Cancer Association of South Africa (CANSA)

Fact Sheet
on Clear-Cell Adenosarcoma
of the Vagina

Introduction

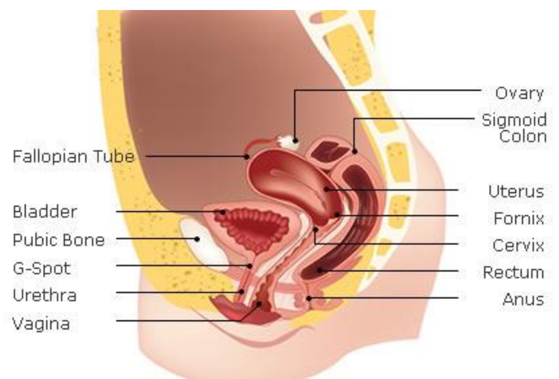
Clear-cell adenocarcinoma (CCA) of the vagina (or cervix) is a rare cancer often linked to the drug diethylstilbestrol (DES), which was prescribed in the mistaken belief that it prevented miscarriage and ensured a healthy pregnancy.

[Picture Credit: Diethylstilbestrol]

This synthetic oestrogen was given to millions of pregnant women, primarily from 1938-1971 but not limited to those years. Internationally, DES use continued until the early 1980s. DES was given if a woman had a previous miscarriage, diabetes, or a problem-pregnancy with bleeding, threatened miscarriage or premature labour. Up until the mid to late 1950s some women were given DES shots. After that, DES was primarily prescribed in pill form. DES also was included in some prenatal vitamins. In the late 1960s through 1971 a cluster of young women, from their teens into their twenties, was mysteriously diagnosed with CCA, a cancer not generally found in women until after menopause.

Clear-Cell Adenosarcoma (CCA) of the Vagina

Clear-Cell Adenosarcoma (CCA) of the vagina is one of the most common subtype of vaginal adenocarcinoma associated with diethystilbestrol (DES) exposure in young females. CCA of the vagina can also occur in postmenopausal women without exposure to DES. It is a rare vaginal cancer, accounting for 5% to 10% of primary vaginal malignancies (PathologyOutlines.com).



[Picture Credit: Female Anatomy]

The relative risk of CCA of the Vagina in DES Daughters

(the daughter of a woman who received diethylstilbestrol (DES) during pregnancy) is much higher compared to the general population.

Poon, C. & Rome, R. 2020.
Background: The malignant transformation of endometriosis within the ovary is a recognised condition. There is less literature surrounding the malignant transformation of extra-ovarian endometriosis (MEOE).
Aims: We report our experience with MEOE in ten patients and present a review of the literature regarding this rare malignancy.
Materials and methods: For this retrospective case series, patients were identified from a practice-based database. Where required, operative notes and pathology reports were reviewed.
Results: Ten patients diagnosed with MEOE between 1991 and 2014 were identified. In each case, the tumour was localised to the pelvis and centred on the pouch of Douglas, broad ligament, obturator fossa, parametrium and rectovaginal septum. Tumour histology was endometrioid adenocarcinoma (six), clear cell carcinoma (two), and adenosarcoma (two). Five patients had a history of endometriosis and four had received oestrogen-only hormone replacement therapy after hysterectomy and bilateral salpingo-oophorectomy. Treatments included surgery (one), surgery and radiotherapy (one), surgery and chemotherapy (one), surgery, radiotherapy and chemotherapy (three), and radiotherapy and chemotherapy (four). Maintenance hormonal therapy was also used in three patients. Curative doses of radiotherapy 45 Gy or more resulted in in-field control in five patients. Six patients had no evidence of disease at a mean follow up period of 15 years (5.5-24 years). Severe G3 long-term bladder morbidity occurred in three patients after radical surgery and radiotherapy.
Conclusion: MEOE is a rare condition for which treatment needs to be individualised. Multicentre studies and registries will hopefully define optimal treatment.

Incidence of Clear-Cell Adenosarcoma of the Vagina
The National Cancer Registry (2016) does not provide any information regarding Clear-cell Adenosarcoma of the Vagina.

Risk Factors for Clear-Cell Adenosarcoma of the Vagina
Age and being exposed to the drug DES (diethylstilbestrol) before birth affect a woman's risk of vaginal cancer.

Anything that increases one's risk of getting a disease is called a risk factor. Having a risk factor does not mean that one will get cancer; not having risk factors does not mean that one will not get cancer. Talk with a doctor if you think you may be at risk. Risk factors for vaginal cancer include the following:

- Being aged 60 or older.
- Being exposed to DES while in the mother's womb. In the 1950s, the drug DES was given to some pregnant women to prevent miscarriage (premature birth of a foetus that cannot survive). Women who were exposed to DES before birth have an increased risk of vaginal cancer. Some of these women develop a rare form of vaginal cancer called clear cell adenocarcinoma.
- Having human papilloma virus (HPV) infection.

- Having a history of abnormal cells in the cervix or cervical cancer.
- Having a history of abnormal cells in the uterus or cancer of the uterus.
- Having had a hysterectomy for health problems that affect the uterus.

Signs and Symptoms of Clear-Cell Adenosarcoma of the Vagina
Patients may have one or more of the following:
Vaginal bleeding
Dyspareunia (painful sexual intercourse)

Diagnosis of Clear-cell Adnosarcoma of the Vagina
The following tests and procedures may be used:

Physical examination and history: Physical examination including a history of the patient's health habits and past illnesses and treatments.

Pelvic examination: an examination of the vagina, cervix, uterus, fallopian tubes, ovaries, and rectum.

Pap smear: A procedure to collect cells from the surface of the cervix and vagina.

Biopsy: The removal of cells or tissues from the vagina and cervix so they can be viewed under a microscope by a pathologist to check for signs of cancer. A biopsy may be done during a colposcopy.

Colposcopy: A procedure in which a colposcope (a lighted, magnifying instrument) is used to check the vagina and cervix for abnormal areas. Tissue samples may be taken using a curette (spoon-shaped instrument) and checked under a microscope for signs of disease.

Treatment of Clear-Cell Adenosarcoma of the Vagina
Approximately 5% of primary vaginal malignancies are adenocarcinomas. Whenever this diagnosis is considered, it is necessary to rule out metastatic lesions from the bowel, uterus, or ovary. The most common variant is the clear-cell adenocarcinoma, which can occur spontaneously and in women with *in utero* exposure to DES. Primary non-DES-related adenocarcinoma of the vagina is rare and occurs predominately in postmenopausal women.

Treatment may involve surgical intervention and radiation therapy. For stage I clear-cell adenocarcinoma in the typical young patient, surgery may be considered to preserve ovarian function. Surgery for vaginal clear-cell adenocarcinoma usually requires a radical hysterectomy and vaginectomy with reconstruction. The vaginectomy is performed only to the level required to obtain an adequate margin. Local excision appears inferior to radical surgery. The role of chemotherapy has not been determined.

About Clinical Trials
Clinical trials are research studies that involve people. They are conducted under controlled conditions. Only about 10% of all drugs started in human clinical trials become an approved drug.

Clinical trials include:

- Trials to test effectiveness of new treatments
- Trials to test new ways of using current treatments
- Tests new interventions that may lower the risk of developing certain types of cancers
- Tests to find new ways of screening for cancer

The South African National Clinical Trials Register provides the public with updated information on clinical trials on human participants being conducted in South Africa. The Register provides information on the purpose of the clinical trial; who can participate, where the trial is located, and contact details.

For additional information, please visit: www.sanctr.gov.za/

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