A study of the Chromosomes In Glioma Cells

Thesis

Submitted for partial fulfillment of M.D. Degree in Anatomy

Presented By

Samy Abd EI-Hameed AbuSikkein

M.Sc. in Anatomy

Supervised by

Professor Doctor/ Mostafa Kamel Ibrahim

Professor and the head of the
Anatomy Department
Faculty of Medicine -Ain Shams University

Professor Doctor/ Hoda Mohamed Mahmoud

Professor of Anatomy
Faculty of Medicine - Ain shams University

Doctor/Azza Salah El-Din Soliman

Assistant Professor of Anatomy
Faculty of Medicine - Ain shams University

Doctor/Hussin EI-Sayed Moharram

Assistant Professor Of Neurosurgery
Faculty of Medicine - Ain Shams University

Doctor/ Ezzat Sayed EI-Sobky

Assistant Professor of Genetics
Faculty of Medicine - Ain Shams University

Faculty of Medicine
Ain Shams University
2005

" وَعَلَّمَكَ مَا لَم تَكُن تَعلَمُ
وَكَانَ فَضلُ اللهِ عَلَيكَ عَظِيمًا "

(سورة النساء جزء من الآية 113)

Acknowledgment

It is not easy to acknowledge all who helped me, directly and indirectly with continuous concern that helped me much during preparation and production of this work.

My profound thanks and appreciation to ***Prof. Dr. Mostafa Kamel Ibrahim,*** *Professor and the Head of Anatomy Department, Faculty of Medicine, Ain Shams University, I owe him a lot of things that can not be enumerated here. However, the inestimable lesson I learned was that the scientific responsibility is hand by hand with coherent thinking. To him, I will be always grateful.*

I would like to express my gratefulness and sincere appreciation to ***Prof. Dr. Hoda Mohamed Mahmoud,*** *Professor of Anatomy, Faculty of Medicine, Ain Shams University, for her endless patience and guidance. She has stood as the motivating power of each aspect of this study.*

I wish to express my greatest gratitude and sincere thanks to ***Prof. Dr. Azza Salah El-Din Soliman,*** *Assistant Professor of Anatomy, Faculty of Medicine, Ain Shams University, for her supervision of this work, valuable remarks and suggestions that helped me in final production of this work.*

I want to express my appreciation to ***Prof. Dr. Hussin El-Sayed Moharram,*** *Assistant Professor of Neurosurgery, Faculty of Medicine, Ain Shams University, for his unforgettable kind assistance, encouragement, valuable suggestions, continuous support throughout the course of this study and his meticulous reviewing of the work.*

I wish to express my thanks to ***Prof. Dr. Ezzat Sayed El-Sobky,*** *Assistant Professor of Genetics Faculty of Medicine, Ain Shams University, and one of the eminences of cytogenetics in Egypt, for his helpful efforts, valuable support and for providing facilities throughout the course of this research. His worthy remarks are beyond words of thanks. He spared no time or effort to help me.*

Furthermore, I wish to express my deepest thanks and gratitude to ***Prof. Dr. Nadia Galal El-Hefnawy,*** *Professor of Pathology, Faculty of Medicine, Ain Shams University, for her guidance and sincere help.*

Finally, I would like to express my deepest thanks and gratitude to all of my professors, colleagues in Anatomy Department, Faculty of Medicine and family members who stood beside me throughout this work giving me their support, sympathy and guidance.

