CASE SERIES

Rare Gynaecological Malignancies –Dilemma In Presentation And Management: A Case Series Of 5 Unusual Cases

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Received: 17April, 2024 Accepted: 15 May, 2024

ABSTRACT
Vulval cancer is a rare gynaecologicalmalignancy.Though it has got excellent prognosis if diagnosed and treated early,but in most instances ,women present late with advanced disease which are difficult to treat ,has got poor prognosis and the treatment itself can cause morbidity and mortality. The present case series of 3 cases, the genital location was the primary site of presentation.

Keywords: Gynaecological, Malignancy, non-Hodgkin's lymphoma

INTRODUCTION

Vulval cancer is a rare gynaecological malignancy. Among vulval cancer squamous cell carcinoma ,which accounts for the majority of cases .However, there are several rare entities of vulval cancer that exhibit unique characteristics and require specific diagnostic and therapeutic approaches. Among this ,DermatofibrosarcomaProtuberans (vulvar sarcomas) comprises only 3.0% of all primary malignancies. [1]. It is a rare, low-grade sarcoma of dermal origin which characteristically presents during early or mid-adult life as a firm, well-circulated nodular mass, fixed to the overlying skin, but movable over the deeper tissues.

Another rare entity being , Aggressive angiomyxoma, a benign slow-growing myxoid neoplasm that occurs almost exclusively in the genital, perineal and pelvic regions of adult women. It mostly occurs during the reproductive years with a peak incidence in the third decade of life. As the tumor is well known for local recurrences, timely diagnosis and management with surgical excision and adjuvant therapy are benefcial for such patients. It was first described in a case series of nine patients by Steeper and Rosai in 1983 [2]

Primary non-Hodgkin's lymphoma (NHL) of the vagina is uncommon. The National Cancer Database reported that only 1.5% of extra-nodal NHL originates in the female genital tract with 5-year overall survival is estimated to be 55% . Surgery does not serve a role in the treatment of this disease, as chemotherapy is relatively effective.[3]

Gynaecologic melanoma are also extremely rare malignancies and primary malignant melanoma of cervix is the rarest among all of them with no associated risk factors, having very poor ;prognosis with only 25% survival rate for even stage I disease.

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CASE 1

A 35-year-old person, inexperienced in pregnancy and labor, approached with a history of a repeated vulval mass lesion. Initially, back in the year 2011, the mass measured 5x6 cm in diameter which got cut out, histopathology revealing DFS for which the person opted out of additional treatment, nevertheless, over the next 1 year it recurred once more at the exact same spot in 2012 measuring at 10X 6cm which was cut out once more at some undisclosed private facility, histopathology indicating low-quality sarcoma, once again avoiding any additional treatment. The vulval mass came back in 2018 and the person sought help from gynaeopd complaining about drainage from local injury where examination brought to light a solid, movable, well-defined 2 x 2-cm nodule on the left mons pubis and a second 1.5 x 1.5-cm nodule on the left labium majus. No obvious suspicious inguinal lymph nodes were detected and the remaining physical assessment was normal. The person underwent radical vulvectomy with a 3 cm

peripheral border focusing on the uretheral region. Histologic testing unveiled Dermatofibrosarcoma Protuberans with the base and surgical edges free of the tumor. Under a microscope, the growth presented itself as 4x3x2 cm in size, situated 1 cm away from the profound resection limit, with cells diffusely infiltrating the dermis and subcutaneous tissue. The central section of the tumor consisted of elongated cells arranged in a woven (storiform) design around an unremarkable vasculature. In the deep areas, the tumor interlocked with lobules of subcutaneous fat but no significant giant cells, necrosis, or mitosis were observed. This person once more disappeared from the radar for 4 years and reappeared at the cancer opd in the year 2022 with an 8x6 cm mass at the post vulvectomy site with no inguinal lymph node abnormalities. CECT Chest and Abdomen scans revealed 2 variably enhancing soft tissue lesions measuring at 5x5 cm and 6x5 cm at the post vulvectomy site hinting at local recurrence without any distant spread. Radiotherapy using Intensity Modulated Radiotherapy Technique was initiated delivering 66Gy/33# (wef 20/10/22-31/12/22) subsequently, she was put on adjuvant Tab Imatinib 400 mg OD from Jan 2023 till now.

