The Pathology of the Endometrium and the Ovary in Association with Uterine Fibroid

THESIS

PRESENTED TO FACULTY OF MEDICINE
AIN SHAMS UNIVERSITY
IN PARTIAL FULFILMENT FOR THE MASTER
DEGREE IN PATHOLOGY

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1982

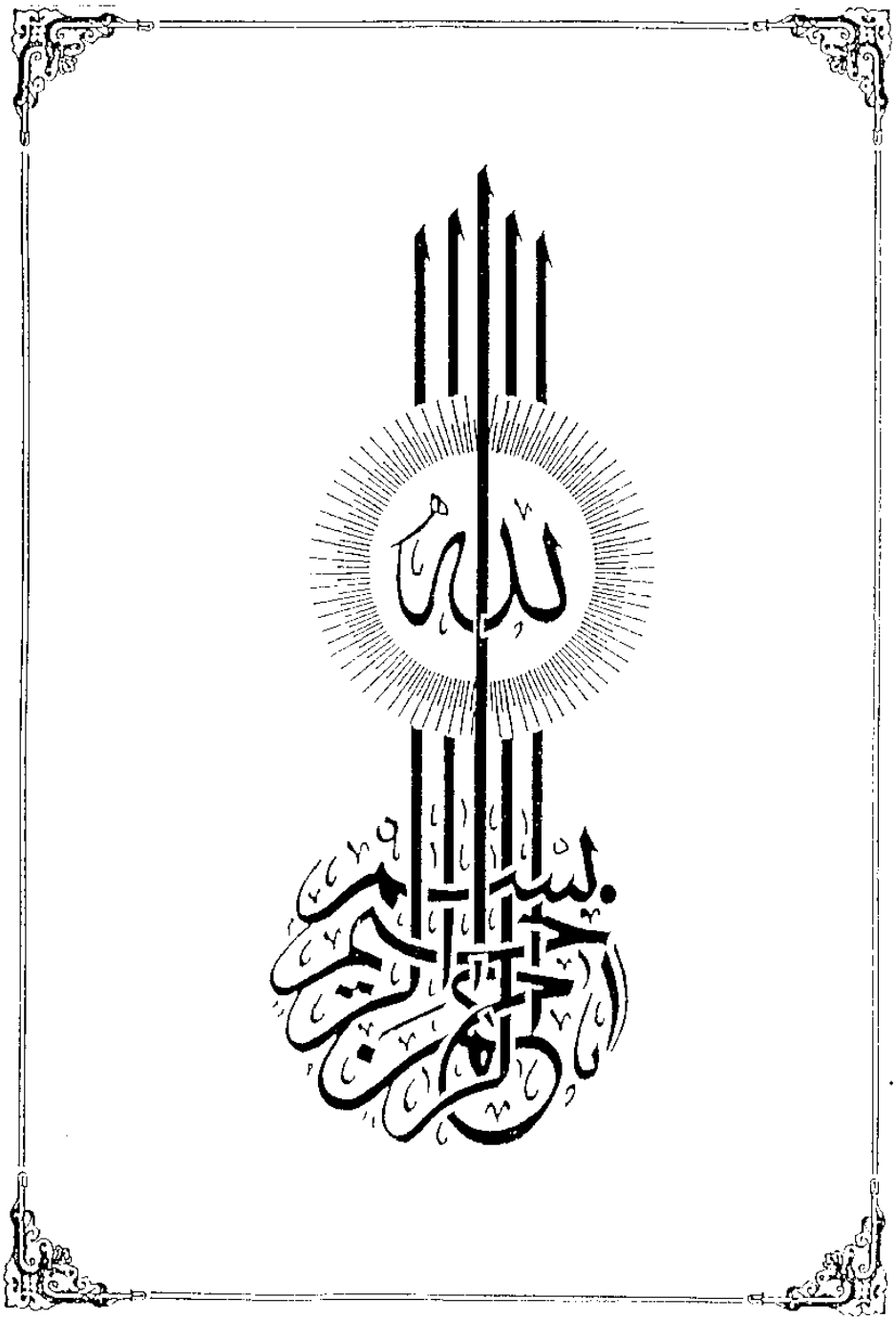
A C K N O W L E D G E M E N T

It is with great difficulty that I endeavour to thank Prof. Mourad Aly Sherif, Head of the Pathology Department, Ain Shams University, who supervised thedetails of the work and enriched me with his vast experience.

