



Gynecologic Cancer: Types, Causes and Therapeutic Approaches

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Abstract

Inflammatory ovarian masses may be difficult to distinguish preoperatively from ovarian malignancies. We present a case of a 54-year old woman with an ovarian mass, diagnosed during a COVID 19-infection. She underwent surgery because of pain and a challenging differential diagnosis on imaging. The frozen section was inconclusive and the final pathological examination showed no malignancy but only an inflammatory mass. Further extensive investigations revealed sarcoidosis, associated with a specific inflammatory changes. In view of the COVID-19 infection and the signs of a systemic inflammatory syndrome, an association with SARS-CoV-2 infection is plausible. With this case report we hope to alert clinicians for the possibility of new COVID-19-related extra pulmonary disease manifestations.

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Introduction

In present days, health issues in women are of great importance in society and have great concern in developing countries. The issues regarding women's hygiene and gynecological diseases are increasing day by day. This is due to only less approach to education and employment, high illiteracy rates and increase in poverty levels. Health improvement in women is slight difficult in developing countries including India. However, in India, the medical technology is still developing so it is quite hard to identify the gynecological problems arising in women. The global comprehensive cancer statistics from international Agency for research on cancer have marked that gynecological

cancers accounted for 20% of the 14.1 million were estimated new cancer cases and 8.2 million cancer deaths among women in the world in 2012 [1]. In India only, cancer among the women is caused mainly due to cancer occurring in four organs i.e, cervix uteri, breast, corpus uteri, ovaries which is about 50-60%. Cancer has become a major Public Health Problem with over 800K new cases occurring every year, and is one of the ten leading causes of death in India [2]. Gynecological cancers have increased in India and about 30% of the total cancers among women India [3]. Among these, cancer of the uterine cervix, ovary and corpus uteri are the most contributors.



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It has been identified that in the age group of 35-64 in most of the female the cases of gynecological cancer were found to be more than 80% and, in the childhood, it was found 3.5-4.5%. Nearly 1,500,000 people require facilities for diagnosis, treatment and follow-up at a given time which is not possible for many women due to the negligence of patient, family and friends to identify early symptoms and expensive procedures regarding treatments and follow ups which is not possible for everyone. This review is aimed to equip the researchers to understand the various types of gynecological cancers, trend, causes and therapeutic approaches.

Sources and methodology

The search was done in electronic databases of PubMed, Scopus, ScienceDirect, Web of Science and Google Scholar for studies using the key term: Gynecological cancer. All the data were extracted and explained in respective subheadings.

Cervical cancer

Cervical cancer is a major public health problem in India, predominantly affecting women of lower socioeconomic status [4]. Cervical cancer accounted for an estimated 96,922 new cases and 60,078 deaths in India in 2018, which is close to one-fifth of the global burden of this cancer [5]. Cervical cancer is the second most common cancer in women aged 15–44 years in India, with more than three-quarters of cases diagnosed at a locally advanced clinical stage with poor prospects of survival [6]. The increasing trend of the cervical cancer in developing countries is attributed to the early beginning of sexual activities, certain sexual behaviors like high number of multiple partners, early age at first intercourse, infrequent use of condoms, multiple pregnancies with Chlamydia association, and immunosuppression with HIV, which is related to higher risk of HPV infection [7].