Figure:1 : Nhl Vagina

CASE 2

In March 2021 , A 40 year-old woman presented with past 2-month history of pain lower abdomen and vaginal bleeding. The patient provided written informed consent to participate in the present case report. The patient did not report any other symptoms, including fever, night sweats, weight loss or fatigue (‘B’ symptoms), and they had no notable past medical history. Upon per vaginal and per speculum examination there was an hard, ulcerative lesion in lower aspect of posterior vaginal wall. Magneticresonance imaging (MRI) (**Fig. 1**) of the pelvis was done which showed ill defined STDL centered along posterior wall of lower 1/3 vagina approximately 3.2x2.9x1.7 cm with infilteration of distal aspect of urethra with loss of fat planes with mesorectal fascia and maintained fat planes with uterus and cervix., there was associated pelvic lymphadenopathy .On admission, the following laboratory parameters were noted: Blood cell count 4.1x1012/l (normal range, 4.0-5.0x1012/l); dehydrogenase 181 U/l (normal range, 109-245 U/l); and cancer antigen-125; 29 kU/ml (normal range, 0-35.0 kU/ml). Baseline renal and liver function test results were also normal. Hepatitis B virus markers, hepatitis C virus antibody (Ab) and human immunodeficiency virus Ab tests were negative. Based on physical examination and laboratory findings, a vaginal biopsy was performed following a suspected diagnosis of cervical carcinoma or primary vaginal carcinoma. and tumor cells were positive for cluster of differentiation 20 (CD20), CD3, CD45, CD2, CD5, CD7 and CD79a The patient was diagnosed as having NHL with a primary location in the vagina, Stage IE . After confirmed diagnosis of NHL vagina , oncologists reviewed the patient and recommended 6 cycles of the R-CHOP regime ,following the 6 cycles of chemotherapy in October 2021 , In Dec 2021 she presented with complaint of abnormal body movement, headache and vomiting episodes and MRI of Brain (fig2) was done which was suggestive of parietal region brain metastasis,

The patient received Whole Brain RT (30 Gy in 10 fractions) for the Brain metastasis.in December 2021.Then she was on oral metronomic chemotherapy with tab cyclophosphamide till November 2023 . the patient was reviewed every three months and no recurrence or other metastasis had been observed.