To my Prof. M.B. Sammour, Prof. of Gynaecology and Obstetrics, Ain Shams University, I express my profound gratitude for his continuous sincere encouragement, supervision,helpful suggestions and valuable advice which were essential for my work to be finally achieved.

I wish heartly to acknowledge my thanks and sincere gratitude for Prof. Iglal Abd El Razek, Prof. of Pathology for her valuable criticism, helpful guidance and directions.

I am also thankful and grateful to Dr. Mahmoud El Shourbagy, Lecturer of Obstetrics and Gynaecology for his continuous supervision and advice. He gave me generously of his time and help throughout the period of this work.



C O N T E N T S

I N T R O D U C T I O N

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One of the most common human tumours and much the most frequent uterine neoplasm, is the myoma. Autopsy studies have shown that approximately 20% of women over 30 years harbour uterine myomas of various sizes, though often there have been no symptoms produced (Novak and Woodruff 1979).

Walker (1976) noted that these common and benign tumours of the uterus, derived from muscle tissue, have been variously designated myomas, leiomyomas and fibromyomas. Although fibroleiomyoma is more strictly accurate, the term which has acquired almost universal usage is the uterine fibroid.

Haines and Taylor (1975) mentioned that the cause of uterine leiomyomas is undetermined. Many factors have been considered on theoretical grounds but practical support is lacking. The fact that these tumours occur during the reproductive era and retrogress after the menopause has been offered to substantiate the possible role of ovarian hormones in the aetiology of uterine myoma.

Jeffcoate (1975) stated that the bleeding , commonly, associating leiomyoma can be mainly attributed

to an increase in size of the endometrial cavity and of the bleeding surface, increased vascularity of the uterus, associated endometrial hyperplasia, compression of veins by the tumour with consequent dilatation and engorgement of venous plexuses in the endometrium and myometrium and interference with uterine contractions.

Novak and Woodruff (1979) said that especially interesting is the condition of the endometrium in association with myoma. The mucosa over submucous tumours exhibits atrophy and thining while the rest of the endometrium may show little or no departure from the normal. The endometrium as well may be non ovulatory or hyperplastic or even of maligunat nature.

The ovary is the main source of estrogen in the female during the reproductive period. It seems that leiomyomas are dependent on estrogen for continued growth and it is possible that estrogen is also a factor in endometrial hyperplasia and carcinoma. Thus one may anticipate the association of estrogen producing lesions of the ovaries with uterine leiomyoma and endometrial lesions as hyperplasia or carcinoma.

R E V I E W

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History Of Leiomyoma

Miller and Ludovici (1955) stated that the long usage of the word "fibroid" has firmly established this term in medical parlance and that the term fibroid is used in its popular sense as referring to all types of uterine myomas.

Ampofo (1964) said that technically, fibroids should be called myomas because they are specifically tumours of smooth muscle, the fibrous component represents the stroma and is not a part of the neoplasm itself.

Haines and Taylor (1975) mentioned the names applied in the past to describe this neoplasm as scleroma by Galen and womb stone by Hippocrates. They added that the term fibromyoma is generally accepted and the description as fibroid is in common use, though in some countries myoma is the preferred term.

Incidence

Miller and Ludovici (1955) stated that one out of every four or five women over 35 years of age has a uterine fibroid. They added that this high incidence does not mean that all these cases have symptom producing tumours.

Novak and Woodruff (1979) in autopsy studies reported 20% of uterine myomas in women over the age of 30 years.

Histogenesis

Novak and Woodruff (1979) stated that there have been differences of opinion as to whether the mature muscle fibres of the uterus, or certain immature indifferent elements in the musculature, are the starting point of tumour formation, and also as to whether or not the tumour arises from muscle elements in the blood vessel wall.

Meyer (1930) observed immature muscle cells in the uterine wall and he suspected that these were tissues from which fibroids could develop.

De Snoo (1934) discovered " genitoblasts" in the uterine wall which he believed that under certain conditions of ovarian dysfunction could grow into uterine fibroids.

Miller and Ludovici (1955) did tissue culture experiments which supported the theory of origin from smooth muscle cells rather than from connective tissue fibres.

Ampofo (1964) stated that leiomyomas are specifically tumours of smooth muscle and the fibrous component represents the stroma of the tumour and is not part of the neoplasm itself.

