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RESEARCH ARTICLE

LOW GRADE ENDOMETRIAL STROMAL SARCOMA PRESENTING AS INFECTED POLYP

[1]Dr. Krishnamma, B.S. and [2,*]Dr. Suryaprabha, V.

[1]Professor of Obstetrics and Gynaecology
[2]Associate professor of Obstetrics and Gynaecology, NRI Institute of Medical sciences, Tagarapuvalasa

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Corresponding author:

ABSTRACT

A 60 yr old post menopausal woman came to Gynaecology OPD with complaints of Bleeding per vagina of 1month duration and H/o of intermittent low grade fever of 4 days. She was changing 4– 5 pads per day, associated with clots, not associated with dysmenorrhoea ,no white discharge , no burning micturition , no retention of urine or no recent loss of weight. She had loss of appetite for the past 10 days. She attained menopause 4 years back. She was anemic and emaciated. Per abdomen there is a mass of 14 weeks size, in lower abdomen , firm, uniformly enlarged, lower border could not be made out. On speculum examination a large necrotic fungating mass covered with slough & purulent foul smelling discharge occupying whole of vagina was found. Finger could be passed around the mass and assumed that the mass could be arising from the body of uterus. Cervix felt separately from growth. On Per rectal examination PV findings were confirmed, rectal mucosa is free. A provisional diagnosis of Infected Polyp was made with suspicion of malignancy. Usually any mass arising from uterus or cervix at this age clinically gives a suspicion of malignancy. Fibroid polyp may arise from body of the uterus or from the cervix. Sub mucous fibroid extrudes into uterine cavity. During this process a broad pedicle forms when it is attached to fundus of uterus. She was admitted in the hospital for confirmation of diagnosis, investigations and further management. Surgical profile was done and found to be anemic which was corrected by three blood transfusions and infection by systemic antibiotics. Retention of urine was treated by continuous bladder drainage. Findings of Ultrasonography and MRI suggested that the mass is benign. Intra operatively also there was no suspicion of malignancy in staging Laparotomy as there were no secondary lesions in Ileo- ceacal junction, liver, under diaphragm and Para-aortic lymphnodes , no free fluid and adnexae were normal. H.P.E report only showed Low grade Endometrial stromal sarcoma. Pathologist advised Immuno – Histochemical studies which was in favour of Endometrial stromal sarcoma. The main reason for presentation of this case is to emphasize on staging laparotomy, when ever a case with such a large polyp with sloughing and infection presents to out-patient department with high index of suspicion of malignancy. Early diagnosis of secondaries has to be kept in mind. To emphasize the need of oncoprotein immunohistochemical staining studies to differentiate Leio-myo sacroma, Endometrial stromal sarcoma, Vascular tumor.

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INTRODUCTION

Fibroids are the most common benign tumors encountered in Gynaecology out patient department. They may arise from the serosal layer (or) Intramural region (or) from the Endometrium . Fibroids arising from the endometrium will present as polyps. Sub-mucous fibroid extrudes in to uterine cavity. Uterine polyps are usually benign comprising endometrial fibroid. Adeno myomatous cervical polyps are mucous and Fibro Adenomatous polyps arise from Endo-cervix. Endometrial polyps mostly arise from hyperplasia of endometrium. They may be single (or) multiple appear as pink swellings with pedicle. Secondary malignant changes may occur in a benign polyp and it is mandatory to study it's histology and Immuno-histochemistry studies.

Some of the complications may arise in polyp. Infection is a common complication in sub-mucous & myomatous polyps. They project into the cervical canal or into the vagina. Infected polyp causes blood stained purulent discharge. Inversion of uterus may also occur in long standing cases moderately large and large sub-mucous fundal fibroids.

Case History: A 60 year old lady came to gynaecology OPD with complaints of fever since 4 days which is on & off , not Associated with chills and rigors . No history of evening rise of temperature. Bleeding per vagina since 1 month , changing 4 – 5 pads per day, associated with clots not associated with dysmenorrhoea, no history of recent loss of weight, no white

discharge or burning micturition. No history of retention of urine. She had loss of appetite for the past 10 days. She attained menopause 4 years back. Her marital life was 42 years, she is Nulliparous. she had similar complaint of bleeding per vagina six months back and underwent medical treatment and relieved. She takes mixed diet. Her bowel and bladder habits are normal. She is a chronic smoker from childhood. No history of Tuberculosis; Epilepsy; Asthma; Thyroid abnormalities. She is non-diabetic and non-hypertensive. On general examination the patient is ill-built and ill nourished. She looks pale, no icterus, no cyanosis, no clubbing , no generalized lymphadenopathy, no pedal edema. Her vitals were stable, pulse rate – 72 B/pm; Bp – 90/70 mmHg CVS examination – Heart sounds (S S_2 heard) Bilateral lungs clear; no focal neurological deficit. Thyroid examination normal; breast – normal, spine – normal.