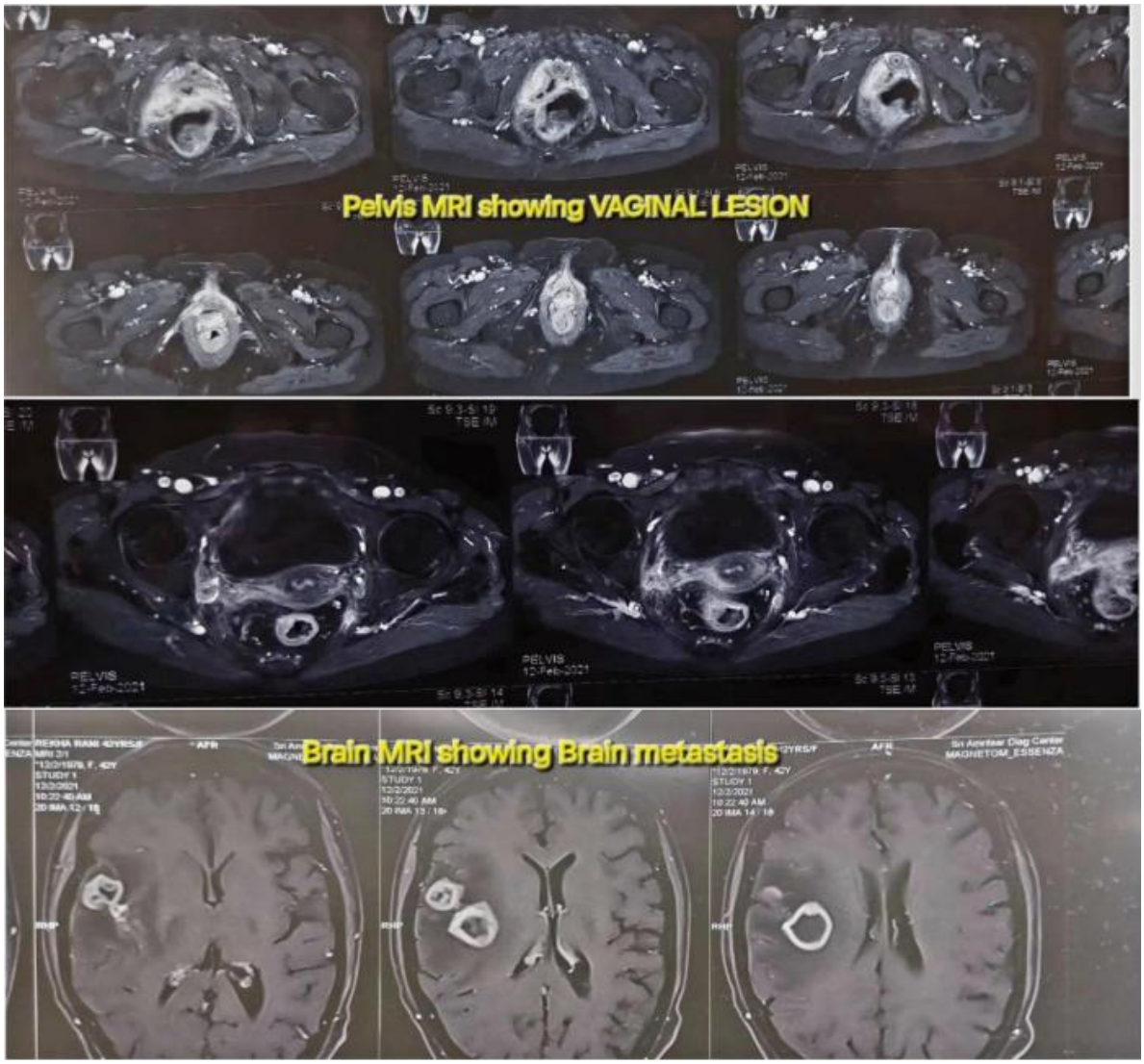

Figure 2: Aggressive Angiomyxoma

CASE 3

An Indian lady, 26 years old, married , P2A0L2 woman approached the gynecology Out Patient Department (OPD) with a swelling happening for 2months on the left labium majora, incrementally increasing in size. History of medical or family background was uneventful. In the general check-up, the patient was reasonably built and afebrile. No signs of jaundice, anemia, cyanosis, lymphadenopathy, clubbing, or any bowel and bladder function anomalies were noticed. Menstrual cycles happened regularly with normal flow. Her abdomen showed softness and lack of tenderness. During local scrutiny, a well-circumscribed, 6x3cm lump surfaced from the left labium majora sidewise of the introitus at five o'clock orientation. When touched, the lump was not tender, non-reducible, and soft in texture. No inguinal lymphadenopathy was detected. In the gynecological assessment, the uterus was average in size with a normal cervix and vagina. Initial checks showed no anomalies. Ultrasonography (USG) of the abdomen and pelvis showed no issues. Magnetic resonance imaging (MRI) wasn't achievable due to monetary restrictions. Post obtaining sanctioned written consent, wide local excision of the lump and surrounding margins was executed under anesthesia. There was some bleeding during the operation. The sample was dispatched for histopathological analysis. The histopathology report showed a growth of unsophisticated spindle cells in a fibromyxoidstroma, which hinted at a spindle cell tumor - favor Deep Aggressive Angiomyxoma. Her recuperation post-surgery was normal . On the fourth day after surgery, the patient was discharged in satisfactory overall

health, with a hemoglobin level of 10 gm%. No relapse has been recorded this far during subsequent appointments q 3monthly for 3 years.

