Effect of Secondary Hyperparathyroidism on Platelet Aggregation & Platelet Count in Uremic Patients

Thesis
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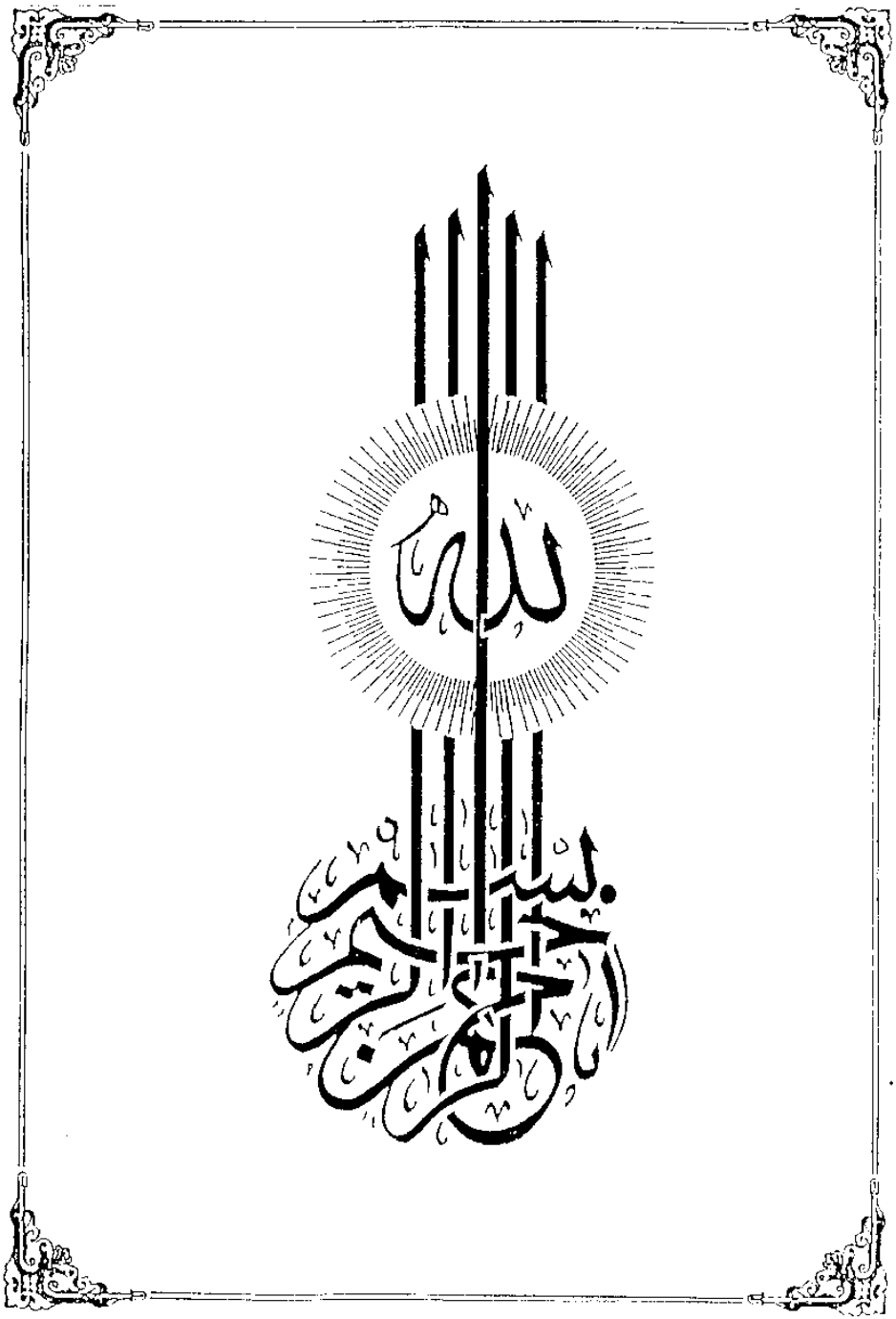