Contents

Subjects ***Page number***

Introduction and Aim of the work ---------- 1

Review of Literature ---------- 3

Chapter 1 (Embryological background)----------**3**

Chapter 2 (Histological background)----------**11**

Chapter 3 (Histopathological review)----------**18**

Chapter 4 (Cytogenetic review)---------- **52**

Subjects and Methods ---------- 138

Results ----------152

Discussion ----------208

Summary ---------- 225

Appendix---------- 228

References ---------- 229

Arabic Summary ----------

List of tables

Number		Page
1	Derivatives of cerebral vesicles from caudal to rostral.	8
2	WHO classification of gliomas.	20
3	WHO classification (2000) of tumors of neuroepithelial tissue.	21
4	Different grading systems of astrocytic tumors.	39
5	Symbols used in describing a karyotype.	82
6	Some transforming retroviruses.	109
7	Functional classification of oncogenes.	114
8a	Age distribution among the studied cases.	152
8b	Gender distribution among the studied cases.	152
9	The clinical and karyotypic findings of the studied cases.	157
10	The clinical and histopathological findings of the different karyotypic groups.	158
11	The clinical and karyotypic findings of the different histopathological groups.	159
12	Relation between age of the studied cases and karyotypes.	203
13		204

14	Relation between gender and karyotyping in the studied cases.	205
15	Relation between symptomatology and karyotyping in the studied cases.	206
16	Relation between histopathology and karyotyping in the studied cases.	207
	Relation between WHO grading of the studied cases and karyotyping.	

List of abbreviations

Abbreviation	Full Name
abl	Abelson leukaemia
BANF	Bilateral Acoustic Neurofibromatosis
CAAT	Cytosine-Alanine-Alanine-Thyronine
C-banding	Constitutive heterochromatin banding
CDK 4	Cyclin Dependent Kinase 4
CDKIs	Cyclin dependent kinase inhibitors
CDKN 2	Cyclic AMP dependent kinase number 2
CDKs	Cyclin dependent kinases
CG	Cytosine-Guanine
CGH	Comparative genomic hybridization
CMF	Calcium and Magnesium Free
CNS	Central Nervous System
CNTF	Ciliary Neurotropic Growth Factor
C-onc	Cellular oncogene
CSF	Cerebrospinal fluid
CT	Computed tomography
CTGF-β	Cytokine Transforming Growth Factor-β
dms	Double minute chromosomes
DNA	Deoxy ribonucleic acid
EGF	Epidermal growth factor
EGFR	Epidermal growth factor receptor

erb-B	Avian erythroblastosis
FBS	Fetal bovine serum
FGF 2	Fibroblast growth factor 2
FGFs	Fibroblast growth factors
FISH	Fluorescence in situ hybridization
fos	FBJ murine ostosarcoma
G0	Gap 0 phase of cell cycle
G1	Gap 1 phase of cell cycle
G2	Gap 2 phase of cell cycle
G banding	Giemsa banding techniques
GBM	Glioblastoma multiforme
GTG	G-bands by trypsin using Giemsa
Ha-ras	Harvey murine sarcoma
Hx&E	Haematoxyline & Eosin
ICP	Intracranial pressure
IL-12	Interleukin 12
INF	Interferone
ISCN	International System for human Cytogenetic Nomenculature
Ki-ras	Kirsten murine sarcoma
LOH	Loss of Heterozygosity
MDM 2	Murine double minute 2
MHC	Major Histocompatibility complex
mos	Moloney murine sarcoma
MRI	Magnetic Resonance Imaging

MTSi	Multiple Tumor Suppressor I
myb	Avian myeloblastosis
myc	Avian myelocytomatosis
NF 2 gene	Neurofibromatosis 2 gene
Nor-banding	Nucleolus organizing regions banding
P arm	Petit arm of chromosome
PBS	Phosphate buffer saline
PCR	Polymerase chain reaction
PDGF	Platelet Derived Growth Factor
PDGFR	Platelet Derived Growth Factor Receptor
PDGFR-α	Platelet Derived Growth Factor Receptor alfa
PNS	Peripheral Nervous System
PXAs	Pleomorphic Xanthoastrocytomas
q arm	Long arm of a chromosome
Q-banding	Quinacrine banding techniques
Q-staining	Quinacrine staining
R-banding	Reverse G-banding
Rb gene	Retinoblastoma gene
RNA	Ribonucleic acid
r.p.m.	Revolution per minute
S	Synthesis phase of cell cycle
SD	Standard Deviation
sis	Simian sarcoma
SPSS	Statistical Program for Social Science
src	Rous sarcoma

