postmenopausal women have predictive value for significant endometrial pathology. Int J Gynecol Cancer. Reporting normal endometrial cells in Pap smears:

Chapter 4 : Endometrial Hyperplasia without Atypia and EIN | Basicmedical Key

This reveals increase in endometrial glands leading to their fusion and causing a common arch bars between the glands. While lack of atypia is noted in simple and complex hyperplasias without atypia, atypical hyperplasias reveal nuclear and cytoplasmic abnormality in the form of lack of polarity, irregular multilayering, and anisocytosis, accompanied by nuclear enlargement, hyperchromasia.

Materials and Methods 4. Introduction Abnormal uterine bleeding AUB is a commonly encountered complaint in gynaecology outpatient department. Although the causes vary with age, the most worrisome cause of perimenopausal or postmenopausal bleeding per vagina is the malignancy of the endometrium. Though various methods have been introduced to know the endometrial status, no widely accepted screening test for endometrial carcinoma exists because of certain issues like cost-efffectiveness and patients acceptance. However, if endometrial cells are observed in smears in second half of cycle, the pathological significance is greater although cell shedding at this time can be associated with use of OCP, IUCD or use of HRT. Hence The Bethesda system has mandated multiple reporting categories meant to apply to endometrial cells. Infact, the LBP method enables storage of a variable amount of cells. However, the cost of most commercially available LBC system is prohibitively expensive for resource-limited settings. Many workers like Alves et al. To explore the role of cervical cytology in the diagnosis of endometrial diseases in all abnormal uterine bleeding cases 2. Materials and Methods Samples were collected using split- smear technique from patients with bleeding history in the age group of 20 to 70 years attending the gynaecology out-patient clinic at JSS Hospital, Mysore, prospectively from July to July for a period of two years. Manual Liquid Based Cytology was strongly advocated as it improves sample quality and reduces the likelihood of false negative results by removing obscuring factors. After fixation, smears were stained using conventional Pap stain. Statistical Analysis Statistical methods applied were Descriptives, Chi-square test and Crosstabs Contingency table analysis. Apart from the above, diagnostic accuracy, sensitivity and specificity were calculated manually. All the statistical calculations were done through SPSS for windows v A P value of less than. The mean age was Remaining 28 cases had irregular menstrual cycle in the form of polymenorrhea, menorrhagia or intermenstrual bleeding. Abnormal uterine bleeding history was most commonly seen in age group of 40 year. Among 52 cases, histopathological correlation in the form of total hysterectomy and endometrial sampling. Out of 46 cases of endometrial cells- 35 were benign and 11 were atypical cells in conventional pap smear. While in manual liquid based cytology 28 were benign and 10 were atypical endometrial cells out of 38 cases. On follow up with histopathology there were 8 cases of malignancy, 1 case of pre cancerous lesion and others were benign pathology. Among benign cases maximum of 8 cases of leiyomyoma with proliferative endometrium , followed by 6 cases of simple hyperplasia without atypia and 4 cases of adenomyomatous polyp. Among 14 atypical endometrial cell cases, 13 had histopathological correlation with 8 cases being malignant, 1 precancerous lesion and 4 cases of benign endometrial pathology. The malignant cases diagnosed were 4 cases as type 1 endometrial carcinoma followed by 3 cases of squamous cell carcinoma and 1 case of type 2 endometrial carcinoma. The remaining benign cases were 2 adenomyomatous polyp, 1 atrophic endometrium and 1 endometritis. Benign endometrial cells did not show any malignant pathology on histopathology follow up. MLBC also showed better sensitivity and positive predictive value. Cells are small with round nuclei and scant cytoplasm Fig. Discussion Our study was conducted among women between year old with history of abnormal uterine bleeding. Although The Bethesda system recommendation is 40 year, our consideration of wide age range was because shedding of normal endometrial cells has been associated with the following conditions: Studies with this stratification and sub analysis are lacking in the literature In our study the youngest patient with endometrial carcinoma type 1 was 36 year , but no family history of uterine or breast malignancy was reported. Previous studies have suggested that reporting nEMCs in premenopausal women has little practical value. However, among 24 postmenopausal patients with atypical endometrial cells, six were diagnosed to have endometrial carcinoma and one person with complex hyperplasia with atypia on follow up. Like our study Simsir et al 23 and Kerpsack et al. Very few studies had clearly mentioned study

