

Mysteries behind the Microscope – The Last Respite ora Rude Shock?

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Abstract: The blatant fact in the field of healthcare that the market is undergoing is rapid and vast knowledge explosion. In recent decades health expectations have risen globally, with all member states of the World Health Organisation committed to Universal healthcare and globalization .As the diagnostic modalities employed in a clinical laboratory are involved in 70% of all healthcare diagnoses and in the procedures involved in the healthcare system, pathology and the clinical laboratory should also scale and reach newer heights as this is key to the growth of the entire healthcare system. This article elaborates the various problems faced by a Pathologist during Frozen sections and Routine Histopathology diagnosis when a malignancy is diagnosed without a prior suspicion of the same by the treating physician or Surgeon and the impact such a diagnosis has on the doctor and the patient¹ – A PEEK BEHIND THE PATHOLOGY DOORS.

Key words: Unexpected malignancy,Anatomic pathology.

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I. Introduction

We are also noticing the upward trend in diagnostic modalities in all fields of laboratory medicine including Anatomic Pathology.The new testing methods are directed towards personalised medicine, also known as genomic medicine as this seems to be the ultimate aim of every treating physician/Surgeon – To mount a Surgical strike to kill only the cancer cells.Just as demand for laboratory services is rising, there is downward pressure to use fewer resources. Nevertheless the health care industry warrants the uninterrupted flow of information from behind the doors of a pathology laboratory to be cost effective for the patient too which puts a Pathologists life into difficulty as the State of the art technologies that give abundant high end information necessary for the precision and personalized therapy comes with a price to pay. Pathologist needs keep the in mind that maximum information shall be provided at a lesser cost. Positive and persistent work is going on in this direction and the strong base on which this dream shall be realised is by the effective and wise use of the tissue obtained from the patients ,Hence,the details of Anatomic pathology need to be analysed systematically with a broader outlook in medicine, an opportunity to correlate his technical knowledge with the clinical aspect of each and every case, and with an intent to pursue the literature in accordance to the clinical case to be resolved.

This article highlights the importance of this vast and indepth knowledge in pathology with special emphasis on the surprises it can throw – to the Pathologist,Clinician and to the Patient and the implications thereon.A series of cases which threw unexpected surprises at a Teretiary Care Centre are discussed with the challenges faced at the time of reporting with a note on how the best possible treatment plan was devised for the patients after discussion in the MDT.

II. Materials And Methods

Patients taken up for surgery during the period 2017 May to 2019 May on the basis of a clinical diagnosis of a benign lesion of Female genital tract were included in the study.The preoperative workup,provisional diagnosis and thepost operative histopathology of the same were collected and analysed.Thepresurgical clinical diagnosis was considered as provisional diagnosis on the basis of which the treatment was planned and the patient taken up for surgery.The diagnosis made on intraoperative frozen section/post operative histopathology was taken as the final diagnosis.The concordance and discordance rates between the provisional and final diagnosis with regards to benign and malignant nature of the tumor was analysed to evaluate for the prevalence of unexpected malignancy.and the clinical profile of the unexpected malignancies.

The presenting symptoms of the 100 patients who were diagnosed to have tumors of the female genital tract were collected,the preoperative radiological findings ,the per operative details were recordedand the

per/ post operative histopathology samples were received in the histopathology laboratory, gross evaluation of the formalin fixed samples were done and the appropriately sampled bits were processed using the rapid processing technique in case of per operative diagnosis or by routine processing. Haematoxylin and Eosin stain was used to stain the sections and careful microscopic evaluation of slides with subtyping of the tumors was carried out using the WHO classification of tumors.

The clinical /demographic data were collected retrospectively for all the patients and analysed for the clinical presentation, serological values, imaging and biopsy findings which led to the pre operative diagnosis. The pre operative diagnosis was compared with preoperative/post operative histopathology. All the patients presented varied from vague abdominal discomfort and abdominal pain to dysmenorrhea, abdominal distension in most of the patients. The radiological findings were cystic masses some of them with solid areas and internal septations. CA 125 ranged from normal to elevated levels.