Per abdomen on inspection, fullness in lower abdomen (Fig-2 a), all quadrants moving equally with respiration, no engorged veins; no visible pulsations, no scars or sinuses. On palpation, a mass of 12 – 14 weeks size is palpable in lower abdomen; firm in consistency; lower border, could not be made out. May be arising from uterus .Rest of the abdomen is soft, no other organomegaly. On per speculum examination a large necrotic fungating mass is seen extending up to introitus, covered with necrotic tissue and slough, purulent foul smelling discharge and no active bleeding. Mass is protruding through external cervical os. Finger could be passed around the cervix and assumed that the mass could be arising from the body of uterus. Cervix felt separately from growth. On Per rectal examination PV findings were confirmed, rectal mucosa is free. A provisional diagnosis of Infected Fibroid polyp is made with suspicion of malignancy. She was admitted in the hospital for confirmation of diagnosis, investigations and further management.

Routine investigations revealed that she is having Hb% 6.9gms on admission. MCV-74.1 /L, MCH-25.8 pg, MCHC-34.8%Blood grouping and Rh- typing O Positive. T.C – 9,900 cells/cmm, D.CP80%, L11%, E 0%B 07% ;ESR :60mm/1hr.HIV &HBsAg Negative. Blood urea 15mgs% and Serum creatinine 0.5%, Serum Electrolytes-Na-130mmol/L,k-3.4mmol/L, Cl-96mmol/L., Random blood sugar -72mgs/dl, FBS-104mgs/dl, PPBS-124mgs/dl, Urine-alb and sugar-nil. Urine for C/S was sent. Escherichia coli isolated (> 1,00,000 cfu/ml) in culture.(ESBL Producer). Treatment given as per sensitivity. Patient's anemia was corrected with 3 PRBC transfusions preoperatively.2D-Echo,X-Ray chest were normal.
Ultra sonography of complete abdomen showed normal Liver and Spleen, Uterus bulky, 117x45x80mms, Endometrial thickness 3mms, an ill defined, cervical single occupying lesion is noticed measuring 74x80 umm, evaluation of internal vascular supply is normal. MRI Pelvis (Multiplanar and multisquential MRI of Pelvis has been performed.--Fig: 1a,b,c,d

FINDINGS

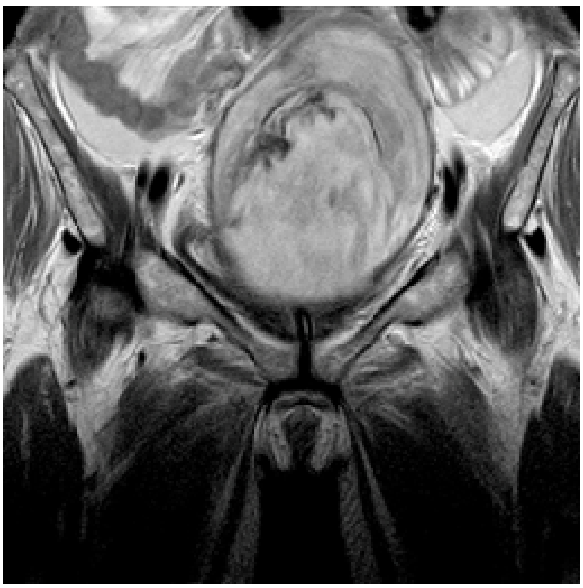
A Large well – defined T1W hypo, T2W and STIR hyper intense heterogeneous SOL noted involving cervix and lower body of uterus, measuring 9.4x9.7x15.2cm(apxtrxcc).No E/o Parametrium /pelvic wall invasion. Antero inferiorly it is compressing the posterior wall of urinary bladder. No E/o wall infiltration. Posterior fat planes with the rectum is maintained. Inferiorly it is bulging into the upper 2/3rd of vagina. No E/o enlarged regional lymph nodes. Visualized bowel loops are unremarkable. Urinary bladder– Foleys bulb seen in- situ. Minimal free fluid noted in pelvis. Free fluid noted in subcutaneous planes and intramuscular planes of pelvis. The femoral heads and acetabula are of normal shape, and the femoral heads are well covered by the acetabular are of normal shape, and the femoral heads are well covered by the acetabular margins. The joint spaces are of normal width. The bone marrow shows normal signal intensity, especially in the femoral head and neck. Both sacroiliac joint are normal.