Cervical cancer occurs when cells undergo changes in women cervix, which connects their uterus with vagina. Cervical cancer has an ability to penetrate deep inside the tissue and commonly spread to the other parts of the body often lungs, liver, bladder, vagina and rectum. It has been found that majority of the cervical cancer are due to the infection with Human Papillomavirus (HPV), which can also be prevented by vaccine. The cancer grows slowly hence there is more pulse so finding and treating it is better before it causes a serious problem. It can be fatal to few women each year if it is not treated. Before the starting of cervical cancer unusual changes in the cells on the surface of cervix which is usually called as squamous intraepithelial lesions which means area of unusual tissue. These are precancerous cells, which might become cancerous or invade deeper layers of tissue for months or years. The majority of the women with cervical cancer present with advanced stage, where surgery may not be suitable. Most of the cervical cancer in their precancerous lesions stage were serve according to the age of women and with regards to their fertility issues. Prior cervical cancer which is in the stage of Ia1 is serve with Hysterectomy, the stage 2 that is Ia2 Early invasive cervical cancer of stage Ia1 is treated with hysterectomy, stage Ia2 unaccompanied by lymph vascular space invasion is expose to extended type II radical hysterectomy with pelvic lymphadenectomy, and stage Ib1 to stage IIa (selected cases) are exposed to radical hysterectomy (Rh type III) along with retroperitoneal pelvic lymphadenectomy with or without sapling o-oophorectomy. Due to prognostic risk factor associated with surgical-pathology few other treatments are recommended like radiotherapy, or chemoradiation. Low risk patients are continued for regular follow up, medium

risk patients are put through the adjuvant brachytherapy and in patients with elevated risk are recommended prognostication and chemoradiation. Cervical cancer which is in stage IIb and selected stage Ib2-IIa recommended chemoradiation treatment. During the treatment of chemoradiation and brachytherapy few of the patient partially responded to those patient surgery was highly recommended. Few of the women with huge early disease are put through to neo adjuvant chemotherapy for 2-3 cycles, which was further continued by surgery at 2–3-week intervals [2].

The primary cause of the cancer related to cervical is Human Papillomavirus (HPV). Infection with these one or more oncogenic HPV types is the prominent reason of almost all cervical cancer. It has been identified that more than 99.7% cervical cancers test were found positive for HPV DNA worldwide. Till now, 15 oncogenic types of HPV have been identified. HPV types 16, 18, and 45 are most predominantly associated with cervical cancer. Most HPV infections are asymptomatic and cleared by the immune system within a year. But in up to 10% of women, the infection can persist, and in very few women the persistent infection with these oncogenic HPV may lead to cervical cancer. Other causes of gynecological cancer can be diabetes, smoking, obesity, reproduction and menstrual history including never having children, starting menstruation before age 12 and or entering the stage of menopause after the age of 55. Family history, estrogen therapy, introduction of pelvic are to radiation, use of birth control pills oral or fertility drugs these causes can vary from women to women [8].

Ovarian cancer

The ovaries found in reproductive system of female are responsible for producing ova, or eggs. And also, reproductive hormones progesterone and estrogen. Ovarian cancer occurs when abnormal cells in the ovary begin to multiply out of control and form a tumor. If the tumor increases it can spread to other parts of the body this condition is known as metastatic ovarian cancer. Nearly ovarian cysts are not cancerous these are called as benign cysts. But in cases, it can cause cancer and ovarian cyst is a collection of fluid or air that develops in or around the ovary. Ovarian cancer has the worst prognosis among all gynecological malignancies. Ovarian cancer is frequently not diagnosed until it is at an advanced stage because of its generally vague symptoms, making it hard to treat on a curative basis [9].

The survival rate of the women with ovarian cancer is almost 45% in 5 years. India has one billion population and the diseases are the biggest burden. Cancer treating centers that offer appropriate care is limited. Many ovarian cancers are first treated by general gynecologists. The experienced gynecological oncologist is very less in number in the country. There are few factors that can gradually increase the mutation of genes associated with ovarian cancer such as BRCA1 or BRCA2. Other factors can be due to endometriosis and older age of women [10].

Epithelial ovarian cancer

Epithelial ovarian malignancies (which account for the majority of ovarian cancers) are divided into two categories: type I and type II tumors. Type I tumors, which are not as lethal as type II tumors, are thought to be caused from continual ovulation cycles, inflammation, and endometriosis [11]. The epithelial tumors are basically developed on the outer layer of the ovaries. Many women suffer from ovarian cancer and the range is about 90% and these are due to epithelial tumors. Most often ovar-

ian neoplasms are either referred with radiological diagnosis or present with pelvic or abdominal -pelvic masses with or without ascites, and rarely with distant metastases. Depending upon the activity status and possibility of surgery, the majority of women are treated with primary cytoreductive surgery which is further followed by six courses of adjuvant chemotherapy, either paclitaxel with carboplatin based, or single agent carboplatinum or cisplatinum with cyclophosphamide chemotherapy [2].

