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Original Research Article

Uncommon Gynecological Pathologies We Had Encountered - A Histopathological Potpourri

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ABSTRACT

Background: Gynecological surgeries are done for both benign and malignant conditions involving the uterus, cervix, tubes, ovaries, vagina and vulva. Very few rare entities are seen in the gynaecopathological practice.
Aim: To analyze the uncommon benign and malignant entities diagnosed in the gynecological specimens.
Materials and Methods: During our one year study period, all the gynecological specimens were retrieved from the records. Rarely encountered specimens were included in our study after reanalysis. The histomorphology and the differential diagnosis are discussed.
Results: Out of 3100 gynecological specimens we received, few rare benign and malignant conditions were diagnosed. Most of them were incidental findings. The commonest presenting symptom was abdominal pain and the provisional diagnosis was leiomyoma in most of the cases. Ten interesting cases were diagnosed during our study period. Brief review of literature and differential diagnosis of these rare entities are discussed.
Conclusion: Rare entities like pure lipomatous lesion of the uterus and adenocarcinoma of mammary gland like arising from hidradenoma papilliferum were encountered during our study period. Diagnostic criteria's of these rare tumors and the review of literature gave us a true learning experience.

Key words: Stromal tumor, Polyp, Apocrine carcinoma, Lipoma.

INTRODUCTION

Among the gynecological surgeries, hysterectomy is the most common surgery performed in the world. The first subtotal hysterectomy was performed by Charles Clay in Manchester, England in 1843 and first total abdominal hysterectomy in 1929. [1] Hysterectomy is performed for abdominal pain, abnormal bleeding, persistent chronic cervicitis, prolapse uterus and for gynecological malignant tumors. [2] Leiomyoma is the commonest entity that is diagnosed among the gynecological specimens. [3-5] Few cases deserve special mention as they are rarely encountered in the gynaecopathological practice. Rare specimens are analyzed and the literatures are reviewed with the learning objective.

MATERIALS AND METHODS

During our one year study period all the gynecological specimens were collected from the records. 3110 gynecological specimens were received during our study period and the rarely encountered tumors were searched and reanalyzed. We had encountered ten rare cases during this one year period. Relevant case history was

taken. Both gross and microscopic reevaluation was done by a panel of pathologists. Literatures were reviewed to establish their rarity and differential diagnosis and markers if relevant were analyzed. Incidence of these rare cases in our setup was calculated.

RESULTS

Relevant case history, gross and microscopic findings are enumerated.

Case1: A sixty year old female came with abdominal pain. Routine investigations were within normal limits. Ultrasound was done and she was diagnosed as having leiomyoma. Hysterectomy was done and the specimen was sent to us for histopathology.

Gross: Hysterectomy specimen we received measured 9x7x5cm. Uterine cavity was compressed by a yellow tumor measuring five centimeter in diameter in the myometrium. The tumor was greasy to cut [Fig 1].

Fig 1: Showa greasy yellow mass measuring 5cm in diameter in the myometrium.

Microscopy: The endometrium was compressed and atrophic and in the myometrium there was a well circumcised mass composed of mature fat cells arranged in lobules. There were neither atypia nor pleomorphism. [Fig2]. It was diagnosed as lipoma of the uterus.

Case2: A fifty four year old female had abdominal pain and distension. She was diagnosed as having leiomyoma in the ultrasound. Hysterectomy was done and sent to our lab.

Gross: Hysterectomy specimen measured 11x9x7cm. On cut surface endometrium was unremarkable and the myometrium showed a tumor measuring 6cm in diameter. On cut surface it was grey white with focal grey yellow areas. [Fig3]

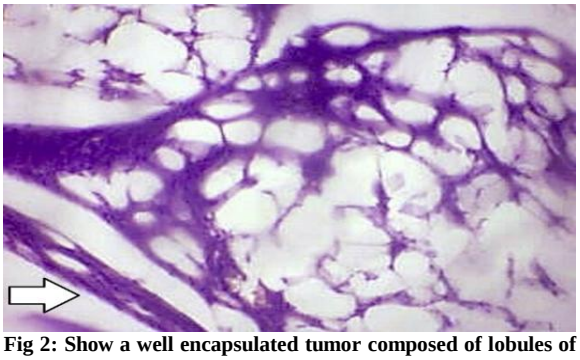

Fig 2: Show a well encapsulated tumor composed of lobules of mature adipocytes. Myometrium is seen in the periphery [arrow]. - Lipoma of the uterus [40x H&E].