CASE 4

In 2019, A 22 year old umarried, nulliparous female presented with past 2-month history of discharge per vaginum. The patient provided written informed consent to participate in the present case report. The patient did not report any other symptoms, including fever, night sweats, weight loss or fatigue ('B' symptoms).On Per Abdomen Examination there was a hard globular mass in pelvic region around 6x6 cm in size ,nontender, nonmobile and with per vaginal examination showing 3x3cm hard mass on right labia majora approximately 3x3 cm in size. Whole Body PET/CT was done which was suggestive of large heterogeneously enhancing mass lesion in lower pelvis in midline location arising in vulval region and vagina with infilteration into adjacent structures , there was associated Reteroperitoneal, pelvic and inguinal lymphadenopathy with bone metastasis . Vaginal biopsy was performed and report came out to be Malignant Round cell tumor and on IHC tumor cells were positive for LCA, and negative for CK,Chromogranin, and HMB-45 .The patient was diagnosed as having NHL with a primary location in the vagina . After confirmed diagnosis of NHL vagina , the patient was recommended 6 cycles of the R-CHOP regime ,following the 6 cycles of chemotherapy in Dec 2019 , Mri Pelvis done in jan 2020 Showed total resolution of vaginal and vulval mass as well as pelvic lymphnodes with 1 cm node being persistant in left inguinal for which she was started on maintainance Rituximab for 3 cycles last in may 2020 . followup W/B PET/CT done in july 2020 showed no disease and patient was kept on follow up. the patient was reviewed every three months and no recurrence or other metastasis had been observed till date.

CASE 5

68-year-old Postmenopausal woman presented with symptoms of bleeding per vaginum. On examination, vulva and vagina were normal. A black pigmented polypoid growth was seen at the cervical os with bilateral fornices being free. MRI Pelvis showing 5.4x5.7cm mass lesion in endocervial canal region with pelvic internal iliac lymphnodes being positive. However, Histopathological examination showed malignant melanoma. On immunohistochemistry (IHC), tumour cells were negative for cytokeratin and diffusely positive for melan-A and Human Melanoma Black 45 (HMB-45) Thetumour was negative for CD20, CD3, CD30, Leukocyte Common Antigen (LCA), synaptophysin and chromogranin. Thus, the case was signed out as malignant melanoma involving the cervix. A complete dermatological, ophthalmological and gastroenterological workup was non-contributory and the tumor was considered as primary tumor of the cervix. Positron emission tomography scan showed an intense uptake in the cervical growth without abnormal uptake in bilateral parametria .Lymph nodes along right common iliac and internal iliac vessels or at any other sites in the body also showed metabolic uptake . The patient underwent radiotherapy to pelvis with 50 Gy/25# with concurrent oral Temozolamide, last fraction being delivered in august 2022 followed by 3 sessions of brachytherapy in September 2022. On follow up cect whole abdomen was done in November 2022 which showed inhomogenously enhancing area with fat standing at cervix and lower uterine body with few subcenterimetriclymphnodes , then patient was taken for Total Abdominal Hysterectomy with Bilateral Salpingo-opherectomy , and the specimen was reported as malignant melanoma confined to cervix (pT1b2Nx) with no lymphovascular invasion. Uterus, bilateral adnexae , bilateral parametria, peritoneum, omentum, abdominal organs and rest of the pelvic organs were unremarkable and lymph nodes were free of tumor, as per the available histopathology report. The patient has been on regular follow-up (regular clinical examination and radiological investigations) with capsule temozolamide 100 mg BD , in view of bleeding per vaginum in may 2023 ,again Whole Body PET/CT was done which was suggestive of disease progression with lung,omental,pancreatic deposits . She refused further chemotherapy and immunotherapy so was kept on palliative treatment with capsule Temozolamide 100 mg.