Germ cell ovarian tumor

Germ cell tumors are heterogeneous tumors that are derived from the primitive germ cells of the embryonic gonad [12]. About 10% of patients present with an acute abdomen resulting from torsion, hemorrhage, or tumor rupture (which is more common with yolk sac tumors or mixed germ cell tumors) [13].

Uterine cancer

Uterine cancer is defined as occurring in the uterine body (corpus), and can arise from the inner lining of the uterus (endometrium) or from the muscular layer of the uterus (myometrium). There are two major types of uterine cancers: adenocarcinomas, arising from the endometrium, and sarcomas, arising in the myometrium.

When a cancer occurs from female uterus, it is known as endometrial cancer. Endometrial cancer occurs from the layer of cells that form the lining (endometrium) of the uterus. Endometrial cancer is also known as uterine cancer. Risk factors are related to excessive unopposed exposure of the endometrium to estrogen, including unopposed estrogen therapy, early menarche, late menopause, tamoxifen therapy, nulliparity, infertility or failure to ovulate, and polycystic ovary syndrome [14].

Vaginal bleeding is the most common symptoms of these types of cancer. If it can be detected early then it can be treated and cannot be fatal which can be carried out by removing the uterus surgically. Abnormal uterine bleeding including postmenopausal bleeding, menorrhagia, or metrorrhagia are the most common presenting symptoms for women with endometrial hyperplasia or carcinoma [15]. According to the stats, endometrial cancer is one the most common gynecological cancer in US and western country [16]. The number of endometrial cancer cases increasing can be due certain factors like obesity, a high – fat diet, diabetes and (RR3) these can give rise to endometrial cancer. The typical age-incidence curve for endometrial cancer shows that most cases are diagnosed after the menopause, with the highest incidence around the seventh decade of life [17].

There are two types of endometrial cancer, type I and type II. The histology of type I is that of an endometrioid carcinoma with several subtypes including secretory and villoglandular carcinoma. Such a patient is more likely to have an estrogen-dependent, superficially invasive Grade I tumor with a low-risk clinical course and resultant good prognosis. Type I carcinomas frequently show mutations of DNA mismatch repair genes (*MLH1*, *MSH2*, *MSH6*), phosphatidylinositol phosphate 3' phosphate (*PTEN*), k-ras and β -catenin genes (*CTNWB1*) [18,19]. Type II endometrial cancer is more likely associated with an atrophic endometrium or with uterine polyps. It contains activation of the ERBB2 oncogene and mutation of the TP53 tumor suppressor gene [20].

Reproductive, menstrual, and medical risk comorbidities can increase or decrease the risk of a woman having development

of endometrial cancer [21]. Continuous estrogen stimulation, albeit it exogenous or endogenous, can alter the normal endometrial cycle. Estrogen-producing tumors, unopposed estrogen therapy, cirrhosis, and tamoxifen also may result in excess estrogen stimulation to the endometrium. Although tamoxifen is an antiestrogen in breast tissue, it can have estrogenic activity in the endometrium [22]. Unopposed estrogen replacement in menopause is associated with a fourfold to eightfold increased risk of disease, whereas estrogen and progesterone replacement therapy in the menopause decreases the risk of disease.

Vulvar cancer

Vulva is the external genital organ which helps in to protect the women reproductive system. In case of Vulvar cancer this external organ got effected, it's a rare type of cancer. Vulvar cancer is an uncommon malignancy and accounts for around 5% of all gynecologic cancers [23]. The cancer results in formation of lumps, itching and bleeding as signs or symptoms. When vulvar got effected directly is called primary vulvar cancer. If the cancer starts from another parts of body and then gets spreads to vulva it is called as secondary vulvar cancer. Co-morbid medical conditions are the most common cause of this cancer and which effects the elderly women (1-3%). However, the majority of undergo radical vulvectomy and inguinofemoral lymphadenectomy. Depending upon the condition of a patient either undergoes surgico-pathological prognosticators or not. Basis of the physical condition the patients will be subjected to either regular follow-up in early-stage low risk patients or adjuvant therapy whenever indicated [2].