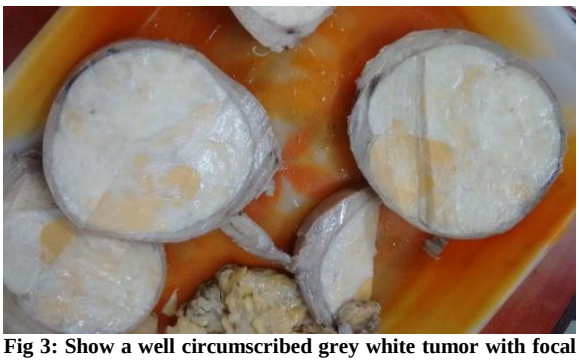

Fig 3: Show a well circumscribed grey white tumor with focal yellow areas in the myometrium.

Microscopy: Sections studied from the uterus showed proliferative endometrium. Sections studied from the myometrium showed a tumor composed of interdigitating fascicles of smooth muscles and scattered among them were adipocytes. Hyaline degeneration was also noted [Fig 4]. It was diagnosed as a case of lipoleiomyoma.

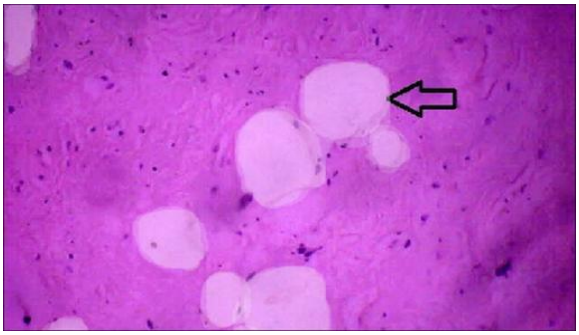

Fig 4: Show smooth muscle fibers arranged in fascicles intermixed with mature adipocytes [black arrow] [40x H&E] - Lipoleiomyoma

Case 3: A thirty four year old female had a chronic lower abdominal pain and white discharge. On investigation she had a mass in the uterine adnexa and was diagnosed as

ovarian mass. Hysterectomy specimen and the peritoneal biopsies were sent to us.

Gross: Uterus and cervix were grossly normal. The fimbrial end of one of the tube showed a grey white mass measuring 4x3x2cm.The other tube and the peritoneum was normal.

Microscopy: Sections studied from the uterus was unremarkable. Sections studied from one of the tube's fimbrial end showed caseating granulomas and many langhans type of multinucleated giant cells. The tubal epithelium was ulcerated. [Fig 5] The diagnosis was caseating granulomas probably of tuberculous origin. AFB stainig show many bacilli confirming the diagnosis. The peritoneum and the other tube were not involved. And there were no other organ nor nodal involvement. Hence the diagnosis of unilateral primary tuberculous salpingitis was made.

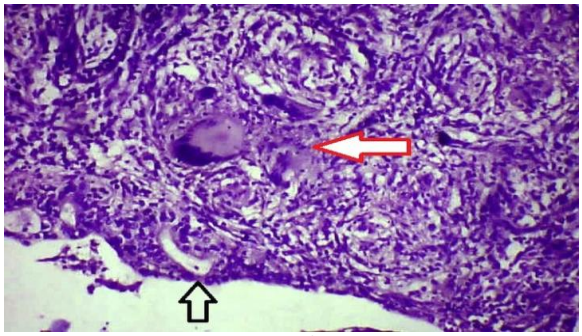

Fig 5: Show serous epithelium of the tube [black arrow] and the stroma shows Langhans giant cell and granuloma [red arrow] [40x H&E]

Case 4: A forty year old female with the complaints of abdominal pain and abnormal uterine bleeding was investigated and diagnosed as having a fleshy growth in the endometrium in the ultrasound. She was on tamoxifen for breast carcinoma since two months. Hysterectomy specimen was sent for evaluation.