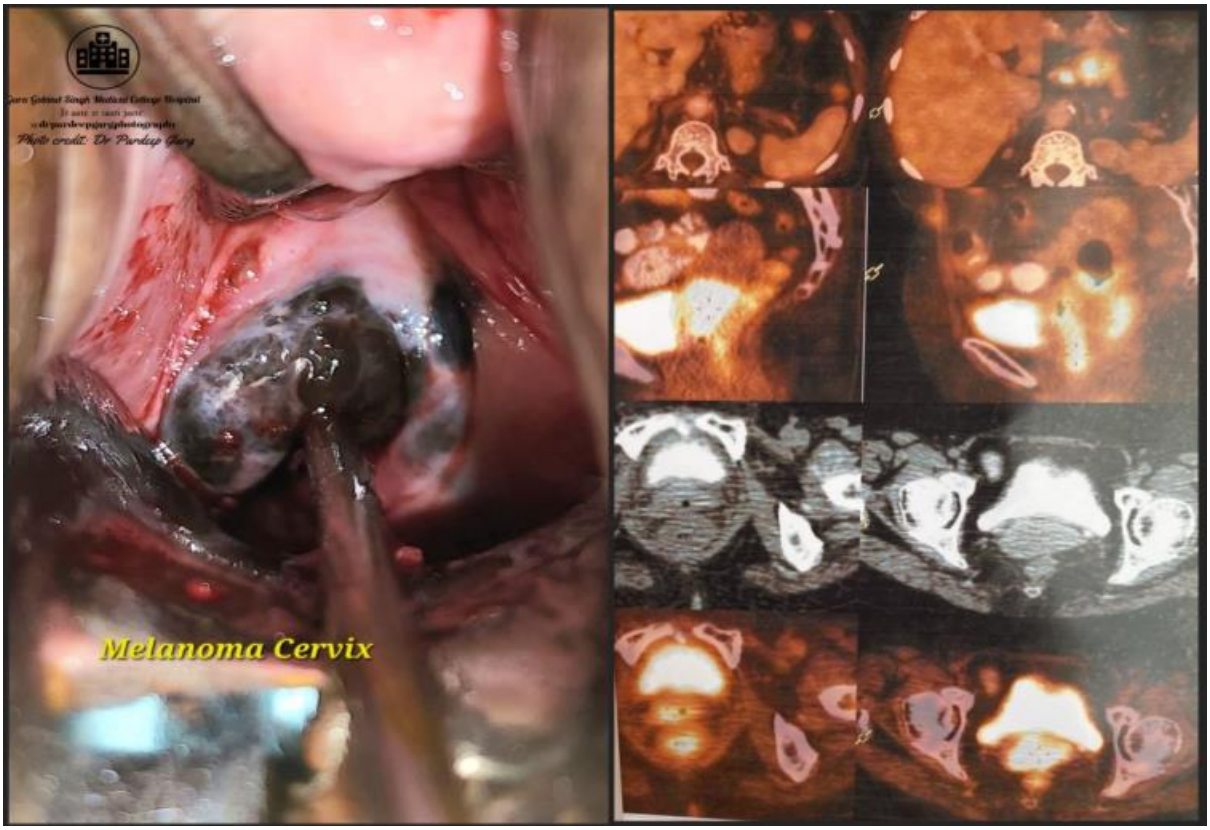

Figure 3: Showing PerspeculumBlackPgmented Growth Over Cervix, Showing Metabolic Active Stdl On Cervix With Lymphadenopathy On Pet/Ct

