ADVANCED GYNECOLOGIC MALIGNANCIES

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By
Hanem Mohamed El-Sayed
(M.B.,B.Ch.)

Supervised By

Prof. Dr. Khalil El Lamie
Chairman & Head of Depart. of Gynecol. & Obst.
Faculty of Medicine
Ain Shams University

Prof. Dr Samia Abd El-Razzak
Professor of Reproductive Biology
National Research Center.

Dr. Hatem Saad Ismail
Lecturer of Gynecol. & Obst.
Faculty of Medicine
Ain Shams University

Faculty of Medicine
Ain Shams University
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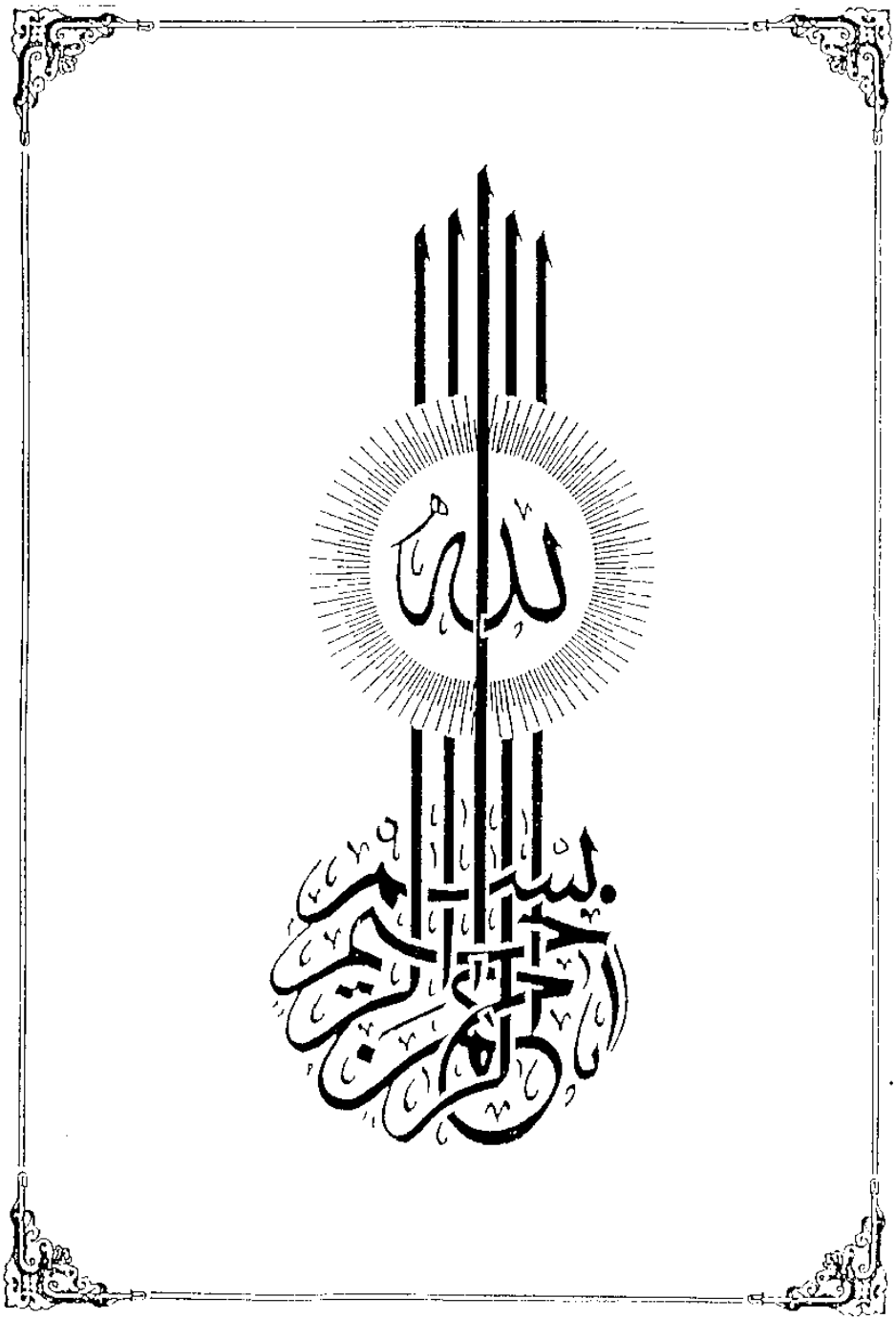
بسم الله الرحمن الرحيم

وقل رب زدني علما

صدق الله العظيم



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Introduction

It is estimated that approximately one woman in 20 will develop cancer of the genital tract during her life-time and about one in 40 will die of the disease.