Gross: Uterus and cervix measured 10x8x6cm. On cut surface the uterus showed a large fleshy polypoidal lesion measuring 6x5cm extending up to the internal os. On cut surface it was grey white and soft.

Microscopy: Sections studied from the uterus showed a polyp consisting of multiple dilated, stag horn shaped glands oriented along the long axis. The stroma was edematous, showed myxoid degeneration and thickened blood vessels. The endometrial glands showed no epithelial hyperplasia, dysplasia nor malignancy. The diagnosis was tamoxifen induced endometrial polyp [Fig 6].

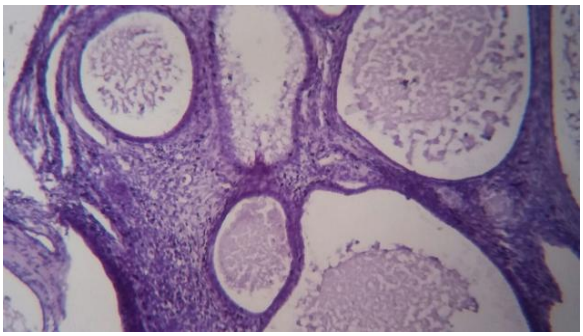

Fig 6: Show multiple dilated stag horn shaped glands and periglandular stromal proliferation- Tamoxifen induced changes [40x H&E].

Case 5 and 6: A sixty year old female and a fifty year old female had abdominal pain. Hysterectomy and bilateral salphingo-oopherctomy was done suspecting leiomyoma.

Gross: Uterus from both the specimen was unremarkable. The ovaries measured 6cm and 5cm in diameter respectively. On cut surface the ovaries were grey white and firm. [Fig7]

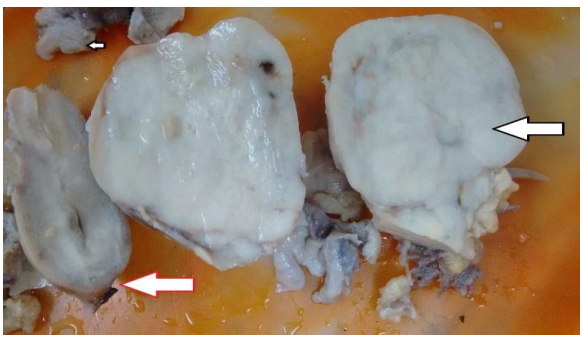

Fig 7: Shows atrophic uterus [red arrow] and the ovarian tumor measuring 5cm in diameter [Large black arrow]. On cut surface tumor were grey white and firm. The other ovary [small arrow] was normal.

Microscopy: Sections studied from the ovaries show replacement of the ovarian parenchyma by a fibrous tumor composed of fascicles of bland spindle shaped cells. There were no mitosis, atypia/ pleomorphism. [Fig 8] The diagnosis was fibroma of the ovary.

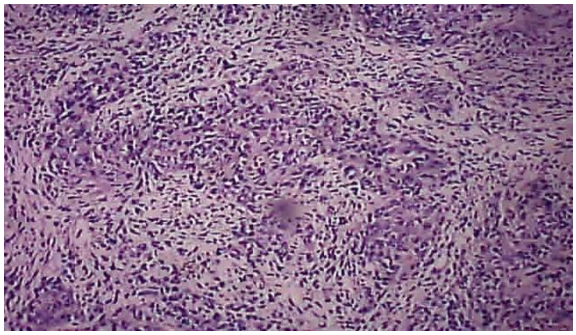

Fig 8: Shows a benign fibrous tumor arranged in fascicles completely replacing the ovary [10x H&E] – Fibroma of the ovary

Case 7: A thirty three year old female had fullness in her stomach and abdominal pain. The ultrasound diagnosis was ovarian tumor. Hysterectomy with bilateral salpingo-oophorectomy was sent.
Gross: Uterus was unremarkable. The ovary measured 6x5x4cm and on cut surface showed a grey yellow mass. [Fig 9]

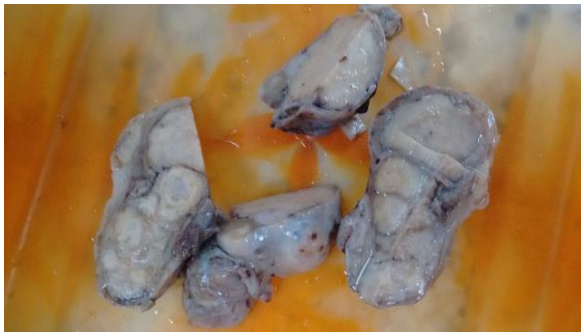

Fig 9: Show an ovary completely replaced by grey yellow and firm tumor.