group population. Comparisons between those studies also were hampered by significant differences in the classification of Pap tests, including a lack of consensus about whether benign-appearing endometrial cells constitute normal or abnormal findings. But available literature suggested compared with conventional cytology, LBC may be associated with a higher prevalence of NECs because of more consistent use of sampling instruments for LBC with better access to this area. There are 3 possible explanations for improved sensitivity: LBC improves sample collection by markedly increasing number of cells that leave collection device into vial. LBC reduces obscuring elements and thus allows for detection of abnormal cells that could have been otherwise hidden on CPS. Better preservation of abnormal cells on LBC slide allows for more definitive categorization of abnormal cells 7. Conclusion Endometrial carcinoma early detection is becoming an increasingly important challenge. So the time has arrived to consider screening for endometrial pathology seriously. Recently, developed countries like Japan has conducted randomized controlled trial comprising liquid based endometrial cytology as screening tool for the early detection of their considerately increasing endometrial cancer and gained a huge response. In developing country specially in low resources set up, MLBC can be of little help. It overcomes the limitations of CPS like removing obscuring factors and increasing diagnostic accuracy. Also, future ancillary techniques like preparation of cell blocks, immunocytochemsitry and HPVtesting becomes possible in testing of new paradigms for screening strategies that are required in such settings. From our study, we like to stress upon that- 1. Clin Exp Obstet Gynecol ; Hysteroscopy in women with abnormal uterine bleeding on hormone replacement therapy: Diagnostic accuracy of liquid-based endometrial cytology in the evaluation of endometrial pathology in postmenopausal women. Screening for endometrial cancer in asymptomatic postmenopausal women with conventional and colour Doppler sonography. Br J Obstet Gynaecol ; Significance of benign endometrial cells in Pap smears from postmenopausal women. Diagnosis of Uterine Cancer by the Vaginal Smear. The Commonwealth Fund; Journal of medical screening ;vol. Liquid-based Papanicolaou test SurePath interpretations before histologic diagnosis of endometrial hyperplasias and carcinomas. Cancer Cytopathology ; 4: Endometrial Cells in Cervical Cytology: Review of Cytological Features and Clinical Assessment. Liquid based endometrial cytology: Utility of thin-layer preparations in the endometrial cytology: Ann Diagn Pathol ; Comparison of manual and automated methods of liquid-based cytology a morphologic study. Validation of a low-cost, liquid based screening method of cervical intraepithelial neoplasia. Am J Obstet and Gynecol The precursors of endometrial cancer: Classification of benign endometrial glandular cells in cervical smears from postmenopausal women. Endometrialtype cells in cervico-vaginal smears: Reportingendometrial cells in women 40 years and older-Assessing the clinical usefulness of Bethesda Am J Clin Pathol ; Glandular lesions of the cervix on thin-layer Pap tests. Validity of cytologic criteria used in identifying significant lesions. Incidence and clinical significance of normal endometrial cells in patients 40 years and older abstract.

Chapter 5 : Pathology of Endometrial Hyperplasia and Carcinoma | Obgyn Key

Endometrial hyperplasia. Endometrial hyperplasia is defined by the World Health Organization (WHO) classification as a spectrum of morphologic alterations ranging from benign changes to premalignant disease, caused by an abnormal hormonal environment.