Advanced gynecological malignancies registered are about 55% of all gynecological cancers which are often diagnosed late with stages III-IV and are so fatal.

Advanced ovarian malignancy is the commonest of all genital cancers. On the contrary the fallopian tube is the rarest site for malignancy in the genital tract but any part may be affected.

For proper diagnosis and treatment planning of advanced gynecologic cancers, the integration of tumour markers, computed tomography, magnetic resonance imaging and fine-needle aspiration biopsy is important.

Management of cases with advanced gynecologic malignancy may be medical, surgical, radiological, by chemotherapy, by immunotherapy or by the integration of two or more of those methods.

Patients with advanced gynecological malignancy that is incurable require treatment with palliative rather than curative intent.

Cachexia is commonly present in patients with advanced cancer. It may be due to diminished food intake, the effect of tumour on metabolism, inherent tumour metabolism or due to treatment of advanced malignancy. Just undernutrition is diagnosed it should be managed by different methods of feeding.

The incidence of pain in advanced gynecological malignancy is high. This pain may be due to the cancer, its therapy, psychological or due

to other factors and the therapeutic approach will vary depending on the underlying pain mechanism.

Classically, pain control depends upon the blockade of afferent pathways by interruption with local anaesthesia, chemical agents, surgical lesions or systemic analytic drugs.

Psychological aspects of caring for patients with advanced gynecological malignancy is so important and this could be reached by communication with the patient, caring of the family and specific psychological problems.

The prognosis of those patients is unfortunately so poor and the five-year survival rate for them may reach 0% specially for stage IV cancer.

The aim is not to give life for those patients but to give them painless exit.

Epidemiology of Advanced Gynecologic Malignancies

The principal aim of studying the epidemiology of cancer is to understand how prevention might be affected. This could be achieved both through the identification of the factors responsible for the differences in risk across populations and population subgroups *(Day, 1992)*.

*Age distribution:-

Each malignancy has its characteristic age distribution.The age distribution of advanced ovarian, uterine and cervical cancer shows some semilarities.Advanced ovarian malignancies show a steady rise of incidence to the mid -50 s, after which the incidence remains roughly constant. Advanced endometrial cancer is rare until age 35, when it rises to reach a plateau at 55 years. Advanced cervical malignancey shows a typical pattern of age distributiion, rising rapidly in the age-span 25 - 40 years, before which it is rare, then reaches a plateau and may even begin to decline in the sixth and seventh decades of life and later *(Day, 1992)*. On the other hand advanced tubal and vulvar malignancies are mostly occurring above the age of 50 *(DiSaia and Creasman, 1993)*.

*Incidence:

-Ovarian cancer accounts for 4% of all cancers among women and one in every 70 women will develop this disease. It also accounts for 23% of all gynecologic cancers.Most of the common epithelial ovarian cancers are advanced and present in stages III and IV.

Approximately 60% of ovarian malignancies present in these stages. Thus, about 47% of all deaths from genital tract malignancies occur in women having ovarian cancer *(Barber, 1988)*. The incidence of cancer ovary differs according to the locality as follows:

Country	Incidence
- Sweden	21/100.000
- Norway	16/100.000
- USA(white)	15/100.000
- England	14/100.000
-Africa	4/100.000
- India	3/100.000

Klostad and Beecham, (1975).

-Fallopian tube, on the other hand is the rarest site for primary malignancy in the female genital tract. Its frequency in relation to all gynecologic cancers is about 1% or less. Cancer tube is mostly advanced as the lesion is usually seen as unexpected operative finding *(DiSaia and creasman, 1993)*.