Microscopy: Sections studied from the ovary showed a tumor composed of cells with abundant eosinophilic cytoplasm and round to oval nuclei. Areas of calcification were also seen. There was neither atypia nor pleomorphism seen. [Fig 10] The diagnosis was luteinized the coma of the ovary.

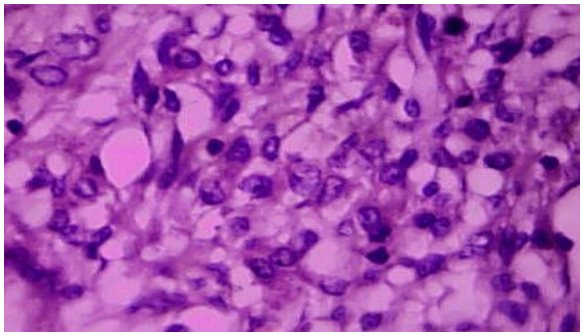

Fig 10: Shows a tumor composed of cells with vacuolated cytoplasm and round nuclei [40x H&E] – Luteinized the coma.

Case 8: A fifty four year old female had abdominal pain and hysterectomy was done with the diagnosis was leiomyoma.
Gross: Uterus and one ovary were unremarkable. The other ovary measured 5x4x3cm and showed a solid and cystic mass on cut surface. [Fig 11]

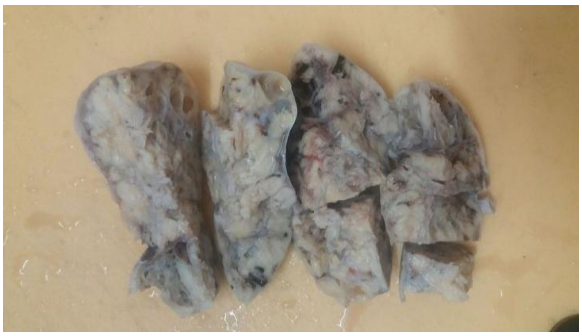

Fig 11: Show entire ovary replaced by a solid and cystic tumor

Microscopy: Sections studied from the ovary showed a tumor composed of uniform cells arranged in sheets. Focal areas showed Call Exner bodies. Individual cells showed scanty cytoplasm and nuclear grooving. [Fig 12] The diagnosis was granulosa tumor of the ovary.

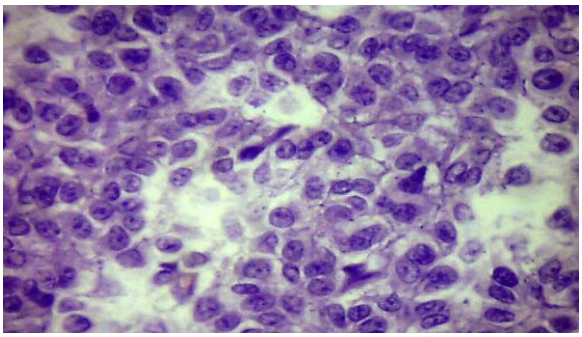

Fig 12: Shows Call Exner bodies composed of cells exhibiting nuclear grooving [40x H&E] - Granulosa tumor.