Vulvar squamous cell carcinoma can be broadly classified as HPV-mediated and non-HPV-mediated and is generally preceded by noninvasive vulvar intraepithelial neoplasia. Most vulvar cancers present symptomatically as either a palpable lump or a visible lesion with or without associated pruritus, dysuria, discharge, or bleeding. Visualization can be difficult due to distortion of labial architecture from atrophy or inflammatory dermatoses [24].

Vaginal cancer

Primarily vaginal cancer is rare because it consists only 1-2% of all female genital tract. Previous data says that these cancers are more common in elderly and postmenopausal women. If the malignancy is found in younger age of woman it is etiologically linked to cervical cancer, but these cancers are now increasingly seen in young women owing to increase in persistent high – risk HPV infections. The vagina has an elastic muscular tube which is compose of many mucosal folds. It extends from the cervix of the uterus to the hymenal ring, posterior to the bladder and anterior to the rectum. The elasticity of the vagina is based on the age of the women, surgeries, and hormonal status. As primary vaginal cancer is rare, treatment is complex. The vaginal cancer can be spread by direct extension, lymphatic spread and hematogenous spread [25].

More than 90% of vaginal cancer cases are squamous cell carcinomas and approximately 5% are adenocarcinomas [26,27,28]. Squamous cell vaginal carcinomas initially spread superficially, but unfortunately, several women are diagnosed with metastatic disease. Frequent sites of distant metastases are in the lungs and liver [29]. Adenocarcinomas differ from squamous disease as they have a peak incidence between 17 and 21 years of age and frequently metastasize to the lung and supraclavicular or pelvic nodes.

Conclusion

Gynecological cancers are important causes of death globally. However, an important fraction of gynecological cancer mortality is preventable by obesity and tobacco control programs, Human Papillomavirus (HPV) vaccination programs, awareness and training programs for recognizing early signs and symptoms of the disease, and national population-based screening programs. An individualized multidisciplinary approach and timely referral to a reproductive specialist is crucial for achieving best results for girls and women to diagnose gynecological cancer at early stage.