- Endometrial carcinoma is the most common invasive carcinoma of the female genital tract and is the fourth most common cancer in women. Cancer uterine corpus is more than 11/2 times as common as cancer of the ovary and almost 3 times as common as cancer cervis. Fortunately, this neoplasm has low virulence when compared to other gynecologic cancers, so advanced disease is uncommon with an average proportion of 7% for stage III cancer and less for stage IV disease *(Ahmad et al.,1990)*. Another study revealed that cancer ovary is the most common cancer of the female genital tract *(Beral, 1990)*.

On the contrary of that , sarcomas of the uterus are rare but the prognosis is very poor,The incidence of it comprise only about 3% - 5% of all uterine tumours *(DiSaia and Creasman, 1993).*

Choriocarcinoma arises only once for every 50 000 - 70 000 pregnancies in Britain and North america. In the far East and central Africa, the incidence is 1/5000 pregnancies. In middle east, the incidence is intermediate *(Jeffcoate, 1987).*

-The frequency with which invasive **cervical cancer** occurs is not known exactly, but the best incidence data indicate a rate of approximately 8 to 10/100,000 woman/year. The incidence appears to change from one locality to another and is less frequent in rural areas than in metropolitan areas. Fortunately the incidence of advanced cancer cervix has declined markedly, and the death rate has been reduced 71% over the past 40 years . This reduction is mainly a result of the use of cervicovaginal cytology and regular pelvric examinations *(Given et al.,1992).* However, in many developing countries, notably in Africa and Latin America, cervical cancer is the most common cancer among women *(Day, 1992).*

-Primary invasive malignancies of the **vagina** accounts for 1% to 2% of all gynecologic malignancies. This tumour is almost always advanced and fatal, because the diagnosis of vaginal cancer is usually delayed *(Eddy et al.,1991).*

-Vulvar carcinoma is rare representing only 3%-5% of all genital cancers. During recent years, it appears that this incidence has been incereasing. Advanced vular malignancies are very rare *(Monaghan, 1990).*

The following table will show the incidence of different gynecologic tumours in selected populations :

	Cervix uteri (%)	Corpus uteri (%)	Ovary (%)
Brazil-Recife	7.7	0.8	0.6
Colombia-Cali	5.3	0.7	0.9
Puerto Rico	1.6	1.0	0.7
Canda			
British Columbia	0.9	1.9	1.2
Manitoba	1.5	2.5	1.5
USA			
Detroit - Black	1.9	1.2	1.0
- White	0.9	2.7	1.4
Iowa	0.9	2.4	1.4
San Francisco-	1.3	1.6	0.9
Chinese			
China - Shanghai	1.1	0.4	0.5
Hong Kong	2.6	0.8	0.6
India			
Bombay	2.2	0.2	0.8
Madras	4.7	0.2	0.5
Isreal - all Jews	0.4	1.2	1.4
Japan - Osska	1.8	0.3	0.5
Singapore			
Chinese	1.9	0.6	0.9
Malay	1.2	0.5	1.0
Indian	3.1	0.4	0.4
Denmark	1.9	1.9	1.7
Finland	0.7	1.5	1.1
France - Liere	1.4	1.2	0.9
GDR	2.5	1.7	1.4
Norway			
Urban	1.9	1.5	1.7
Ruural	1.3	1.4	1.7
Spain - Zaragoza	0.6	0.9	0.6
UK			
South Thames	0.9	1.1	1.3
Merse	1.7	0.9	1.3
Scotland	1.2	0.8	1.3
New Zealand			
Maori	2.9	1.7	1.0
Non - Maori	1.2	1.2	1.2

From *Muir et al., (1987)*

-Aetiological factors:-

It has long been suspected that hormonal influences, reproductive factors and sexual behaviour are important for all advanced gynecologic malignancies, but recently the way in which they affect cancer risk has been studied in details *(Beral, 1990)*.

-The main factors affecting risk for **ovarian** cancer are reproductive including parity and use of oral contraceptives. Associated factors, include age at menarche, menopause and first or last birth, the evidence of which is less clear. There is a smoothly decreasing risk of ovarian cancer with increasing parity *(Kvale et al., 1988)*. The risk of ovarian cancer with respect to oral contraception use decreases even after stoppage of oral contraception *(Wu et al.,1988)*. Genetic factors clearly play an important role in the development of ovarian cancer. The risk was substantially elevated among women with a first- degree relative with the disease. The specific gene or genes have not yet been identified *(Ponder et al.,1989)*.

