EARLY OVARIAN CANCER AND GERM CELL TUMORS

ESSAY

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BY

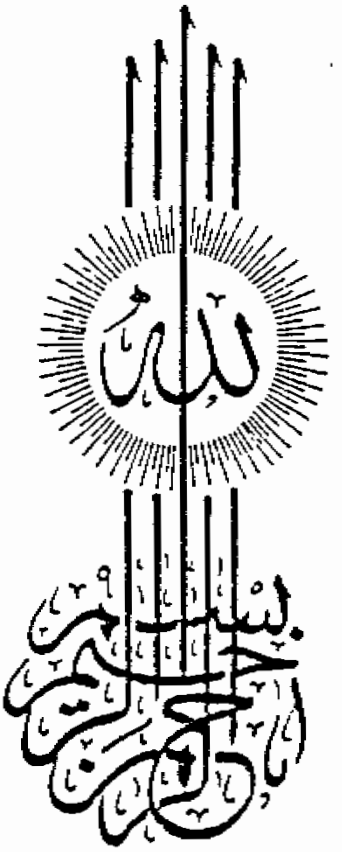
MONA AHMED EL KHATIB
(M.B.B.Ch.)

Supervised by

PROF. DR. KHALIL ISMAIL EL LAMEY
Prof. & Head of Obstetrics and
Gynecology Department
Faculty of Medicine
Ain Shams Unviersity

Dr. GAMAL ABD AL SALAM WAFA
Ass. Prof. of Obstetrics & Gynecology
Faculty of Medicine
Ain Shams University

Faculty of Medicine
Ain Shams University
1993



قالوا سبحانك لا علم لنا إلا ما
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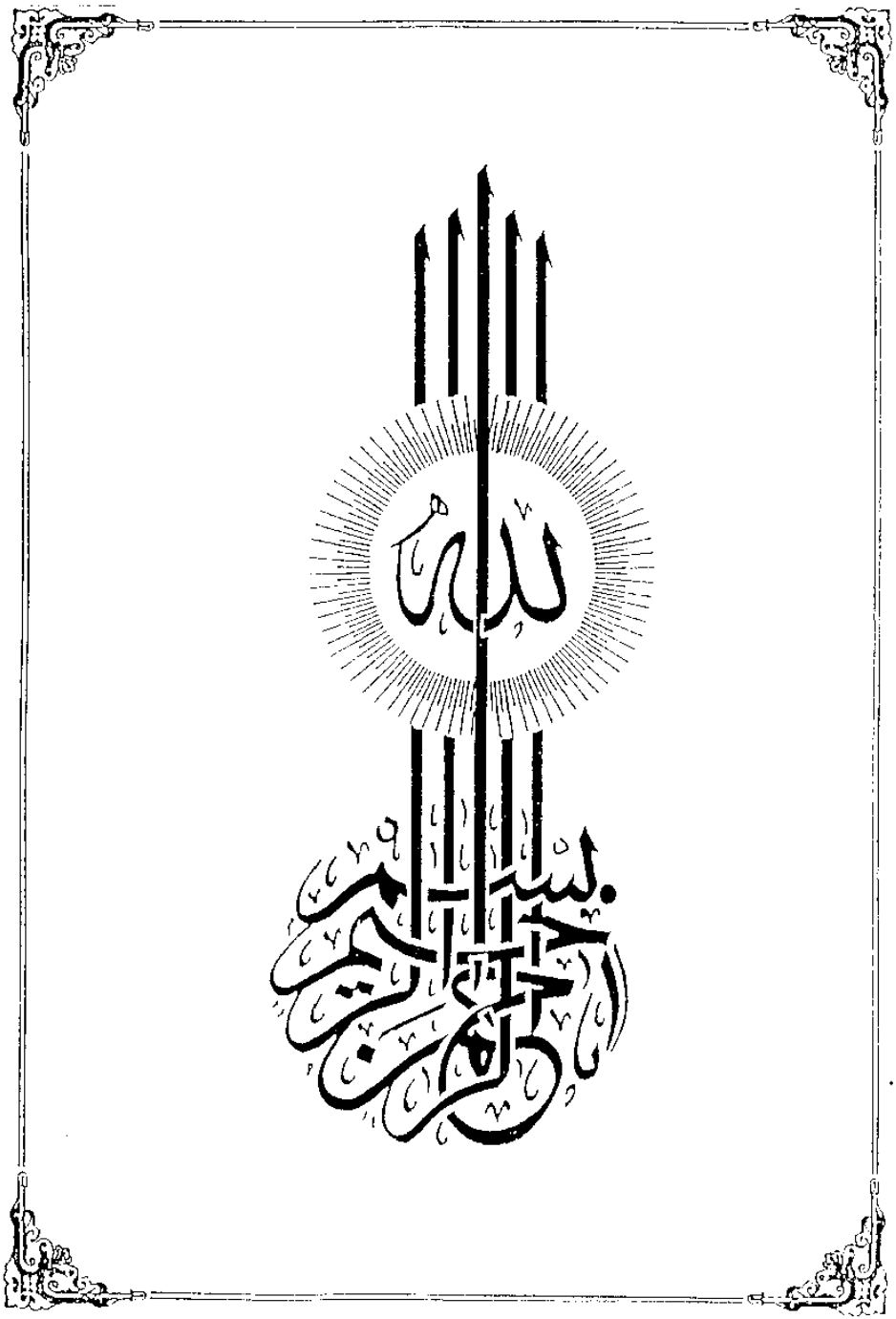