III. Results

S.N O	AG E	TUMOR CHARACTERISTICS	PREOPERATIVE DIAGNOSIS	INITIAL SURGERY	PER OPERATIVE/POST OPERATIVE DIAGNOSIS	PEROPERATIVE/POST OPERATIVE REVISION OF DECISION
1	32/ F	7X4 CM CYSTIC MASS WITH FOCAL SOLID AREAS CA125 16U/ml	CYSTADENOFIBROMA RIGHT OVARY	RIGHT OVARIECTOMY	ATYPICAL SEROUS PAPILLARY TUMOR RIGHT OVARY	N/A
2	36/ F	ASCITIS +, 6X4 CMS BILATERAL SOLID OVARIAN MASS, CA 125 11 U/ML	FIBROMA – THECOMA OVARIES BOTH	TOTAL ABDOMINAL HYSTERECTOMY WITH BSO	KRUKENBERG TUMOR OF GASTRIC ORIGIN	SYSTEMIC CHEMOTHERAPY AFTER SURGERY
3	49/ F	VAGINAL BLEEDING, POLYP MEASURING 2X1 CMS IN THE ENDOMETRIAL CAVITY.	ENDOMETRIAL POLYP	LAPAROSCOPIC HYSTERECTOMY	ENDOMETRIOID ADENOCARCINOMA ENDOMETRIUM GRADE 1 STAGE I	N/A
4	32/ F	10X7 CMS SOLID MASS RIGHT OVARY. CA 125 9U/ML	FIBROMA /SEXCORD STROMAL TUMOR ON IMAGING	RESECTION OF THE TUMOR	DYSGERMINOMA ON FROZEN SECTION	UNILATERAL SALPINGO OOPHORECTOMY FOLLOWED BY PLATINUM BASED CHEMOTHERAPY
5	51/ F	ABDOMINAL DISTENSION, POLYURIA, INTRAMURAL MASS AT THE UTERINE FUNDUS MEASURING 4X3 X3CMS	LEIOMYOMA	HYSTERECTOMY	ENDOMETRIAL STROMAL SARCOMA – HIGH GRADE	CHEMOTHERAPY RADIO THERAPY AND HORMONAL THERAPY SUGGESTED AFTER SURGERY.
6	48/ F	POST MENOPAUSAL BLEEDING	ENDOMETRIAL HYPERPLASIA ON CURRENTING	TOTAL ABDOMINAL HYSTERECTOMY WITH BSO	ENDOMETRIAL ADENOCARCINOMA – ENDOMETRIOID TYPE GRADE 1 STAGE II	POST OP BRACHYTHERAPY AND EXTERNAL PELVIC RADIATION AFTER SURGERY
7	43/ F	DYSMENORRHEA, ABDOMINAL DISTENSION, SOLID AND CYSTIC MASS RIGHT OVARY, CA 125 100U/ML	ENDOMETRIOSIS OVARY	TAH WITH BSO	ENDOMETRIOID ADENOCARCINOMA OVARY	CHEMOTHERAPY AFTER SURGERY
8	35/ F	ABDOMINAL DISTENSION AND PAIN, LEFT ADNEXAL SOLID MASS 6X5 CMS CA 125 60U/ML	OVARIAN FIBROMA/LEIOMYOMA	HYSTERECTOMY WITH BSO	LEIOMYOSARCOMA – LOW GRADE ON FROZEN SECTION	FOLLOW UP
9	49/ F	BLEEDING PV, POLYPOIDAL MASS 3X2 CMS OCCUPYING THE ENOMETRIAL CAVITY	ENDOMETRIAL POLYP	TOTAL ABDOMINAL HYSTERECTOMY WITH BILATERAL SALPINGO OOPHORECTOMY	MALIGNANT MIXED MULLERIAN TUMOR STAGE II	CHEMO AND RADIOTHERAPY SUGGESTED AFTER SURGERY

10	38/ F	K/C/O ENDOMETRIOSIS OVARY, MASS MEASURING 6X5X4 CMS WITH FOACL SOLID POLYPOID AREAS	ENDOMETRIOTIC CYST LEFT OVARY	TOTAL ABDOMINAL HYSTERECTO MY	PEROPERATIVE DIAGNOSIS- CLEAR CELL CARCINOMA OVARY	HYSTERECTOMY WITH BSO, PELVIC PARA AORTIC LYMPHADENECT OMY AND OMENECTOMY FOLLOWED BY CHEMOTHERAPY.
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Fig 1. Clear cell carcinoma – Gross appearance