-The main risk factors identified for **endometrial** cancer relate to hormonal status and reproductive history.Early age at monarche and low parity increase risk as for breast cancer but of greater importance are late menopause, the use of oestrogen replacement therapy and obesity.In contrast to this , a decrease in risk for advanced endometrial cancer has been seen both for cigarette smokers and for users of the combined oral contraceptive *(Day, 1992)*. Uterine carcinoma is also more common in Jewesses than in women of other races. There is a significant association between diabetes and endometrial cancer. Fifty per cent of patients suffering from endometrial carcinoma can be shown to have abnormal glucose tolerance curves, and 10-30% are frankly diabetic. The obese diabetic patient is more susceptible for cancer uterus. Obesity alone is a predisposing factor. The combination of diabetes, obesity and hypertension, in association with endometrial carcinoma, is sometimes

called the "corpus cancer syndrome". It is suggested that the link between these conditions is a disturbance of hypothalamic-pituitary function

In 50% of cases of **choriocarcinoma** the condition is preceded by hydatidiform mole. In the remainder it follows abortion, ectopic pregnancy or delivery of anormal foetus *(Jeffcoate, 1987).*

- It has been recogniced for many years that the major risk factors of **cervical** cancer relate to sexual activity, as exeplified by the high rates seen among prostitutes and the virtual absence of the disease among nuns. Other risk factors include cigarette somking, oral contraception, immunosuppression and dietary factors. Sexually transmitted diseases have also a role as a risk factor for advanced cervical cancer.Attention is now focused on human papilloma viruses (HPV), particularly HPV 16 and 18. Previously, herpes simplex virus type2(HSV2) had been extensively investigated but neither the epidemiological nor the experimental data relating HSV2 to cervical cancer have proved convincing. Women of certain races, notably Orthodox Jewesses, are almost immune to cervical cancer. It is more common amongst women living in poor socioeconomic conditions *(Munos and Bosch,1989).*

The following simplified table will show the relation between sexual activity and probability of occurrence of cervical cancer :

Number of sexual partners	Relative risk	Age at first intercourse	Relative risk
1	1.0	>21	1.0
2	1.5	20-21	1.9
3-4	2.2	18-19	2.2
5+	2.8	< 18	2.5

Brinton et al (1987), Modified by Day (1992).

- For advanced **vulvar** malignancies the incidence increases in immunosuppressed patients and decreases with syphilis *(Managhan, 1990)*. In older women there is almost invariably a long history of vulvar irritation and pruritus, often associated with a vulvar skin dystrophy. A viral factor, possibly the herpes or papilloma viruses are the most popular aetiological agents proposed.

Downey et al. (1988) have shown the presence of human papillomavirus in 55% of cases of vulvar condylomatous carcinoma with equal distribution of type 6 and 16.

Stages and Pathology of Advanced Gynecologic Malignancies

-Advanced **ovarian** malignancies are those of stage III and IV disease. Approximately 60% of ovarian cancers present as these stages *(Barber, 1989).*

According to staging of International Federation of Gynecology and Obastetrics (FIGO staging 1988), ovarinan malignancies are dealt with as stage III if:

Tumour involving one or both ovaries with peritoneal implants outside the pelvis and/or positive retroperitoneal or inguinal nodes. Superficial liver metastasis equals stage III. Tumour is limited to the true plevis but with histologically proven malignant extension to small bowel or omentum.

Stage III ovarian cancer is subdivided into :-

IIIa :

Tumour grossly limited to the true pelvis with negative nodes but with histologically confirmed microscopic seeding of abdominal peritoneal surfaces.

IIIb :

Tumour involving one or both ovaries with histologically confirmed implants of abdominal peritoneal surfaces not exceeding 2cm in diameter. Nodes are negative.

IIIc :

Abdominal implants greater than 2 cm in diameter and/or positive retroperitoneal or inguinal nodes.