Course in the Hospital: General condition improved by correcting anemia, hypoprotienemia .Control of infection of polyp by giving 3rd generation cephalosporines and vaginal douching and cleaning .While on treatment patient developed acute retention of urine which was treated by continuous urinary bladder drainage using Foleys catheter. Staging Laparotomy was performed and intra operatively on opening the abdomen the findings are 1) Minimal ascetic fluid in pouch of Douglas, 2)Uterus is uniformly enlarged to 12-14wks,3)Bilateral Fallopian tubes and Ovaries normal .There was a small depression at fundus of uterus where pedicle of mass is attached ? Inversion. Parametrium is free and no palpable enlarged lymphnodes. The ascitic fluid was sent for cytology. Total abdominal hysterectomy with bilateral salpingo - oophorectomy was done and specimen sent for histopathology.

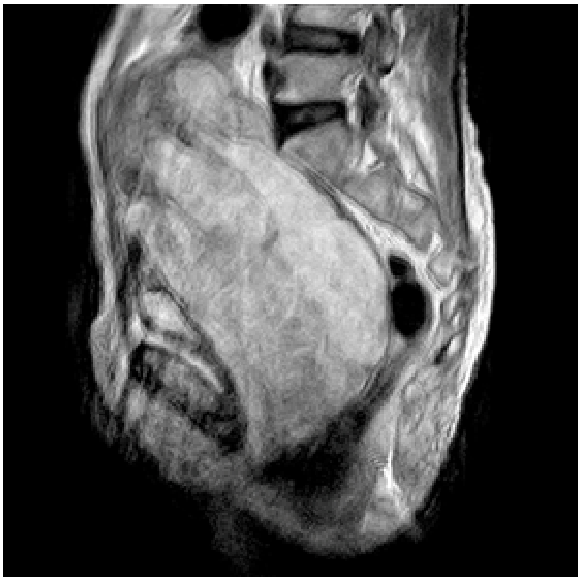
Macroscopic examination of cut section of the specimen showed a large infected polyp arising from fundus of the uterus with inversion of uterus. There were no dense adhesions between mass & uterine wall

Infected Polp Histopathology Report Of Specimens, Fig---4

- Uterus along with infected polyp
- Left unilateral ovary along with fallopian tube
- Unilateral right ovary sent for HPE.



Mass Deliniated From Uterus-A



Sagital view-B

Mass up to Vagina----D

MRI---FILMS-fiG-1a,b,c.d

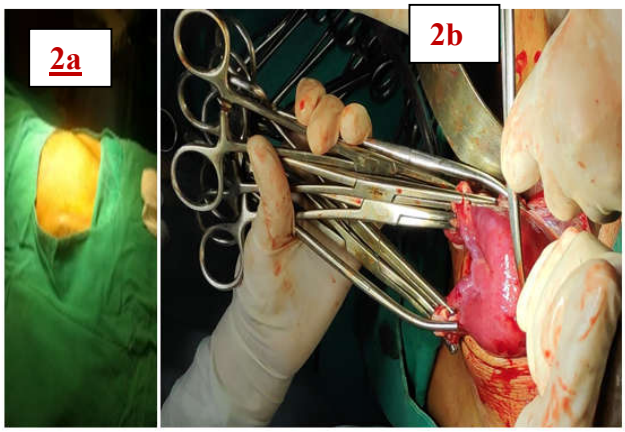


Fig. 2.