Most endometrial carcinomas maintain endometrioid differentiation; these also can contain areas of mucinous or squamous differentiation. Other nonendometrioid subtypes seen in routine practice include clear cell carcinoma, papillary serous carcinoma, and other rare variants. Tumor grading is of greater independent prognostic value for endometrioid endometrial adenocarcinoma and its related types i. Papillary serous and clear cell cancers do not show the grade-dependent changes in aggressiveness seen with the endometrioid tumors; instead, as a group they are consistently aggressive. Division of endometrial adenocarcinomas into the clinicopathologic classes of endometrioid and nonendometrioid types is paralleled further by differences in epidemiologic risk factors and precursor lesions. It has traditionally been suggested that endometrioid endometrial adenocarcinoma is preceded by endometrial hyperplasia EH. These do not cleanly correspond to four distinctive biologic categories, nor are there comparable numbers of clinical interventions individually matched to each hyperplasia subtype. A contraction of the number of categories to three was suggested by merging all atypical hyperplasia AH groups into one diagnostic category atypical endometrial hyperplasia which contained the highest endometrial cancer risk. New data that have emerged in the last decade have changed the underlying assumptions upon which endometrial precancer diagnosis is constructed. Endocrine induced endometrial changes, such as those conferred by unopposed estrogens, do produce a field-wide effect that gradually changes the histologic pattern as a function of time and dose. This can be described as a dynamically changing histotype, which early on has the appearance of a disordered proliferative endometrium, and with subsequent remodeling assumes a variable gland density that we prefer to designate as the benign endometrial hyperplasia sequence. Bona fide premalignant lesions, however, are of an entirely different character. Precancerous lesions of the endometrium originate focally as a result of clonal outgrowth of genetically mutated glands which have a differing cytologic and architectural pattern relative to the background. EIN is not synonymous with carcinoma but indicates a lesion that may regress, persist, or progress to invasion. Approximately one third of women diagnosed with EIN will have a concurrent carcinoma diagnosed within the first year, and the long term cancer risk is 45 times increased beyond benign endometrial hyperplasia. Even when present in the patient, myoinvasion is rarely evident in an endometrial curettage or biopsy, which rarely succeeds in sampling the underlying myometrium. For this reason, distinction between EIN and adenocarcinoma must commonly be performed in isolated endometrial samples devoid of myometrium. EIN lesions are made up of aggregates of individual glands which may have some branch points, but lack the complex folded sheets that produce a maze of interconnected lumens or villoglandular architecture in some carcinomas. Functional changes which correspond to malignant behavior in vivo include loss of anchorage dependent growth. The histologic equivalent of this feature is growth of epithelial cells without a requirement for contact with a basement membrane. This is evident histologically by areas of solid epithelial growth without lumen formation or a cribriform pattern of multiple gland lumens within a single gland. The presence of myoinvasion, or any one of the above described patterns solid, cribriform, villoglandular, maze-like , is diagnostic of adenocarcinoma. In contrast, EIN is a clonal proliferation of abnormal endometrial glands which arises at a point in space and spreads peripherally, eventually involving the entire endometrial compartment in approximately a quarter of women at the time of initial EIN diagnosis. The diagnostic, nomenclature, and therapeutic distinctions between these processes are projected into the EIN diagnosis schema which is described below. This is intended to replace, rather than supplement, older classification using the WHO hyperplasia standards. Below we review the expanded evidence base for revised criteria, and summarize diagnostic implemetation strategies. Topography of hormonal and neoplastic endometrial disease. The diffuse field-wide endometrial effects of unopposed estrogens in benign endometrial hyperplasia are randomly scattered throughout the endometrial compartment