Case 9: A fifty year old female had a mass in the vulva. A biopsy of the lesion was sent. On microscopy the tumor showed abundant eosinophilic cytoplasm, dispersed nuclear chromatin with prominent nucleoli and marked pleomorphism. A provisional diagnosis of malignancy was given and later wide local excision was sent for analysis.
Gross: Vulvectomy specimen was received measured 6x5x4cm.Skin was intact and on cut surface the tumor was in deep dermis, grey white infiltrating and measured 3x3x2cm with an all-around clearance ranging from 2-3cm. [Fig 13]

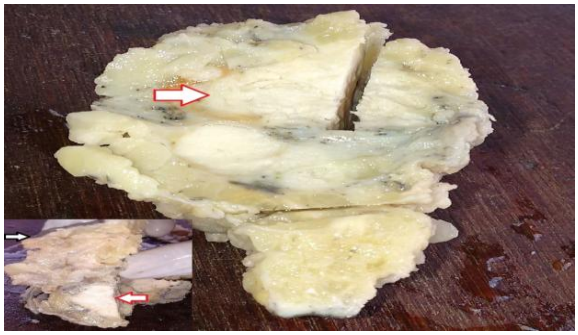

Fig 13: Shows Vulvectomy specimen with a skin [Black arrow] and a grey white tumor [Red arrow] in the dermis.

Microscopy: Sections studied from the tumor showed skin and the dermis showed benign hidradenoma area and its transition into a malignant tumor. The individual cells had abundant eosinophilic cytoplasm and exhibited marked nuclear atypia and pleomorphism arranged in glandular, tubular pattern and in sheets. [Fig 14& 15] The diagnosis was mammary type adenocarcinoma arising from hidradenoma papilliferum.

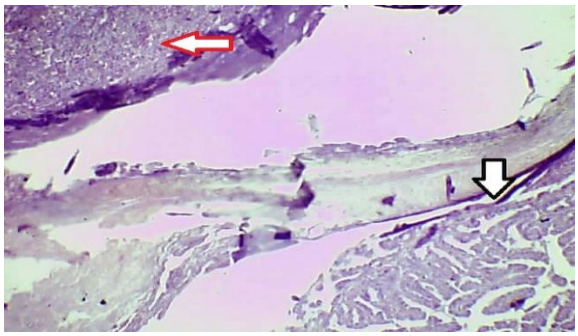

Fig 14: Shows benign hidradenoma papilliferum area[Black arrow] and malignant adeocarcinoma area[Red arrow].[4x H&E]

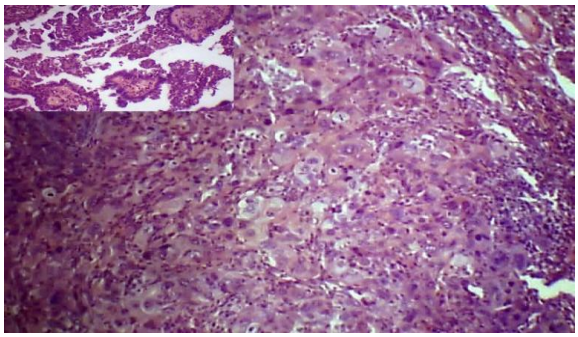

Fig 15: Show malignant epithelial cells arranged in sheets. Individual cells show abundant eosinophilic cytoplasm, vesicular nuclei and prominent nucleoli [40x H&E] Inset show benign hidradenoma area [40x H&E].

Case 10: 35 year old female was evaluated for her abdominal pain and on ultrasound uterine tumor with nodal metastasis was diagnosed. Hysterectomy specimen, peritoneal biopsy, ascitic fluid along with cervical nodes was sent for evaluation.

Gross: Hysterectomy specimen we received measured 9x8x7cm. On cut surface the endometrial cavity was dilated and showed a polypoidal homogenous white mass measuring 5x4x3cm, extending up to the os and invading the myometrium grossly. Ovaries and peritoneal samples were unremarkable grossly. Out of the three nodes we had received, one node was enlarged and was homogenous white. [Fig 16]

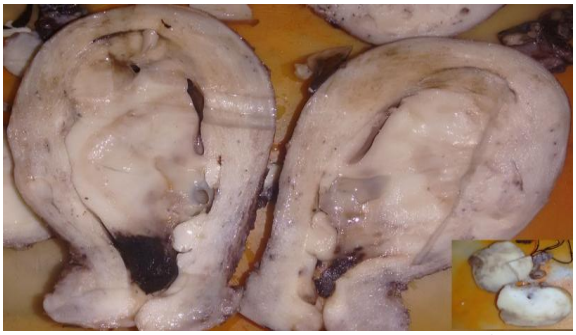

Fig 16: A polypoidal homogenous grey white mass filling the endometrial cavity and extending up to the cervical os. Inset shows cervical node involved by the tumor.