DISCUSSION

Even though the term dermatofibrosarcoma protruding was first applied by Hoffmann [4] in 1925, this uncommon fibrous tumor was initially mentioned by Darier and Ferrand [5] in 1924. It is an unusual, less-grade sarcoma of dermal source which typically presents during early or mid-adult life as a firm, well-circumscribed nodular bunch, fixed to the overlying skin, but movable over the deeper tissues [6-8]. A majority of patients are asymptomatic; however, pain, tenderness, and ulceration may develop with tumors in an accelerated growth phase. Although these neoplasms may occur at almost any site except the palms and soles [5], they are most frequently reported to involve the trunk and proximal extremities [4, 8].

Dermatofibrosarcoma protruding of the vulva is an extremely unusual diagnosis. Incidence of this tumor is about 4.2 per 1 million in the United States, with primary vulva cases making up a striking minority (9). While many histological variations for DFSP exist, one underlying genetic abduction is common. Translocation of chromosomal 17 and 22 [t(17:22)(q22:q13)] is seen in over 90% of DFSP(10). Translocation of these chromosomes causes alterations in platelet-derived growth-factor beta (PDGFB1) and collagen type I alpha 1 (COL1A1 resulting in aberrant growth),Presenting patients will often notice a slow growing process, confined to dermal or superficial subcutaneous tissues. If large-sized tumors are encountered, it can often reveal a more malignant process with fibrosarcomatous overgrowth on histology. Management hallmarks for vulvar sarcoma include radical local resection with negative margins. Mohs' microscopic surgery has been reported for smaller lesions, while large lesions require a 2-3 cm margin of normal tissue (11,12). Routine lymph node assessment has not been described for DFSP, however positive lymph nodes do have prognostic implications. Vulvar reconstruction following large resection may require myocutaneous flap coverage. Adjuvant therapy for DFSP is based on the risk of recurrence. Treatment regimes must be based on experience. Wide local surgery, if anatomically possible, can provide adequate local control of DFSP. We recommend radiotherapy in DFSP patients where repeated surgery may cause mutilation or functional impairment. A high probability of local control may then be expected.

Two studies showed activity for imatinib in phase II trials (13,14) with excellent response rates described. Patients on trial with a durable response were treated for at least 48 weeks, providing the rationale for our patient's planned treatment course. These studies lead to an FDA approval label for DFSP.

Angiomyxomas are recognized as superfcial (cutaneous myxoma) and are aggressive. Angiomyxomas occur more commonly in middle-aged patients presenting as a single nodule or a polypoidal mess in the head and neck region, trunk,

and lower extremities. Angiomyxoma report almost exclusively in womans of reproductive ages, with occasional cases seen in perimenopausal females and children's. This may be attributed to the hormone-responsive nature of the tumor, as its growth is stimulated by estrogen and progesterone. The exact pathogenesis of Angiomyxoma is still not clear. However, since the tumor cells express desmin and smooth muscle actin, it is believed to originate either from specialized mesenchymal cells or from the multipotent perivascular progenitor cells [15]. High-mobility group protein isoform I-C (HMGI-C) gene located in the region 12q13-15 of chromosome 12 seems to play a role in the pathogenesis off this tumor. Abnormal expression of this gene, HMGI C, detected using the immunoperoxidase technique, may be a possible marker of microscopic residual disease [16] . The patients are usually asymptomatic and presents with a slow-growing pedunculated mass in the vulva, gluteal region, or suprapubic region. Preoperative imaging is extremely important to see the extent of the tumor and plan surgical excision accordingly. The MRI is the investigation of choices for diagnosis and follow-up of recurrences. Radical surgical excision with negative margins is the conventional treatment of choice. However, it is not always possibly to achieve negative resectionmargins as tumor is locally infiltrative, leading to high operative morbidity. Therefore, less radical surgery is recommended nowadays. Adjuvant therapy with raloxifene, tamoxifen, or GnRH agonists like leuprolide acetate and goserelin have proven beneficial where the tumor is estrogen and progesterone receptor sensitive. In a case report by Fine et al., recurrent Aggressive Angiomyxoma of the vulva was treated solely by 3 months off GnRH agonist without needing any other medical therapy or surgery [17] No evidence-based recommendations are unavailable for post-surgery management off AA, but due to the rate of local recurrences and possible metastases, patients should be advised to undergo long-term follow-up until 15 years after the primary excision.