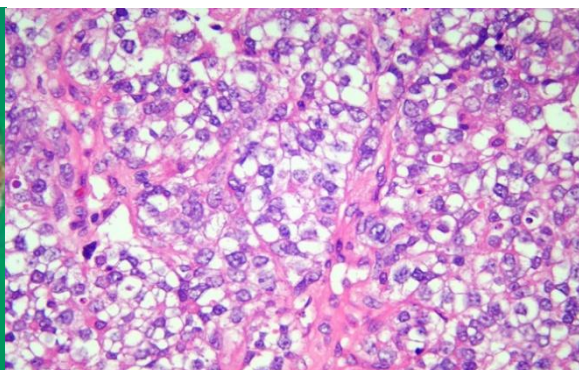


Fig .2 Clear cell carcinoma H&E X 400



Fig 3 Leiomyosarcoma – Gross appearance

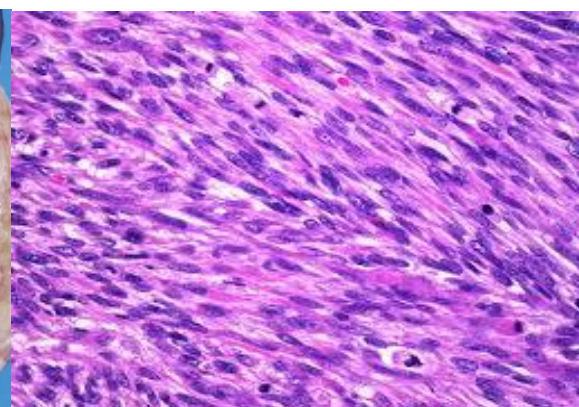


Fig 4 Leiomyosarcoma H & E X 400

Out of the 100 patients who underwent surgery for a diagnosis of benign tumor pre operatively, Ten patients had unexpected malignancies which were diagnosed either of frozen sections or on post operative permanent histopathology sections. Out of the ten cases of unexpected malignancies, three patients underwent frozen section which changed the course of surgery in one patient .The remaining two patients were diagnosed per operatively as malignancies and had the same histological findings on permanent sections which altered the post operative course of treatment for the patient. In 3 out of the remaining seven 7 patients, frozen section, if done could have altered the course of surgery .The prevalence of unexpected malignancies in our study is 10% and it was found in our study that diligent pre operative evaluation with a high index of clinical suspicion leading to per operative frozen section evaluation in clinically suspicious cases would have altered the course of surgery in 50% of the patients.

IV. Discussion

Ovarian cancer is the second most common and the #1 cause of death³ among malignancies of the female genital tract and epithelial ovarian cancer accounts for more than 95% of ovarian malignancies⁴. The non epithelial ovarian cancers are uncommon and constitute, the germ cell tumors, sexcord stromal tumors and metastasis. The clinical presentation of epithelial ovarian cancers can either be acute or subacute. Acute cases present with symptoms which may not be attributed to the ovarian pathology such as pleural or peritoneal effusion, ileal obstruction and venous thromboembolism. Subacute cases also may present with symptoms like abdominal fullness, bloating, an adnexal mass, vague pelvic or abdominal pain and gastrointestinal symptoms. Blood test for CA-125 marker and transvaginal ultrasound are neither sensitive nor specific for ovarian cancer. They can be abnormal and misleading. Benign conditions such as endometriosis, menstruation, pregnancy, and malignancies of fallopian tube, breast or the GI tract. Hence, diagnosis of ovarian tumors requires

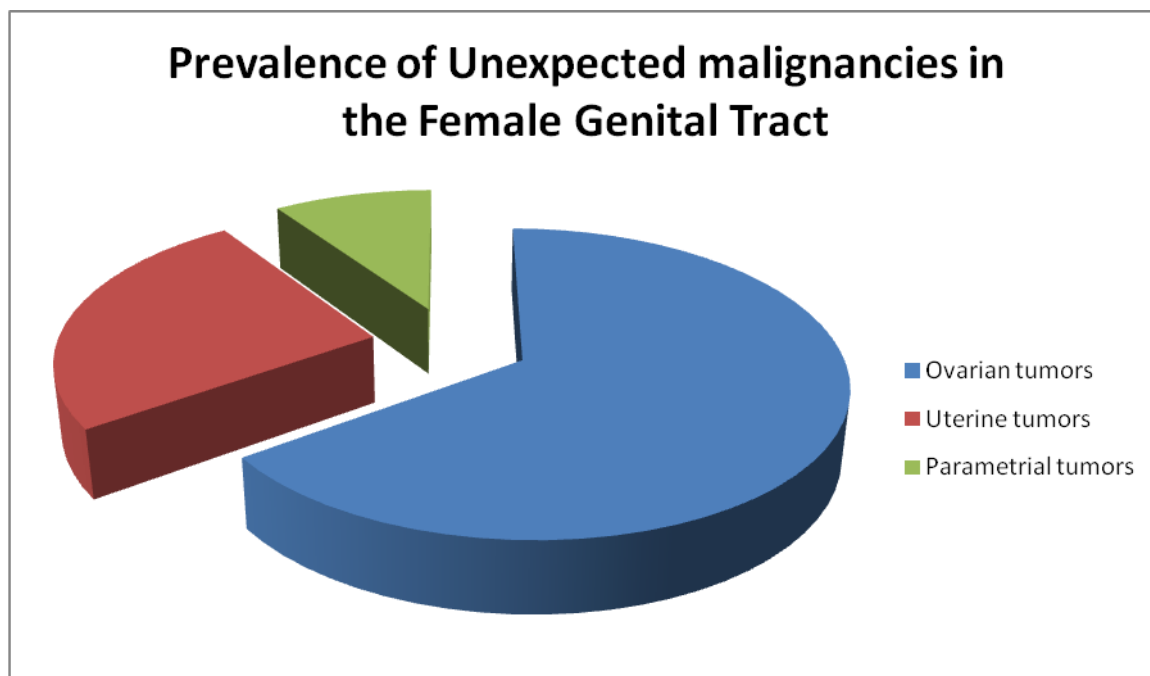
careful correlation of the symptomatology with biochemical values and imaging studies and careful treatment planning .