Microscopy: The endometrium was completely replaced by tumor tissue consisting of uniform bland cells with oval nuclei, dispersed chromatin arranged in sheets and infiltrating the myometrium in a tongue like fashion. Many capillary sized blood vessels were seen among the tumor cells. Mitosis was 2/10 high power field. [Fig 17] Out of the three cervical nodes sent, one showed metastatic deposits from the endometrial tumor. The peritoneal biopsy was unremarkable. Smear studied from the ascitic fluid was hemorrhagic and showed tumor cells arranged in sheets. [Fig 18] The diagnosis was endometrial stromal sarcoma- Low grade with metastatic deposits in a cervical node and ascitic fluid was positive for malignancy.

When the incidence of these tumors was calculated, almost all the tumors included in our study except ovarian fibroma had an incidence of 0.003% proving their rarity [Table1].

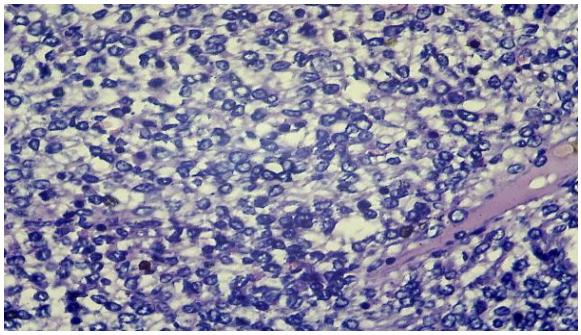

Fig 17: Shows uniform bland oval shaped cells arranged in sheets - Endometrial stromal sarcoma [40x H&E].

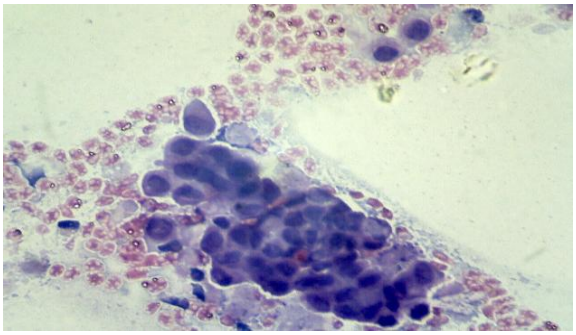

Fig 18: Shows deposits from the endometrial stromal sarcoma in the ascitic fluid [40x H&E].

Table 1: Incidence of these tumors encountered in our study

Name of the tumor		Incidence
Lipomatous tumor	Lipoma of the uterus	0.003%
	Lipoleiomyoma of the uterus	0.003%
Unilateral primary tuberculous salpingitis		0.003%
Tamoxifen induced endometrial polyp		0.003%
Ovarian fibroma		0.006%
Ovarian Granulosa tumor		0.003%
Mammary type adenocarcinoma arising from hidradenoma papilliferum in the vulva		0.003%
Endometrial stromal sarcoma - Low grade with metastasis to a cervical node		0.003%

DISCUSSION

Gynecological pathology encompasses a wide array of entities. Of which some are very rare in the routine practices. Awareness of these rare entities increases the diagnostic acumen of the practicing pathologists.

The lipoma of the uterus is a rare tumor with an incidence of 0.03 to 0.2%. [6-8] Lipomatous tumor may be benign - pure or mixed with other components [Lipoleiomyoma, Angiolipoma] or malignant [Liposarcoma]. It was first described by Lopstein in the year 1816. [9] It is common in postmenopausal women. [10] Uterine bleeding and abdominal pain are the most common presenting symptoms. Theories that were proposed for the origin of the lipoma in the uterine wall include migration of adipose cells through the uterine arteries, mesenchymal remnant of a pluripotential stem cell or from the metaplasia of the uterine smooth muscle. [11-13] Diagnosis of purelipoma of the uterus should be made when the smooth muscle cells are confined to the periphery of the tumor. [14] Fat cells are immunoreactive for vimentin, desmin and actin [smooth muscle markers]. [15] Direct transformation of the fat cells from smooth muscle cells may be the reason for this immuno reactivity. Differential diagnosis include mixed lipomatous tumor, liposarcoma component of carcinosarcoma or lipoma may be a part of ovarian teratoma. Absence of other component ruled out mixed lipomatous tumor. Absence of atypia and other malignant epithelial component ruled out carcinosarcoma. Ovarian teratoma also has other components like squamous epithelium, adnexal structures to name a few and it was also ruled out confirming the diagnosis of pure lipoma of the uterus. The incidence of pure lipoma of the uterus in our study was 0.003% in correlation with others studies. [6-8]