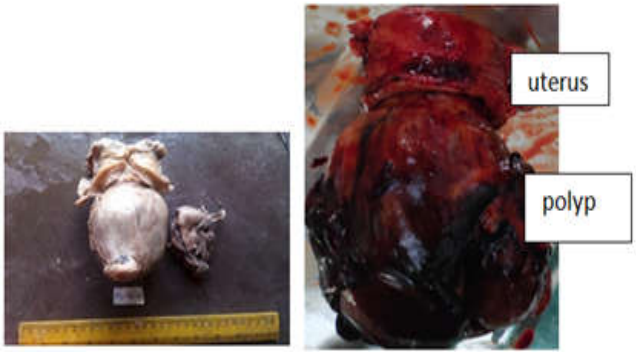
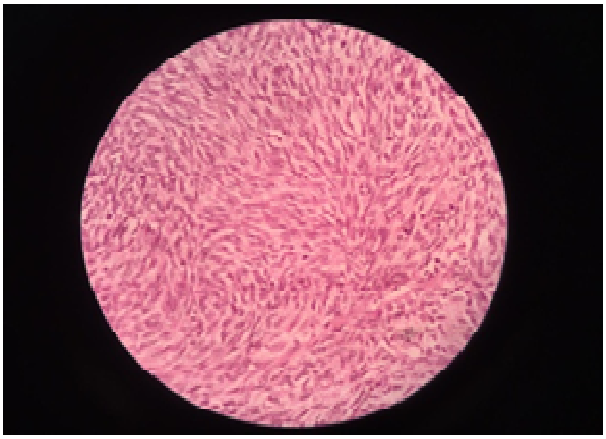


Fig. 3.

Fig. 4.-Microscopic view Herringbone appearance



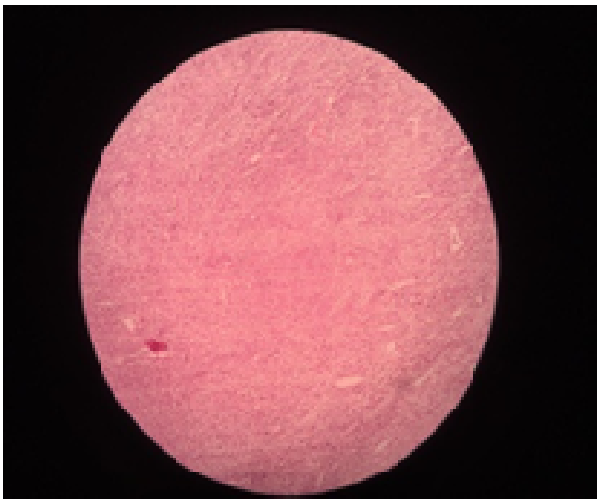


Fig-5,6. Nuclear pleomarphic features mitosis --40x highpower

Microscopic Features & Impression: Multiple sections show a poorly circumscribed infiltrating malignant lesion, composed of sheets, irregular fascicles, bundles, discretely arranged and herring bone pattern of tumor cells invading into the Myomatrium and extending upto the lower uterine segment. The cells are large pleomorphic oval to spindle with indistinct cytoplasmic borders, increased N/C ratio, large vesicular nucleus with prominent nucleoli. Mitotic rate is >15 / 10 HPF, multinucleated tumor giant cells, areas of myxoid changes, widely dispersed areas of necrosis and multiple fibrin thrombi with trapped tumor cells seen. Dispersed blood vessels with hemangio-pericytomatous pattern of arrangement are evident.

Endometrium: Proliferative phase with no evidence of tumor invasion. Sections from cervix show chronic cervicitis with no evidence of tumor invasion. Sections from specimen labeled as left fallopian tube show patent lumen with no tumor involvement. Sections from specimen labeled as right ovary show extensive foci of hyalinization with scanty ovarian stroma and foci of calcification. No evidence of malignancy. Sections from glistening mass show myxohyaline changes with entrapped tumor cell clusters.

Features are in favour of "Soft tissue sarcoma " with the following possibilities:

Leiomyosacroma 2: Endometrial stromal sarcoma 3.Vascular tumor Herringbone appearance Nuclear pleomarphic features .mitosis --40x highpower Fig-5,6. Advised IHC panels for confirmation and better evaluation. Immunohistochemical Profile

Microscopy: Microscopic picture showed sheets of spindle shaped cells with elongated nuclei. There is focal nuclear atypia. Chromatin is coarse and occasional nucleoli are prominent. Mitotic activity is 3 to 4/10 HPF. Intervening stroma is scanty but vascular.Fig—4,5.

