Serum Prolactin As A Diagnostic Marker For Uterine Fibroid

Thesis
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Abstract

Objectives: To evaluate the use of serum prolactin as a tumor marker in diagnosing uterine fibroid(s).

Methods: A case control study was carried out from March 2010 to October 2010, at El Kasr El-Aini University maternity Hospital. Thirty patients with uterine fibroid(s) and 30 healthy normal women were involved in the study. Blood samples were collected from uterine fibroid patients before and after surgery. The serum prolactin was measured by ELISA technique.

Results: The serum of patients with uterine fibroid before surgery showed an elevated prolactin level (57.43 $\pm$ 57.85) compared with their prolactin after surgery (21.16 $\pm$ 16.04), and with the control group (12.43 $\pm$ 4.67). This also increased with increasing the fibroid number, size and duration of fibroid related symptoms, independently of the site or the type of the fibroid.

Conclusion: Serum prolactin can be used as an adjuvant biochemical marker to confirm the diagnosis of uterine fibroid(s).

Keywords: Uterine fibroid, prolactin, leiomyoma, tumor markers.

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Pancé Mohamed

List of Abbreviations

5'-UTR	:	5' Untranslated region
ATP	:	Adenosine tri-phosphate
BMI	:	Body mass index
cAMP	:	Cyclic adenosine monophosphate
COCs	:	Combined oral contraceptives
CT	:	Computed tomography
CX	:	Cervix
D1-R	:	Dopamine type 1 receptor
D2-R	:	Dopamine type 2 receptor
DA	:	Dopamine
dPRL	:	Decidual prolactin
DR	:	Dopamine receptor
E	:	Estrogen
ECD	:	Extra cellular domain
ECM	:	Extracellular matrix
EGF	:	Epidermal growth factor
ER	:	Estrogen receptor
ET	:	Endothelins
FGF-2	:	Fibroblast growth factor-2
FGF-R	:	Fibroblast growth factor receptor
FSH	:	Follicle stimulating hormone
GABA	:	Gamma Amino butyric acidγ
GH	:	Growth hormone
GHR	:	Growth hormone receptors
GIT	:	Gasrointestinal tract
GnRH	:	Gonadotropin releasing hormone
GnRHa	:	Gonadotropin releasing hormone agonist
HCG	:	Human chorionic gonadotropin
hGH	:	Human growth hormone

List of Abbreviations *(Cont.)*

HPCM	:	Human placental conditioned medium
HPF	:	High power field
HRT	:	Hormone replacement therapy
HSE	:	Sonohysterography
ICD	:	Intra cellular domain
IGF1-2	:	Insulin growth factor
ILs	:	Interleukins
IUD	:	Intra-uterine device
IVF	:	In vetro Fertilization
IVP	:	Intravenous pyelography
Jak-stat	:	Janus kinase signal transducer and activator of transcription
KDa	:	Kilo Dalton
LH	:	Lutinizing hormone
LIF	:	Leukemia inhibiting factor
LPL	:	Lipoprotein lipase
M	:	Micron
MPA	:	Medroxyprogesterone acetate
MRI	:	Magnetic resonance imaging
mRNA	:	Messenger ribonucleic acid
ng	:	Nanogram
NMR	:	Nuclear magnetic resonance
NSAIDs	:	Non steroidal anti-inflammatory drugs
Ob/ Gyn	:	Obstetric / Gynacology
OCS	:	Oral contraceptives
P	:	Progesteron
P53	:	Tumour suppressor gene
PDGF	:	Platelet-derived growth factor
PGs	:	Prostaglandins

List of Abbreviations *(Cont.)*

PES	:	Post-embolization syndrome
PI3K	:	Phosphoinositide-3 kinase
PIF	:	Prolactin inhibitory factor
Pit-1	:	Pituitary- specific transcription factor
PKA	:	Protein kinase A
PKC	:	Protein kinase c
PL	:	Placental lactogens
PRF	:	Prolactin releasing factor
PRL	:	Prolactin
PRLR	:	Prolactin receptors
PTHrP	:	Parathyroid hormone related peptide
PVA	:	Polyvinyl alcohol
RIA	:	Radioimmuno assay
RT-PCR	:	Reverse Transcriptase – Polymerase chain reaction
RU 436	:	Mifepristone
SERMs	:	Selective estrogen receptor modulators
SIS	:	Saline infusion sonography
SMCs	:	smooth muscle cells
SOCS	:	Suppressor of cytokine signaling
SPRMs	:	Selective progesterone receptor modulators
TGF-B	:	Transforming growth factor-B
TIDA	:	Tuberoinfundibular neurons
TM	:	Transmembrane domain
TNF-α	:	Tumour necrosis factor-α
TRH	:	Thyrotropin releasing hormone
TV	:	Transvaginal
u/s	:	Ultrasound
UAE	:	Uterine artery embolization
UFE	:	Uterine fibroid embolization
VEGF	:	Vascular endothelial growth factor
VGCCs	:	Voltage gated Ca^{2+} channels
VIP	:	Vasoactive intestinal peptide

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INTRODUCTION

Uterine fibroid (leiomyoma) is the most common bengin uterine tumors in women of reproductive age which originates from the smooth muscle layer and the accompanying connective tissue of the uterus ***(Jolley, 2009).***

Although the incidence and natural history of the uterine fibroids are not fully understood. Uterine fibroid formation and development varies with age, increasing in the middle and late reproductive period and with ethinc origin, with African American women being disproportionately affected ***(Hoffman, 2009).***

Many studies have suggested that uterine leiomyomas are monoclonal tumors derived from a single neoplastic myometrial cell, and neoplastic transformation of myometrium to leioymyosarcoma occurs in less than 1% of fibroids ***(Tai et al., 2003).***

prolactin **(PRL)** is trophic horomone produced mainly by the pituitary gland but also secreted by extrapitutary site as (uterus, colon, …. etc). **I**n addition to the decidualized endometrium of the late luteal phase and of pregnancy the human myometrium has been proposed as a second source of **uterine PRL** ***(Gellersen et al., 1991)***.

Many studies showed increasing evidence of **PRL** effects and say that **PRL** plays a role in several types of cancer in the reproductive and non reproductive tissues via local production or accumulation ***(Ben-Jonathan et al., 2002)***.

PRL production may be a potential marker for detecting an early occult fibroid tumor or for gauging the effectiveness of therapy ***(Flake et al., 2003).***

Considering **PRL** as an active participant in tumorigenesis should inspire and encourage the development of novel therapies aimed to reducing PRL production or by blocking its receptors ***(Somiglanaa et al., 2007).***

AIM OF THE WORK

A case control study aimed to evaluate the possible relationship between circulating levels of **PRL** with **uterine fibroid(s)** and the possibility of these parameters to be used as a diagnostic marker of the tumor.

Uterine fibroid

Definition:

Uterine fibroid also called (uterine leiomyoma, myoma, fibromyoma, leiofibromyoma and fibroma). It is a bengin tumor that originates from the smooth muscle layer (myometrium) and the accompanying connective tissue of the uterus (**Fig 1)** ***(Jolley, 2009)***.

Fig. (1): Uterine Fibroids (leiomyomas) ***(Jolley, 2009*).**

Incidence (prevalence):

Fibroids are the most common bengin solid pelvic tumors in females. Fibroids tend to develop in women in their thirties and forties. Although estimations of the number of women whose are affected vary considerably with figures ranging from 20% to 70%, it is generally accepted that about one in three women will develop fibroids ***(Cornforth, 2009).***