Lipoleiomyoma is most common among the lipomatous tumor of the uterus. [16] Lipoleiomyoma was first described by Meis and Enzinger in 1991. It is common in obese postmenopausal women. [17] It is an asymptomatic tumor. Inclusion of the fat cells in the uterine wall during surgery and fatty degeneration of the connective tissue were the theories proposed for the origin of these tumors. [18] Malignant transformation in uterine lipoleiomyoma was reported in the literature. [18] Surgery is curative.

Genital tract tuberculosis constitutes about nine percent of all the extra-pulmonary tuberculosis. [19] The prevalence of genital tuberculosis in the female is 1-2%. [20] The

mean age incidence is 20-40 years. It is commonly asymptomatic. If symptomatic, the presenting symptoms include infertility, amenorrhea, menorrhagia, abdominal pain and dyspareunia. It is incidentally diagnosed during the investigations for infertility. Morgagni was the first to describe the signs of female genital tuberculosis infection. [21] Unilateral primary tubal tuberculous infection is very rare. Criteria to diagnose primary genital tuberculosis include: No other site should be infected with tuberculosis and the genital lesions should be the first tuberculous infections and the regional lymph node should also be involved by tuberculous lesion. In the absence of a peritoneal lesion, tuberculosis of the fallopian tube is likely to be primary in origin. [22] Diagnosis is by histopathology, demonstration of the bacilli using AFB stain, fluorescent aura mine stain, culture and PCR. Culture is negative in one third of the cases. [23]

Tamoxifen is a non-steroidal ant estrogenic agent which is used as an adjunct to treat breast cancer. It also has a weak estrogenic effect leading on to various estrogen induced side effects on the female genital tract which includes estrogenic effect on the vagina, stimulate the growth of fibroid, and stimulate endometriosis, causes endometrial polyp, endometrial hyperplasia, atypical endometrial changes and carcinoma endometrium. Atypical lesions are seen when there is preexisting endometrial lesion and carcinoma is seen in postmenopausal female. [24,25] The patients may be symptomatic or asymptomatic. Grossly, the uterus is bulky and there is increased endometrial thickening. Microscopically, the polyp may be single or multiple and show periglandular proliferation of the stroma, glandular and epithelial proliferation, metaplasia, dysplasia and carcinomatous changes. The polyps are larger and consist of stag horn shaped glands arranged along the long axis with edema and myxoid change isseen in the stroma. [26,27] Low-grade endometrioid and serous carcinoma are three to four times more common following tamoxifen therapy. Follow up of these patients with hysteroscopy and endometrial sampling is necessary even in asymptomatic patients on tamoxifen.

Ovarian fibroma constitutes 4% of all ovarian tumors. [28] This tumor occurs in the perimenopausal women. [29] Usually asymptomatic, ovarian fibroma can cause abdominal pain due to torsion. 90% of ovarian fibromas are unilateral. It is associated with two syndromes- Gorlin and Meig. Bilateral, nodular and calcified ovarian fibroma is associated with Gorlin syndrome. [28] In Meigs syndrome, ovarian fibroma is associated with hydrothorax and ascites. This syndrome is observed with 1-10% of ovarian fibromas. Most of the tumor is solid and firm and have grey white cut surface. Cyst formation is also seen. Microscopically, this tumor show intersecting fascicles or a storiform arrangement of bland spindle cells with ovoid to elongated nuclei. Cellular variant is also noted. It shows diffuse vimentin, WT-1 and CD56 positivity. [30] It is a benign neoplasm and treated with surgical excision.