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Before all and above all thanks to God.

Mona El Khatib

Aim of the Work:

This essay study will deal with the various methods of diagnosis and treatment of ovarian malignancy. Treatment will include, surgery as regard its possible therapeutic role as well as the role of radiotherapy, chemotherapy. The side effects and complications of these measures will be discussed. The new items in the therapy of ovarian malignancy including immunotherapy will be discussed. Finally, the prognosis of ovarian malignancy will be discussed.

INTRODUCTION

Ovarian carcinoma is now the most common fatal gynaecologic malignancy in many countries of the western world, it is the fourth most frequent cause of death from cancer among women surpassed only by cancer of the breast, lung and colon. The overall cure rate reported in large series is 30%, this poor prognosis is mainly because it is usually not detected until advanced state (stage III and IV) when existing therapeutic measures become ineffective. (Lynch et al., 1990).

Recently little evidence that long term survival is being improved with the advent of combination chemotherapy using cisplatin and other individual active drugs. Prevention, early detection, morbidity and survival issues continue to challenge health professionals involved in the care of women with ovarian cancer.

While advances indiagnosis, staging and treatment have been made, survival rates remain grim.

Continuing research in the areas of screening, diagnosis and treatment is the key to improved survival.

The hope of new drug therapy such as cisplatin containing regimens, intraperitoneal therapy, immunotherapy and bone marrow transplantation needs further investigation to become reality. (Presbyterian et al., 1990).

DEVELOPMENT AND ANATOMY OF THE OVARY

DEVELOPMENT OF THE OVARY

Genetically, the sex of the individual is determined at the time of fertilization, but it is not until the embryo has reached the 17 mm. stage that it is possible to identify the gonads as either a testis or an ovary (Hamilton et al., 1945).

The primitive gonad is first evident in embryos of 5.5 - 7.5 mm. crown rump length (5 weeks). According to Gillman (1948) the gonad is of triple origin from the coelomic epithelium of the genital ridge, the underlying mesoderm and primitive germ cell which come from an extragenital source. The gonad forms as a bulge on the medial aspect of the mesonephric ridge. There is a proliferation of cells in and beneath the coelomic epithelium of the genital ridge. By 5 or 6 weeks, these cells are seen spreading as ill-defined cords (sex-cords) into the ridge, breaking up the mesenchyme into loose strands. Primitive germ cells are distinguishable as much larger structures, lying at first between the cords and then within them (Dewhurst, 1986).

It is now generally accepted that the germ cells arise in the endoderm before the formation of the

mesoderm of the lateral plate and somite formation (Pinkerton et al., 1961). Pinkerton and his colleagues described germ cells as migrating along the endoderm of the yolk sac, into the gut, through the mesenchyme at the root of the mesentery and into the primitive gonad.

After the embryo reaches 14 to 18 mm. (6 to 7 weeks), the conversion of the gonad into an ovary is not so prominent as its conversion into a testis.

The young ovary seems to remain in the indifferent stage for a longer period of time.

Finally, the germinal epithelium becomes thicker and more prominent. In places, massive clumps of sex cells are visible. The first follicles, constituted of oocytes surrounded by recognizable layers of granulosa cells appear initially in the center of the ovary when the fetus measures about 150 mm. crown rump length (slightly younger than 5 lunar months).

After arrival in the gonad of the female, the germ cells may be called oogonia. They are noted as early as the first week, although the gonad cannot be identified as an ovary at that time. According to Baker (1963), whose account is followed, oogonia may be found through the seventh month of fetal life. They undergo mitotic

division with great frequency, and their maximal number is at the first month , when their estimated number is about 2.6 million.

The oogonium is said to become an oocyte when it enters the first of its two meiotic divisions. The first oocyte may be recognized at about 8 weeks, and their maximum number is likewise at about 5 months, when their number approximates 4.2 millions. At birth, no oogonia remain, and the oocytes have been reduced to 2 millions. At the age of the seventh postnatal year, the remaining oocytes are only about 300,000.

The primary oocyte remains in a kind of hibernation in the prophase of the first meiotic division for many years. Completion of the first meiotic division is simultaneous with pre-ovulatory follicular maturation and ovulation. The second meiotic division usually occurs after ovulation and is completed only if there is sperm penetration (Novak et al., 1981a).

ANATOMY OF THE OVARY

The ovaries are homologous with the testes. They are situated one on each side of the uterus, close to the lateral wall of the lesser pelvis, and attached to the posterior superior aspect of the broad ligament of the uterus, posteroinferior to the uterine tube. They are of greyish-pink color, and present at a smooth surface before regular ovulation begins, but thereafter, the surface is distorted by the cicatrization which follows degeneration of successive corpora lutea. Each ovary is almond-shaped or amygdaloid and is about 3 cm long, 1.5 cm wide, and about 1 cm thick. The position of the ovary is subjected to a wide range of variation in women who have born children, because it is displaced in the first pregnancy and probably never returns again to its original location. It is also variably mobile and may change its position to some degree, according to the state of surrounding organs, such as the intestines (Gray et al., 1973).

Relations (Gardner et al., 1975):

When the ovary is in its usual position, its long axis is nearly vertical. It has medial and lateral

surfaces, tubal and uterine ends, and mesovarian and free borders. It lies in a depression, the ovarian fossa, which is bounded in front by the obliterated umbilical artery and behind by the ureter and internal iliac artery.

The lateral surface is in contact with the parietal peritoneum lining the ovarian fossa and is separated by this peritoneum from the extraperitoneal tissue that covers the obturator vessels and nerve. Most of the medial surface is covered by the uterine tube, elsewhere, this surface is related to the coils of the ileum.

The mesovarian or anterior border is attached to the mesovarium and faces the obliterated umbilical artery. The hilus of the ovary, through which blood vessels, lymphatic vessels, and nerves pass, is located on this border. The free or posterior border is related to the uterine tube and, behind this, to the ureter. The tubal or upper end is closely connected to the uterine tube; the suspensory ligament of the ovary is attached to this end. The uterine or lower end gives attachment to the ovarian ligament.

The mesovarium is a short, double-layered mesentery that extends backward from the posterior layer of the broad ligament to the mesovarian border of the ovary. Its two layers are attached one on each side of this border. The suspensory ligament of the ovary, or infundibulopelvic ligament, extends upwards over the external iliac vessels and become lost in the connective tissue covering the psoas major. It contains the ovarian vessels and the ovarian plexus of nerves. The ovarian ligament passes from the uterine end of the ovary to the body of uterus, just below and behind the entrance of the uterine tube. It is a rounded cord and contains some smooth muscle fibers (Gardner et al., 1975).

Structure (Gray et al., 1973):

The surface of the ovary is covered with a layer of cubical cells in the young female, which become flattened later in life. This so-called germinal epithelium gives to the ovary a dull grey color as compared with the shining smoothness of the peritoneum; the transition between the flattened mesothelium of the peritoneum and the cubical cells covering the ovary is usually marked by a fine white line around the anterior, or mesovarian, border of the ovary.

The ovary, after puberty, has a thick cortex which contains the ovarian follicles and corpora lutea and surrounds, except at the hilus, a richly vascular medulla. The interstitial framework or stroma of the cortex is of a dense texture and consists of networks of reticular fibers and numerous spindle-shaped cells which resemble non-striated muscle cells, though they contain no fibrils and are possibly mesenchymal elements. These stromal cells contribute to the growth of the theca folliculi, and they may secrete estrogens. The stroma of the medulla is of a loose texture and consists of connective tissue, with many elastin fibers, non-striated muscle cells and numerous large blood vessels, particularly veins. At the hilus, strands of non-striated muscle cells enter the medulla from the mesovarium. The cortex is much less vascular than the medulla. Immediately beneath the germinal epithelium, the connective tissue of the cortex is condensed to form a delicate tunica albuginea, which increases in density with advancing years. It is a collagenous layer, in contradistinction to the general stroma of the ovary. During prenatal life, the stroma of the cortex contains small groups of interstitial cells, but after puberty these cells are only present