List of Errata

Page	Line	Wrong	Correct
List of abbreviations	7	CLIS	CLIA
1	14	1990	1991
4	2	Remuzzi et al.	Remuzzi
5	4	Cycloxygenase	Cyclooxygenase
6	18	clothing	clotting
7	1	Sizinger	Sinzinger
7	2	arochidonic	arachidonic
7	2	cycleooxygenase	cyclooxygenase
7	18	1980	1960
8	13	guanidinosuccinec	guanidinosuccinic
10	11	Fernandez et al. [1982]	[Fernandez et al., 1982]
11	12	clothing	clotting
13	10	B-thromboglobulin	β-thromboglobulin
13	15	maintain-ing	maintaining
15	5	there by	thereby
15	14,20,22	B-TG	β-TG
16	4	B-TG	β-TG
16	5	where as	whereas
17	2	collaegues	colleagues
18	18	lubbecke	Lubbecke
20	16	extra cellular	extracellular
22	18	exagerated	exaggerated
24	19	hyperpara-throidism	hyperparathyroidism
24	20	hemtochemical	hematochemical
24	22	bsis	basis
24	24	hyperparthyroidism	hyperparathyroidism
25	11	elevated triglycerids	Elevated triglycerides
25	17	aggregaation	aggregation
26	8	near	mean
26	20	corelation	correlation
27	1	patient	patients
29	8	lipo-oxygenase	lipooxygenase
34	9	dyslipoprotein-emia	dyslipoproteinemia
34	12	Avriam	Aviram
35	8	Knudsen et al.	Knudsen and Dyeberg
35	15	show	shows

List of Errata (Cont.)

Page	Line	Wrong	Correct
35	16	Dyerberg	Dyeberg
38	8	jujenum	jejunum
40	8	. With	, with
41	4	1991	1992
41	13	Kumar	Kumar and Clark
42	4	PTH	vitamin D
42	11	PTH	vitamin D
42	16	1991	1992
43	1	PTH	vitamin D
45	9,10	Thyroxine	Thyroxin
47	9	extra-acellular	extracellular
47	16	1991	1992
48	3	1991	1992
50	9	1991	1992
50	14	osteoclsts	osteoclasts
51	22	electroence-phalogram	electroencephalogram
54	2	for	far
55	5	equilibriate	equilibrate
55	6,7	═══	⟸
56	3	heterogenity	heterogeneity
56	19	in	is
60	6	Calorimetrically	Colorimetrically
65	16	Oldman	Oldham
68	4	hemodialy-sis	hemodialysis
69	15	chromic	chronic
70	16	are	is
72	14	normocacemic	normocalcemic
74	4	glomenrulonephritis	glomerulonephritis
74	4	pyelonephiritis	pyelonephritis
75	6	Urease	Urease →
76	3	Units litre	Units/litre
80	14	an vitro	an in vitro
85	8	91.28	91.22
102	12	x 100	x 1000
103	1	Table (2)	Table (8)
104	1	Table (3)	Table (2)

List of Errata (cont.)

Page	Line	Wrong	Correct
105	1	Table (4)	Table (3)
106	1	Table (5)	Table (4)
107	1	Table (6)	Table (5)
108	1	Table (7)	Table (6)
108	5	Table (8)	Table (7)
123	1	patient	patients
124	14	Dyerberg	Dyeberg
127	16	PH	pH
129	22	correlations	correlation
131	12	hypercatabolsim	hypercatabolism
137	5	Avriam	Aviram
137	7	Avriam	Aviram
137	26	1983	1982
138	15	Blumen Krantz	Blumenkrantz
139	21	Brumbough	Brumbaugh
139	24	Buccianrti	Buccinarti
142	7	Deuel	Duel
146	16	Harries	Harris
147	17	1985	1975
148	10	Janson	Jonson
148	13	Jargensen	Jorgensen
148	24	1975	1984
148	26	Dyerberg	Dyeberg
160	11	Warrell	Warell
160	24	1985	1983
161	1	Whittle and Moncader	Whitle and Moncadar
161	7	1985	1981
161	17	Yardmuian	Yardumian
161	22	Zuker	Zucker