Honore (1977) supported the theory of "vascular" origin of leiomyomas as he found a uterine leiomyoma with hemangiopericytomatous foci, so he supposed that the vascular pericyte is the mother cell of both uterine leiomyoma and hemangiopericytoma.

Aetiological Factors

Various theories of the origin of leiomyoma have been proposed, but no accepted theory has yet been advanced.

1. Racial factors

Torpin et al. (1942) in an analysis of nearly 2000 cases, found leiomyomas to be three times as common in the American Negroes as in the white population.

Miller et al. (1953) reported that leiomyoma is commoner in the pure African Negroes, as the American Negroes represent a mixture of races.

2. Age

Ampofo (1964), Haines and Taylor (1975) and Jeffcoate (1975) independently reported that uterine leiomyomas are extremely rare before the age of 20 years old and for the first time after the age of 50 years. They also noted

that these tumours most commonly cause symptoms in women 35-45 years of age.

3. Parity

Witherspoon (1933), Miller et al. (1953) and Jeffcoate (1975) independently stated that leiomyomas are common in virgins, nulliparae and absolutely or relatively infertile females but it was not known whether sterility causes leiomyoma or visa versa.

4. Role of estrogen

Moench (1929) was one of the first to write on this subject. He suggested that the role of estrogen in the development of leiomyomas is based upon the observation that these tumours develop only during the active sexual and reproductive life of the woman. He explained that human female shows leiomyomas more frequently than other primates as being due to continued ovarian activity present in human female. He also stated that there are few leiomyomas of the tube and cervix as these structures are normally incapable of reacting much to the ovarian hormones.

These observations were greatly amplified and given widespread appreciation by Witherspoon (1933) who

emphasized the frequency with which he had found endometrial hyperplasia accompanying uterine leiomyoma. He reached the hypothetical conclusion that " the unopposed action of estrogen in the absence of corpus luteum influence, if prolonged sufficiently would result in leiomyomatous growths". This conclusion was largely based on a 100% incidence of endometrial hyperplasia in a series of 124 uteri which contained myomatous tumours and 26 cases of endometrial hyperplasia which later developed leiomyomas.

Kanter et al. (1936) in a careful study of 100 patients with leiomyomas, found hyperestrinism to play a part, but not the only one in the aetiology of leiomyoma, so concluded that various factors must be associated. They found endometrial hyperplasia in 55% out of their 100 cases.

Wharton (1943) agreed with the hypothesis of Witherspoon and stated that this neoplasm's dependence upon ovarian stimulation is shown by the effect of ovariectomy which was formerly a method of treating myomas and he mentioned a case in which bilateral oophorectomy was followed by complete disappearance of a huge myoma.

Granjon et al. (1961) found high estrogen levels in women with uterine leiomyomas.

Rechnitz and Domotori (1964) examined 1,255 cases of myomatous uteri and they found increased estrogenic activity in 59% of the cases.

On the other hand, Nelson (1937) injected 32 guinea pigs with various estrogenic substances over a period of 2 to 10 months and was able in 6 cases to produce growths in and about the uterus but the growths were fibrous tissue only, not leiomyomatous and usually were not in the myometrium.

Furthermore Henderson (1941), found Swiss-cheese type of endometrial hyperplasia in 6.5% of 727 leiomyomatous uteri and he stated that in his group, endometrial hyperplasia as an evidence of prolonged unopposed or excessive estrogen stimulation did not occur with sufficient frequency to justify a conclusion that such a disturbance of estrogen production plays any role in the origin of uterine fibroids.

Theophanidis and Mantalenakis (1966) found no significant difference in percentage of endometrial hyperplasia between 360 with myomatous and 120 with non myomatous uteri.

Hecht (1951) in an analysis of 4, 461 cases by vaginal smears, found hyperestrinism in 8% of the total and it showed further that 89.33% of these had pathology; most commonly leiomyoma, in 66.86%. Hecht believed that the picture of hyperestrinism as seen in vaginal smear if persistently associating leiomyoma, indicates that this leiomyoma is growing and functionally active even if there are no symptoms associating it. Also his observations revealed that many patients with asymptomatic myomatous uteri do not present the cytological picture of hyperestrinism and he assumed that the leiomyomas in these cases are not activity growing and are of no significance.