and include cysts, and locally variable gland density. EIN lesions arise through local proliferation of genetically mutated glands which are characterized by an altered cytology and gland area exceeding stromal area. Adenocarcinoma has a similar clonal origin often within a pre-existing EIN lesion but with solid, cribriform, or maze-like architecture. With time, EIN and adenocarcinoma lesions can expand to occupy the entire endometrial compartment and thus no longer retain their earlier localizing character. Endometrial precancers first were identified as premalignant lesions by virtue of their temporal and spatial association with cancer in large patient series. A low precancer-to-cancer progression efficiency predicts that most premalignant lesions will never display a malignant end point. Further difficulty in standardizing diagnosis of endometrial precancers comes from poor reproducibility by pathologists of histopathologic criteria used for lesion classification. Even if such a laboratory approach were impractical for everyday use, it would constitute a powerful tool for critical evaluation and refinement of current histologic diagnostic practices. Initiation of carcinogenesis is accompanied by clonal expansion of a mutated cell, which subseqently undergoes additional mutation to generate new subclones with malignant behavior. The clonal expansion of mutated cells at each step is what generates a sufficient burden of abnormal glands to be seen by a pathologist. Monoclonal growth and mutation of tumor-suppressor genes are measurable features of the premalignant phase of endometrial tumorigenesis that can be directly ascertained in paraffin-embedded tissues and correlated with histology on a case-by-case basis. The idea that endometrial precancers are monoclonal proliferative products of a single transformed cell is based on a multistep model of tumorigenesis 16 in which progression is driven by sequentially acquired mutations manifest as altered morphology and increasing aggressiveness. Although initial stages may not show an invasive phenotype, it is anticipated that premalignant lesions have sufficient growth advantage relative to their source tissues that they expand monoclonally. This expansion has now been shown to be the case for putative endometrial precancers using a variety of polymerase chain reaction-based molecular genetic methodologies applied to DNA isolated from targeted regions of paraffin sections: Early stages of carcinogenesis are characterized by incremental growth advantages, which are necessarily small in relation to normal tissues and exquisitely sensitive to environmental modification. Hormonally mediated selection 20 of latent transformed clones is one mechanism that might link genetic and endocrine events in genesis of this disease. This selection may occur through changes in precancer clone proliferation rates or remodeling of adjacent normal tissues. In the case of precancers confined to the functionalis, persistence is enhanced by absence of regular shedding anovulation. Shedding is also a key part of progestin therapy for precancers because patients who have biopsies before a withdrawal bleed often have persistent lesions, albeit with an altered cytology. For this reason, repeat biopsy for confirmation of postprogestin precancer ablation is best accomplished after a withdrawal bleed to realize the full benefit of shedding and to avoid the confounding effects of progestins on histopathology interpretation. In cases that do have an associated carcinoma, conservation of acquired genetic changes between matched premalignant and malignant tissues has provided a highly specific basis to conclude evolution from the former to the latter. Detailed lineage reconstruction, including hierarchical ordering of steps from precancer to cancer, has been accomplished in cases in which the repertoire of informative genetic markers is sufficiently rich. Disordered proliferative endometrium has scattered cystically dilated glands but a low gland density overall. Randomly distributed glands may have tubal metaplasia, and fibrin thrombi can cause microinfarcts with symptomatic bleeding. With additional duration of estrogen exposure, gland remodeling and expansion can lead to a higher gland density overall. Although the same underlying process as the less severe disordered proliferative endometrium, this is an example of benign endometrial hyperplasia. Crowded glands have not undergone any coordinated cytological change. A tight cluster of cytologically altered glands comprises the EIN lesion in this oriented section. Residual normal glands are visible on the right aspect of the endometrium. Note the change in cytology between the neoplastic glands left and background endometrium right. Endometrial adenocarcinoma, endometrioid type, well differentiated. Unlike the EIN lesion above, the glands are no longer visible individually, but are arranged as folded villoglandular sheets.

Chapter 6 : Endometrial hyperplasia - Libre Pathology

DOWNLOAD PDF CYTOPATHOLOGY OF ENDOMETRIAL HYPERPLASIAS

The Spectrum of Non-Atypical Endometrial Hyperplasias. Non-atypical endometrial hyperplasia is a spectrum of hormonally induced pan-endometrial changes, characterized by increased gland density and variation in gland size and shape.

Chapter 7 : Endometrial Hyperplasia and Neoplasia: Definition, Diagnosis, and Management Principles | G

Cytologic Diagnosis of Endometrial Carcinoma and Hyperplasias positive or suspect cervicovaginal cytology report. The women were divided into two groups: A.

Chapter 8 : [Thin-layer cytology in endometrial diagnosis] | Read by QxMD

The aim of this study was to evaluate liquid-based endometrial cytology to manage endometrial polyps in postmenopausal age by its ability to exclude hidden premalignant and malignant changes within polyps.

Chapter 9 : Papers with the keyword Endometrial liquid-based cytology (Page 4) | Read by QxMD

Abstract: Abnormal uterine bleeding is common gynaecologic complaint. Causes may vary with age, the most worrisome cause is malignancy of endometrium. No widely accepted screening test for endometrial carcinoma exists, but cervical cytology has been found to be of some use in detecting endometrial diseases.