References

- Barman D, Sharma JD, Barmon D, Kataki AC, Sharma A, et al. Epidemiology of gynecological cancers in Kamrup Urban District cancer registry. *Indian Journal of Cancer*. 2017; 54: 388-391.
- Uma Devi K. Current status of gynecological cancer care in India. *Journal of Gynecologic Oncology*. 2009; 20: 77-80.
- Takiar R, Nadayil D, Nandakumar A. Projections of number of cancer cases in India (2010-2020) by cancer groups. *Asian Pacific Journal of Cancer Prevention*. 2010; 11: 1045-1049.
- Singh GK, Azuine RE, Siahpush M. Global inequalities in cervical cancer incidence and mortality are linked to deprivation, low socioeconomic status, and human development. *Int J MCH AIDS* 2012; 1: 17-30.
- Global Cancer Observatory. India fact sheets. 2019.
- Sankaranarayanan R, Basu P, Kaur P, Bhaskar R, Singh GB, et al. Current status of human papillomavirus vaccination in India's cervical cancer prevention efforts. *The Lancet. Oncology*. 2019; 20: e637-e644.
- Gustafsson L, Ponten J, Bergstrom R, Adami HO. International incidence rates of invasive cervical cancer before cytological screening. *Int J Cancer*. 1997; 71:159-165.
- Manikandan S, Behera S, Naidu NM, Angamuthu V, Mohammed O, Debata A. Knowledge and awareness toward cervical cancer screening and prevention among the professional college female students. *Journal of Pharmacy & Bio allied Sciences*. 2019; 11: S314-S320.
- Jayson GC, Kohn EC, Kitchener HC, Ledermann JA. Ovarian cancer. *Lancet*. 2014; 384: 1376-1388.
- Song YS, Kim HS, Aoki D, Dhanasekaran DN, Tsang BK. Ovarian cancer. *Bio Med Res. Intl*. 2014; 764323.
- Chien J, Poole E. Ovarian cancer prevention, screening and early detection: report from the 11th Biennial Ovarian Cancer Research Symposium. *Int J Gynecol Cancer*. 2018; 27: S20-S22.
- Shaaban AM, Rezvani M, Elsayes KM, Baskin H, Jr Mourad A. et al. Ovarian malignant germ cell tumors: Cellular classification and clinical and imaging features. *Radiographics: A review publication of the Radiological Society of North America, Inc*, 2014; 34: 777-801.
- Pectasides D, Pectasides E, Kassanos D. Germ cell tumors of the ovary. *Cancer Treat Rev* 2008; 34: 427-441.
- Braun MM, Overbeek-Wager EA, Grumbo RJ. Diagnosis and Management of Endometrial Cancer. *American Family Physician*, 2016; 93: 468-474.
- Sorosky JI. Endometrial Cancer. *Obstetrics & Gynecology*. 2012; 120: 383-397.
- Leslie KK, Thiel KW, Goodheart MJ, De Geest K, Jia Y, et al. Endometrial cancer. *Obstetrics and Gynecology Clinics of North America*. 2012; 39: 255-268.
- Amant F, Moerman P, Neven P, Timmerman D, Van Limbergen E. et al. Endometrial cancer. *Lancet (London, England)*. 2005; 366: 491-505.
- Mutter GL, Lin MC, Fitzgerald JT, Kum JB, Eng C. Changes in endometrial PTEN expression throughout the human menstrual cycle. *The Journal of clinical endocrinology and metabolism*, 2000; 85: 2334-2338.
- Mutter GL, Lin MC, Fitzgerald JT, Kum JB, Baak JP, et al. Altered PTEN expression as a diagnostic marker for the earliest endometrial precancers. *Journal of the National Cancer Institute*, 2000; 92: 924-930.
- Ambros RA, Sherman ME, Zahn CM, Bitterman P, Kurman RJ. Endometrial intraepithelial carcinoma: a distinctive lesion specifically associated with tumors displaying serous differentiation. *Human Pathology*. 1995; 26: 1260-1267.
- Brinton LA, Berman ML, Mortel R, Twiggs LB, Barrett RJ, et al. Reproductive, menstrual, and medical risk factors for endometrial cancer: results from a case-control study. *Am J Obstet Gynecol*. 1992; 167: 1317-1325.
- Fisher B, Costantino JP, Wickerham DL, Redmond CK, Kavanah M, et al. Tamoxifen for prevention of breast cancer: report of the National Adjuvant Breast and Bowel Project P-1 Study. *J Natl Cancer Inst*. 1998; 90: 1371-1388.
- Rajaram S, Gupta B. Management of Vulvar Cancer. *Reviews on Recent Clinical Trials*. 2015; 10: 282-288.
- Weinberg D, Gomez-Martinez, Ricardo A. Vulvar Cancer. *Obstetrics and Gynecology Clinics of North America*. 2019; 46: 125-135.
- Maheshwari A, Kumar N, Mahantshetty U. Gynecological cancers: A summary of published Indian data. *South Asian Journal of Cancer*. 2016; 5: 112-120.
- Davis KP, Stanhope CR, Garton GR, et al. Invasive vaginal carcinoma: Analysis of early-stage disease. *Gynecol Oncol*. 1991; 42: 131-136.
- Merino MJ. Vaginal cancer: The role of infectious and environmental factors. *Am J Obstet Gynecol*. 1991; 165: 1255-1262.
- Macnaught R, Symonds RP, Hole D, Watson ER. Improved control of primary vaginal tumors by combined external-beam and interstitial radiotherapy. *Clin Radiol*. 1986; 37: 29-32.
- Gallup DG, Talledo OE, Shah KJ, et al. Invasive squamous cell carcinoma of the vagina: A 14-year study. *Obstet Gynecol*. 1987; 69: 782-785.