Germ cell tumors of the ovary results insymptoms not localizing to the ovary like pelvic fullness, polyuria or dysuria. Menstrual irregularities in patients, and lower abdominal pain or pressure on the small intestines may be present. Some of these symptoms can be misinterpreted as due to pregnancy which leads to further delay in diagnosis and treatment.Sometimes,torsionof the ovarian cyst or rupture of the adnexa can develop. These symptoms may be confused with acute appendicitis. In more advanced cases, ascites may develop and the patient can present with extensive abdominal distension⁵If imaging if the lesions are principally solid or a combination of solid and cystic, as might be noted on an ultrasonographic evaluation, a neoplasm is probable and a malignancy is possible⁵.

Uterine corpus is the second most common site of malignancy in the female genital tract and comprises of the epithelial,mesenchymalmixed epithelial mesenchymal and trophoblastic tumors.Vague abdominal symptoms including abdominal distension,discomfort ,vaginal bleeding.Imaging studies shows the presence of a mass involving the uterus either in the endometrial cavity or involving theendomyometrium.The diagnosis of malignancy requires a high index of suspicion in these cases.

Cervical cancer screening methods and colposcopy have enabled earlier diagnosis and monitoring of patients with cervical cancers and helps in planning out treatment decisions accordingly.Inadvertant hysterectomies leading to a post operative diagnosis of unsuspected carcinoma cervix have declined to a significant extent because of the vigilance and awareness created by the cervical screening programme among others.

Malignancies of the fallopian tubes constitute 0.5% of all female genital tract malignancies and the vaginal and vulval malignancies are also uncommon constituting 5% of all female genital tract cancers.They present with abnormal vaginal bleeding .Careful clinical examination and biopsy will be necessary to identify the pathology and proceed in line with the standardtreatment protocol.



In the literature, only sporadic reports regarding unsuspected gynecologic malignancies discovered during or after gynaecological surgeries are available. Hence, the real magnitude of this problem is still unknown but probably has been underestimated and the literure reports on such cases is yet to be published and recorded. Theoretically, the incidence of unexpected malignancies at gynecologic surgery varies depending on various factors i.e. the experience of attending physicians, an availability of laboratory investigations, and the complexity of patients' conditions. However, major discordance between preoperative and postoperative diagnoses such as encountering an unsuspected malignancies should be considered as a major problem during the time of medical audit .This kind of a situation may be avoided as much as possible if qualified surgical practice is to be achieved for which opting for peroperative diagnosis whenever the clinical scenario demands is one viable option .Having said this,the knowledge and experience of the pathologist performing the frozen section also becomes pertinent for an accurate diagnosis to be made during surgery as this will alter the course

of the surgery in cases of unsuspected malignancies many a times. For this, careful perusal of the findings, clinical and biochemical along with diligent gross examination of the surgical specimen becomes mandatory on the part of the reporting pathologist. Obviously, preoperative counseling about the risks of encountering unexpected cancer at surgery is of paramount importance in everyday surgical practice.

V. Conclusion

Encountering unexpected cancers during or after surgery may result in suboptimal treatment performed because of the potential of failure to follow standard treatment guidelines for such cancer. In addition, failing to prepare patients for a possibility of unsuspected cancer is an extremely difficult situation and may complicate the relationship with the surgeon.

All pathology departments shall be in a prominent position in the hospital, so that patients and healthcare professionals can come to the department to talk to the pathologists and scientists who work there, discuss results and find out more about how the specialty contributes to everyone's care.

This would mean that pathology would be valued for the vital contribution it makes to patient care, which hopefully would ensure appropriate investment in the people, equipment and IT infrastructure that is needed for a responsive, high quality pathology service for the benefit of patients.

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