T-banding	Telomeric region banding
TGF-β	Transforming growth factor-β
T S gene	Tumor suppressor gene
VEGF	Vascular Endothelial Growth Factor
V-onc	Viral oncogene
WHO	World Health Organization

List of figures

Number		Page
1	The formation of neural folds, tube and neural crest.	4
2	Flexures of the early developing brain.	7
3	Histogram of cells in the central nervous system.	9
4	Layers of the cerebral cortex.	12
5	Different types of non-neuronal cells in the CNS.	17
6	Diffuse astrocytoma involving the left cerebral hemisphere.	23
7	Anaplastic astrocytoma of the left cerebral hemisphere.	26
8	Glioblastoma involving both	29
9	hemispheres.	34
10	Subependymal giant cell astrocytoma.	43
11	Oligodendroglioma.	47
12	Ependymoma of 4^{th} ventricle.	53
13	Stages of mitosis.	55
14	Stages of meiosis.	59
15	Types of chromosomes.	61
16	G-banding of X-chromosome.	63
17	Chromosomes 1 and 2 using G-banding.	65

18	Chromosome 3 using G-banding.	65
19	Chromosomes 4 and 5 using G-banding.	67
20	Chromosome 6 using G-banding.	67
21	Chromosomes 7 and 8 using G-banding.	69
22	Chromosome 9 using G-banding.	69
23	Chromosomes 10 and 11 using G-	71
24	banding.	71
25	Chromosome12 using G-banding.	73
26	Chromosomes 13 and 14 using G-	73
27	banding.	75
28	Chromosome 15 using G-banding.	75
29	Chromosomes 16 and 17 using G-	77
30	banding.	77
31	Chromosome 18 using G-banding.	80
32	Chromosomes 19 and 20 using G-	84
33	banding.	85
	Chromosome 22 using G-banding.	
34	Chromosomes X and Y using G-banding.	89
35	Simplified diagram showing DNA	91
36	coiling.	93
37	Structure of the DNA.	94
38	Diagram of the structure of a typical	96
39	human structural gene.	100
40	Generation of somatic mosaicism.	113
41	Karyotype showing triploidy.	116

42	Types of translocation.	119
43	Chromosome inversion.	128
	Karyotype showing ring chromosome.	
44	Normal G-banded male karyotype.	140
45	Steps of signal transduction pathway.	142
46	loss of constitutional heterozygosity.	142
47	Multistage evolution of cancer.	143
48	Clonal numerical chromosome changes in pediatric astrocytic tumors.	143
49	Laminar flow.	144
50	Culture flask.	148
51	CO_2 incubator.	149
52	An inverted microscope.	149
	Growing colonies under inverted	
53	microscope.	153
54	Chamber slide.	154
55	Slides stained using Geimsa stain.	155
56	Imaging analyzer system.	156
57	metaphase spread as shown by imaging analyzer.	164
58	Clinical presentation of the studied cases.	165
	Different sites of the studied tumors.	
59	Histopathological types of the studied	166
60	cases.	167
61	WHO grading of the studied cases.	168

62	Photomicrograph of normal cerebral cortex (superficial layers).	169
63	Photomicrograph of normal cerebral cortex (deep layers).	170
64	Photomicrograph of astrocytoma grade II.	171
	Photomicrograph of astrocytoma grade II.	
65	Photomicrograph of astrocytoma grade II.	172
	Photomicrograph of anaplastic	
66	astrocytoma grade III.	173
67	Photomicrograph of anaplastic	174
68	astrocytoma grade III.	175
69	Photomicrograph of anaplastic	176
70	astrocytoma grade III.	177
71	Photomicrograph of anaplastic	178
72	astrocytoma grade III.	179
73	Photomicrograph of GBM.	180
74	Photomicrograph of GBM.	181
75	Photomicrograph of GBM.	182
76	Photomicrograph of GBM.	183
77	Photomicrograph of GBM.	184
78	Photomicrograph of GBM.	185
79	Photomicrograph of GBM.	186
80	Photomicrograph of GBM.	187
81	Photomicrograph of pilocytic	190
82	astrocytoma.	191