The coma is very rare and the incidence is about 1% of solid ovarian tumors. [31] It is common among postmenopausal female. The symptomatology includes vaginal bleeding, symptoms related to estrogen secretion and virilizing symptoms related to androgen excess. Luteinized the coma is associated with androgenic excess. It is a solid grey yellow tumor. Microscopically this tumor show sheets and nests of ovoid to spindle cells with round to oval nuclei, inconspicuous nucleoli, abundant pale or vacuolated cytoplasm with indistinct cellular borders. [32] Reticulin stains the individual cells. Inhibin, calretinin, CD10, and vimentin are positive in the coma. [30] They are benign neoplasm and surgery is the treatment of choice.

There are two types of granulosa tumor - Adult and Juvenile. Adult granulosa tumor is common in peri and postmenopausal women. It is an estrogen producing, solid and cystic tumor.

Unilateral involvement of the ovary is common. Microscopically, variable growth patterns such as diffuse sheets, trabecular, insular, tubular, corded, micro follicular; macro follicular and watered silk are seen. Call Exner bodies that ismicrofollicle filled with eosinophilic basement membrane material is seen in this tumor. The tumor cells have scant cytoplasm, angulated nuclei and have nuclear grooves [coffee bean]. [33] Juvenile granulosa cell tumor is common in the first three decades and presents with hyper estrogenic symptoms. [34] It is associated with Maffuci syndrome and Ollier disease. [34] It is unilateral grey yellow or tan colored tumor. Microscopically, the tumor exhibits follicle like spaces lined by cells with hyperchromatic non grooved cells and filled with eosinophilic material. The cytoplasm is abundant eosinophilic to vacuolated. Increase in mitosis and atypia is noted in this type. This tumor is inhibin and calretinin positive. This is a benign tumor with good prognosis. Recurrence is seen in adult granulosa tumors.

Hidradenoma papilliferum is a benign tumor arising from specialized anogenital mammary-like sweatgland. [35,36] Hidradenoma papilliferum is composed of numerous tubules and acini linedby a single or double layer of cuboidal cells and outer myoepithelial cells. Intraductal carcinoma resembling mammary-type apocrine epithelium arising in hidradenomais a rare entity. [37] It was first reported in 1936 by Greene. Approximately 30 to 40 cases of adenocarcinoma of mammary-like glands were reported in the literature to date. [38] The presence of a transition zone between normal mammary-like glands and the carcinoma component is necessary to establish a diagnosis. The loss of the myoepithelial layer, nuclear pleomorphism and invasiveness are used to diagnose invasive adenocarcinoma. Histopathologically, these tumors show varied patterns. They show predominantly ductal to lobular pattern. Other patterns include mixed ductal and lobular, tubulolobular, mucinous, and adenoid cystic likes areas. The tumor exhibits an aggressive behavior, with 60% of patients having regional lymph node metastasis at the time of presentation. [39] Immuno histochemically, loss of s100, ER and PR help to differentiate benign hidradenoma from its malignant counterpart. In addition, markers like mammaglobin and gross cystic disease fluid protein 15[GCDFP15] are positive in this tumor.

Endometrial stromal sarcomas were once called as endolymphatic stromal myosis. Typicallythis tumor infiltrates the myometrium and has a tendency to permeate lymph vessels. The lymphovascular invasion can be seen grossly as a yellow ropy mass. The risk of nodal metastases ranges from 0% to 44%. [40] Endometrial stromal sarcoma is divided into low grade and high grade based on the mitotic figure [<10/ 10 high power field or more than10]. [41] The size of the tumor, mitotic figures and extension of the tumor are the prognostic factors. Histological differential diagnosis include epithelioid variant of leiomyosarcoma. The presence of thin walled vessels, Multinodular pattern and CD10 positivity helps to differentiate endometrial stromal tumor from leiomyosarcoma. Endometrial stromal tumor has a tendency to recur and rarely metastases.

CONCLUSION

Diagnostic criteria of lipoma of the uterus, primary fimbrial tuberculosis and mammary type adenocarcinoma of the vulva turned out to be an eye opener for us. Stromal tumors of the ovary are rarely encountered and their incidence was 0.003% in our study, thus proving rarity. Very few cases of mammary type adenocarcinoma arising from hidradenoma papilliferum had been reported so far. One such case is documented in our study.

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