The Lymphomas are divided into two main categories: Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL). The latter is mainly currently divided into Precursor Lymphoid Neoplasms, B-cell neoplasms, and mature T/NK-Cell lymphomas. The incidence of non-Hodgkin lymphoma is 2–5% of all cancers [18].

The mean age at onset for NHL is 50 years, with most of the women having entered menopause. The most common form of presentation of this neoplasm is the abnormal vaginal bleeding; associated with abdominal or perineal pain, dyspareunia, dysmenorrhea, and urethral obstruction [19]. It usually appears as a large, fast growing and endophytic mass. In our case, the patient consulted due to vaginal bleeding as the sole symptom and it presented itself as an exophytic mass.

The diagnosis is confirmed by biopsy. The tissue obtained through biopsy must be sufficient in order to perform conventional histology and immunohistochemical and molecular genetics studies to determine the subtype of lymphoma [19, 20].

The prognosis for the vaginal lymphoma is encouraging, with an mean survival of 5 years depending on the tumor stages: 80% during the initial stages (I and II) and 30% in advanced stages (III and IV) [21, 22].

The treatment of this type of tumor is not clearly established because of its low incidence. Radiotherapy has been used as the sole treatment in some cases, while chemotherapy has been used in others [23]; nevertheless, it seems that the combination of both treatments is the most accepted alternative [5]. Surgery may also be used in treatment-resistant cases associated with chemotherapy, although its role is not generally accepted.

Malignant melanoma can appear in diverse mucosal locales. yet, the female genital region is a truly odd spot .Approximately 3% to 7% of all cases in ladies ensue within the genital tract. The preferred sites are vulva and vagina. Malignant melanoma of the uterine cervix is an amazingly uncommon tumor, with merely 80 documented instances. Worst site, some may say, for tumors to grow, the main cause is cervix's restricted blood supply and fibrous stromas; this malignancy's incidence is 5 times lower than primary vaginal or vulva mucosal melanomas (24-29). However, what adds to the challenge is the paucity of melanocytes within the vaginal and cervical mucosal membranes – making diagnosis of malignant melanoma of the cervix tricky. Cervical malignant melanomas may assume diverse shapes, such as mimicking malignant lymphoma, carcinoma, and sarcoma. Plus, they spread out quickly (29-30). From age, the likelihood of cervical malignant melanoma increases, but no one's quite sure how that impacts the patient's outcome. The pitiful survival rates of cervical cancer compared to those of the vagina or vulva might point to the reality that mass detection generally occurs at progressively improved stages, and riskier treatments are typically shied away from due to possible post-therapy complexities. Hence, the bleak prognosis ascribed to this neoplasm and limited agreement on curing primary malignant melanoma of the cervix exists (31-32).

Despite radical hysterectomy with pelvic lymph node dissection being recommended for cervical malignant melanomas, convincing evidence supporting this strategy remains scant and fewer case reports have transpired.

CONCLUSION

Rare gynecological malignancies, though less common than their prevalent counterparts like squamous cell carcinoma or adenocarcinoma, present unique challenges and can be a diagnostic and

management dilemma for physicians. These cancers often require a high level of clinical suspicion and specialized diagnostic techniques, including advanced imaging and molecular profiling (IHC). Treatment strategies are typically individualized, combining surgery, chemotherapy, and radiation therapy, tailored to the specific histological type and stage of the disease.

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