Diagnosis: H & E slides: * Low grade, Endometrial stromal sarcoma. Vimentin: * Positive. SMA: Negative, BCL2: *Positive. Immunohistochemical profile is in favour of Endometrial stromal Sarcoma. Specimen has been processed by the HRP polymer method. Protein. Retrieval has been done by HIER technique. The following antibody Clones have been used:

- Smooth Muscle actin Clone 1A4 (SMA).
- Monoclonal mouse Anti – Human Bcl2 Oncoprotein Clone
- Monoclonal mouse Anti – Human Vimentin Clone V9.

DISCUSSION

Fibroid polyp may arise from body of the uterus or from the cervix. Sub mucous fibroid extrudes into uterine cavity. During this process a broad pedicle forms. When it is attached to fundus. As the size of the fibroid is increases, it may cause inversion & also get exposure to infection. The toxin ends of the pseudocapsule are retracted in the base of the pedicle. The uterus contracts to expel the polyp out through cervix to lie even in the vagina. It should be differential from chronic inversion, malignancy and fibroid polyp. The infected polyp will be presented with history of blood stained purulent discharge & mass per vagina as in this particular case. They also present with history of menstrual disturbances and retention of urine. The possibility of fibroid turning into sarcoma is not more than 0.28 - 0.5%. They usually come with history of pain & postmenopausal bleeding. Endometrial stromal sarcoma is a perplexing neoplasm; the tendency has been to make the diagnosis when, by the process of elimination, other mesenchymal neoplasms can be ruled out. The diagnosis of endometrial stromal sarcoma is easiest when the neoplasm arises within a polyp; the portion considered malignant usually is quite distinct from the polyp due to the greater cellularity and more prominent nuclei.

The cells are usually pleomorphic with indistinct cell borders and have a tendency to be spindle-shaped. They may have areas of decidual alteration. Larger stromal sarcomas invade the uterine wall and often there is extensive necrosis. They may extend through the uterus to adjacent tissues of the pelvis. The clinical findings in this case have not suggested the possibility of malignancy. After controlling the infection, the slough and purulent discharge decreased. MRI films showed clear demarcation between mass and uterine cavity suggesting that there is no infiltration in to myometrium. Exploration of peritoneal cavity was normal without palpable secondaries though the Histopathology report showed features in favor of soft tissue sarcoma with the possibilities of leiomyosarcoma or endometrial stromal sarcoma or vascular tumor. Apoptosis or programmed cell death is a well known fundamental feature that provides an efficient mechanism for eliminating cells, thus keeping cell numbers at constant levels in different organs. The B cell leukemia, lymphoma-2 gene (Bcl-2) was the first gene identified that inhibits apoptosis in many cell systems. A chromosomal translocation between chromosomes 7 and 17 has been identified in low-grade endometrial stromal sarcoma. These tumors can be viewed as stromal proliferations of varying degrees of malignancy: low-grade endometrial stromal sarcomas show an indolent natural history and can often be cured by appropriate surgery alone, whereas the high-grade endometrial stromal sarcomas (now commonly referred to as undifferentiated uterine sarcomas) typically have very aggressive behavior with a predilection to metastasize early and widely. Cyclical variation in Bcl-2 expression in normal endometrial glandular epithelium has been suggested. As Bcl-2 gene might increase the proliferative activity of the glandular

endometrium. it might eventually lead to the development of endometrial hyperplasia and possibly neoplasia. The apoptotic mechanism has been shown to take place due to change in the expression of the gene family controlling the apoptosis. Anti-Bcl-2 targeted therapy has been used in several tumors. vimentin is well known to be strongly positive in endometrioid adenocarcinoma of primary uterine corpus origin, and is useful in the distinction of the latter from endocervical adenocarcinomas, its expression in primary ovarian endometrioid carcinoma has not been analyzed in detail previously.

Immunohistochemical procedures have shown endometrial stromal sarcomas to be positive for S100 protein and vimentin and negative for desmin and alpha-actin. The main reason of presentation this case is to emphasize on staging laparotomy. Whenever a case with such a large polyp with sloughing and infection presents to out- patient department with high index of suspicion of malignancy has to be kept in mind. Early diagnosis of secondaries has to be kept in mind.

Need of oncoprotein immunohistochemical staining studies to differentiate Leiomyosacroma, Endometrial stromal sarcoma, Vascular tumor and also normal through complex and atypical hyperplasia into well differentiated adenocarcinoma Counseling of Patient and attendants regarding the possibility of malignancy is mandatory. It helps psychologically motivated patient and relatives to accept such circumstance. It will also reduce Medico-Legal problems.

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