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LIST OF ABBREVIATIONS

ADP	Adenosine diphosphate.
ATP	Adenosine triphosphate.
ATP-ase	Adenosine triphosphatase.
B.TG	Beta-thromboglobulin.
cAMP	Cyclic adenosine monophosphate.
CLIS	Chemiluminescence immunoassay.
CRF	Chronic renal failure.
C-terminal	Caboxy terminal (i.e. carboxy terminal fragment of PTH)
CUP	Cuprophane membrane
$(Ca^{2+})_i$	Intracellular calcium
ECF	Extracellular fluid
ICMA	Immunochemiluminometric assay
IRMA	Immunoradiometric assay
mRNA	Messenger ribonucleic acid
N-terminal	Amino terminal (i.e amino terminal fragment of PTH
PF-3	Platelet factor-3
PGE_2	Prostaglandin E_2
PGI_2	Prostacyclin
P.T.H.	Parathyroid hormone
RIA	Radioimmunoassay
vWF	von Willebrand factor
1,25 $(OH)_2D_3$	1,25 dihydroxycholecalciferol
VIII:C	Clotting component of factor VIII

INTRODUCTION

INTRODUCTION

Abnormal hemostasis is a common derangement in chronic renal failure (i.e. tendency to hemorrhagic events). The modern management of renal failure has definitely reduced the incidence of severe hemorrhage but bleeding complications still represent a problem for uremic patients, particularly during surgery or invasive procedures, **[Remuzzi, 1989].**

A number of qualitative platelet defects have been reported in chronic renal failure including impaired availability of platelet factor-3, reduced platelet retention on glass bead columns, increased calcium content within the platelet, reduced adenosine diphosphate and serotonin levels and increased platelet cyclic adenosine monophosphate.

Also, changes in platelet prostaglandin production have been found in uremia e.g. decreased thromboxane A_2 production in response to ADP and decreased production of prostaglandin E_2 and prostacyclin, **[Eschbach and Adamson, 1990].**

There is a recent suggestion that calcium metabolism and parathyroid hormone may affect platelet functions in renal failure since secondary hyperparathyroidism with markedly elevated blood levels of parathyroid hormone is an almost universal characteristic in chronic renal failure, it has been suggested that parathyroid hormone is a major uremic toxin which could be responsible for many manifestations of uremic syndrome. Thus an excess of

parathyroid hormone may play a part in pathogenesis of uremic thrombocytopathy, **[Docci et al., 1986].**

Aim of study:

The aim is to investigate the possible relation between parathyroid hormone and in vitro platelet aggregation and count in chronic renal failure patients on hemodialysis or on conservative treatment.

REVIEW OF LITERATURE

CHAPTER I

PLATELET DYSFUNCTION IN UREMIA

Numerous hemostatic abnormalities have been associated with chronic renal failure. Many studies were conducted in the last 30 years that showed that uremic patients manifested abnormal platelet adhesiveness, aggregation, reduced platelet factor-3 and prolonged bleeding time.

Castaldi and Colleagues [1966], concluded that the bleeding disorder in uremia is due to a qualitative platelet defect which is reversible by dialysis in many cases. They found prolonged bleeding time, impaired platelet aggregation and clot retraction in patients with evident bleeding. In about half of these patients, in vivo platelet adhesiveness and availability of platelet factor-3 were also abnormal. Reduced platelet aggregation and clot retraction were found in half of the group of patients without any bleeding diathesis.

Eknoyan and coworkers [1969], observed a significant inverse correlation between the level of serum creatinine and blood urea, and adhesiveness of platelets. However, **Remuzzi et al. [1978]**, found no correlation between platelet retention on glass beads (which assess platelet adhesiveness and release reaction) and bleeding time and a number of blood chemistry parameters altered in uremia (such as urea, creatinine, uric acid, sodium, potassium, calcium and phosphorus) though both tests were significantly altered in uremics.

Recently, several studies were carried out , in an attempt to define the possible mechanisms underlying platelet dysfunction in uremia, **[Remuzzi et al., 1988; Barradas et al., 1991 and Fluck et al., 1992].** They summarized the most important changes in platelet function as follows:

1- Abnormal platelet arachidonic acid metabolism.

2- Platelet inhibition by uremic plasma metabolites e.g. urea, guanidinosuccinic acid.

3- Abnormalities of factor VIII von Willebrand complex.

4- Anemia.

5- Increased levels of parathyroid hormone (P.T.H.).

6- Platelet storage pool deficiency.

7- Abnormalities of platelet - vascular wall interaction.

I. Abnormal Platelet Arachidonic Acid Metabolism:

The main features of the normal pathway are outlined in the figure: