ROLE OF ULTRASOUND DURING MANAGEMENT OF MALIGNANT GESTATIONAL TROPHOBLASTIC NEOPLASIA

THESIS
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1992

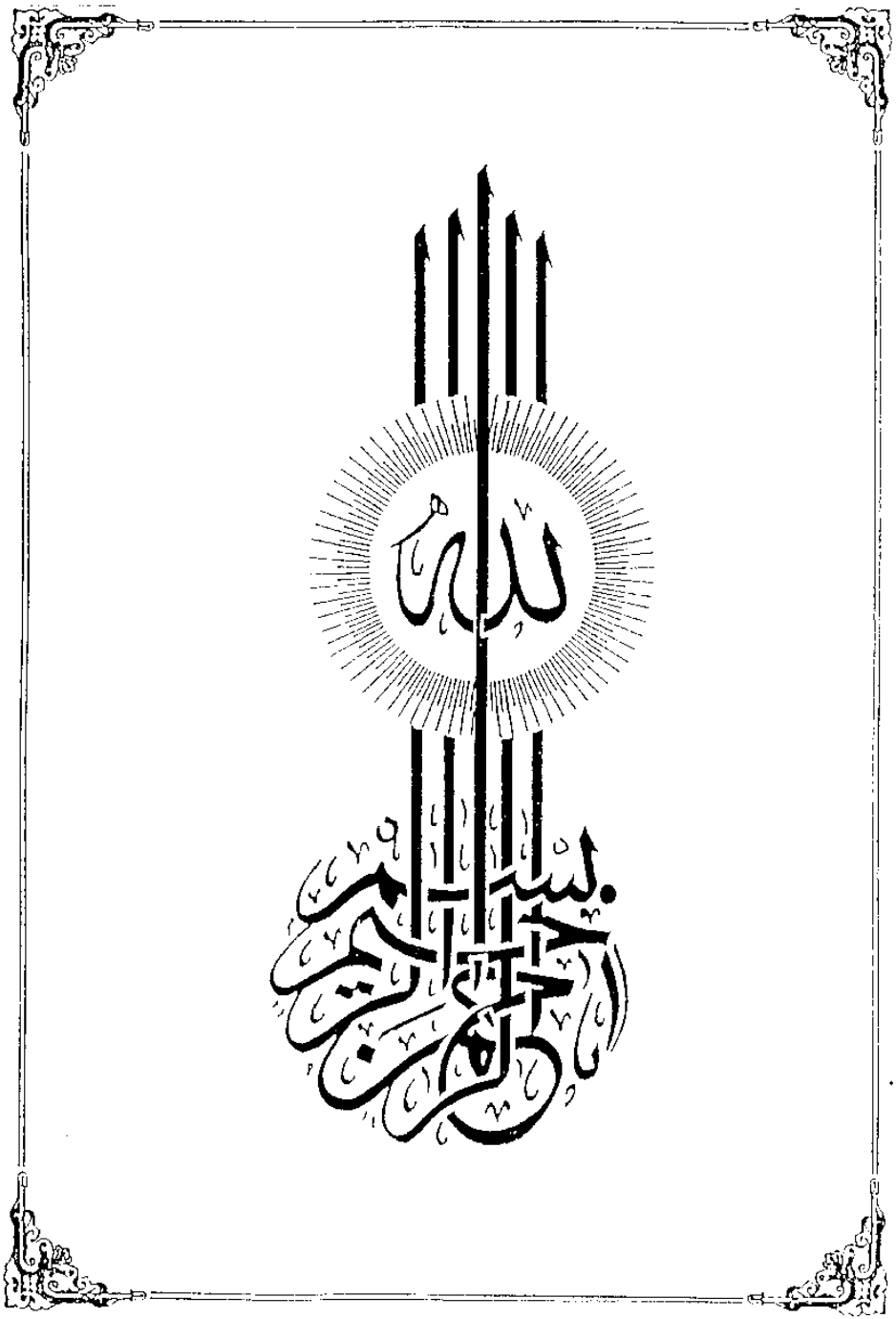
To

My Parents

My Husband

and

My Daughters



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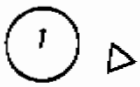
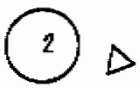


List Of Abbreviations

ABBREVIATIONS

- GTN : Gestational Trophoblastic Neoplasia.
- HCG : Human Chorionic Gonadotrophin.
- RIA: Radio Immuno Assay.
- L.H: Luteinizing Hormone.
- MRI : Magnetic Resonance Imaging.
- MAC : Methotrexate, Dactinomycin, Cyclophosphamide.



Introduction and Aim of The Work

INTRODUCTION

Trophoblastic disease is a clinical term used to indicate three closely related conditions that are characterized by active proliferation of trophoblastic cells; hydatidiform mole, invasive mole and choriocarcinoma (Begent, 1990). Hydatidiform mole is the result of degenerative changes following the death of the embryo and may be precursor for invasive mole and choriocarcinoma which are considered to be malignant neoplasms (Ramzy, 1983).

Tumours arising from the trophoblast form a continuous spectrum, from the benign behaviour of the majority of hydatidiform moles which die out spontaneously following evacuation to highly aggressive tumours, which are histologically choriocarcinoma, that can be fatal within a matter of weeks. During normal pregnancy the trophoblast has special properties which allow it to invade the myometrium and form intimate connection with the maternal circulation. Tumours deriving from the trophoblast retain this capacity to invade locally into the myometrium and have a high propensity to spread via the blood stream to the lungs and other sites (Jones, 1990).

Trophoblastic tumours arising from epithelium of trophoblast which result from fertilization of ovum or may occur primarily in teratomas (Tindall, 1987).

AIM OF STUDY

This study is undertaken to evaluate the role of ultrasound in the management of malignant gestational trophoblastic neoplasia at Ain Shams Obstetrics and Gynaecology Hospital.

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Review of Literature (Normal Trophoblast & Gestational Trophoblastic Neoplasia

A. HISTORY

In 1889 Sanger first suggested that there was a special tumour which was derived from the decidua of pregnancy.

In 1895 Marchand demonstrated that these tumours originated exclusively from the chorionic epithelium, consisting of syncytiotrophoblastic & cytotrophoblastic cells. However, Marchand adhered to the prevalent idea that syncytiotrophoblast was of maternal origin & cytotrophoblast of fetal origin. It was Gottschalk (1894) who said that choriocarcinoma was a tumour of fetal tissue.

In 1903 Teacher wrote his classic paper on chorionic tumours further defining the spectrum of trophoblastic tumours of uterine origin. Since then a great amount of information has been accumulated regarding the natural history of the disease, its histopathogenesis, hormonal production and host tumour relationship (Ratnam and Ilancheran, 1982).

B. EMBRYOLOGY

After fertilization of the ovum, the zygote is formed and diploid number of chromosomes is restorted, cleavage begins at once and soon a solid cluster of cells called the morula. Fluid accumulates in the centre and blastocyst stage is reached (Ratnam and Ilancheran, 1982).

The blastocyst become attached to the uterine mucosa 6 to 7 days after ovulation and fertilization. In human it is embeded in the endometrium by 7.5 - 8 days. It is a flattened plate of cells surrounded by a small amniotic vesicles and the yolk sac, and these contained within the fluid-filled coelomic cavity. The trophoblast defined as "nourishing tissue" grows rapidly and in a formless manner. It surrounds the chorionic shell and interposes and appreciable cell mass between the maternal tissue and coelomic cavity. As the trophoblastic cells multiply they become hydropic and small pockets of fluid occur within and among them. The pockets increase in size and number, just as in the morula when fluid accumulate within the free ovum during formation of the blastocyst (Reynolds, 1972).

There is a substantial increase in the trophoblastic elements between 6-9 and 10-12 days after implantation (Hamilton et al., 1962).

In this early stage the endometrium itself provides sufficient nourishment for the ovum. Erythrocytes and white cells are seen in early trophoblastic vacuoles, some lacunae contain clotted blood. Necks of uterine glands are

compressed and their coils distended with blood tinged secretion; fibrinous exudations appear between the trophoblast and maternal tissues in the wall of area (Ratnam and Ilancheran, 1982).

Previllous stage :-

Two or three days after implantation the primitive trophoblastic cells contain fluid and these fluid filled pockets enlarge. Where there is extracellular fluid, the trophoblastic cells form a special covering layer without boundaries between the cells. These form the syncytiotrophoblast, and parent cells are called cytotrophoblast. when the fluid filled vacuoles touch and coalease the enlargement are called lacunae these form the primitive intervillous spaces of the future placenta.

The walls of maternal veins weaken and blood begins to enter the lacunae. The circulation of maternal blood through lacunae is delayed untill maternal capillaries open into the lacunae twelves days after ovulation (Ratnam and Ilancheran, 1982).

Villous period :

Significant changes occur in these period between ten and twenty-one days after ovulation. Numerous columns of cytotrophoblastic cells covered with syncytiotrophoblast form within the chorionic trophoblastic shell. This is associated with enlargement of lacunae. This shell invades and ingests adjacent maternal tissue, the columns increase in diameter and a cone of mesodermal cells is formed inside each one. Angioblast cells develop and

are numerous through out each villus, but don't yet from blood capillaries. Angiogenic and haematopoietic foci formed around the yolk sac of the embryo at 13.5 to 15 days after conception (Ratnam and Ilancheran, 1982).

Deportation of trophoblast :

In the course of erosion into maternal endometrium some trophoblastic villi become detached and are carried into systemic circulation to reach distant parts of the body, most frequently the lungs, this trophoblastic embolisation was noted as early at 1893 by schmorl in German literature.

Douglas et al (1959) and Attwood and Park (1961) have shown that trophoblastic deportation is an apparently innocuous and almost physiological phenomenon. It is well tolerated in normal woman. It remains to be determined with that frequently this process of deportation leads to pulmonary noduler lesions. Attwood and Park (1961) found some clearly identifiable trophoblast cells in the lungs of nearly half of 220 patients reviewed. There is an obscure defence mechanism where by most of the emboli are presumably quiety and unevent fully held in check and removed. At term the placenta is expelled and the trophoblast ectopic sites undergo resorption usually within a fortnight or so of delivery, the normal trophoblast, therefore shows some of the characteristic of malignancy, such as invasiveness, rapid growth and embolisation (Ratnam and Ilancheran, 1982).