Perinatal Neuropathology

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Preface

The realm of Neuropathology is a special terrain in its own right, compared to other Pathology fields such as general Autopsy or Surgical Pathology. This is in part because of the unique (and daunting!) complexity of the brain's functional organization, which is the core of our minds, personalities, and all of humanity. Add to this complex terrain a fairly rapid shifting of the sands with time (i.e., development). Even seasoned Pathologists may throw up their hands in frustration! It is for these practitioners, trainees, and interested colleagues who may not have had much exposure to Perinatal Neuropathology that we decided to write this book.

So many times, each of the authors have had the experience of delivering a lecture on some topic in Perinatal Neuropathology, and then having been besieged by attendees with specific, practical questions of "how to handle" certain cases, "how to report perinatal findings", and so on. We also have been continually asked "what is normal" in the brain at different developmental stages. To us, these questions have reflected a void in the available teaching resources, and it is our most sincere hope that this book will, to some degree, begin to fill that void. We acknowledge that this book is not a comprehensive "reference text", which every so often assumes the reader is already knowledgeable about the subject matter before they even open the book, but rather this is a practical guide to begin one's understanding of the more usually encountered perinatal case materials in a hospital (and even a forensic) setting. We also acknowledge the ever-accelerating pace of diagnosis of underlying genetic variants, which plays a critical role in the phenotypes illustrated here. We encourage our readers to seek readily available internet sources, some of which are provided within the book, to further refine their comprehension of specific disorders, as needed. Thus, we consider this text but a "starting point" along the path to recognizing the normal as well as abnormal fetal and infant nervous system.

May our experience and intent in sharing this work with the Pathology community, along with our colleagues in Neonatology, Child Neurology, Perinatal Imaging, and Obstetrics, be beneficial to all, and ultimately to our patients and their families.

Lechpammer, Del Bigio, and Folkerth

Acknowledgments

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Dr. Lechpammer: I would like to express my gratitude to all teachers, mentors, colleagues, students and patients who influenced my learning, teaching and practicing in the unsurpassable field of Neuropathology. Professors Zvonko Kusić, Josip Lukač and Mladen Belicza have forever indebted me as I grew into a field of Pathology. Professor Frances Jensen thought me how to think critically and appreciate neuroscience, while I shall never forget the advice of my inspiring mentor Professor Umberto De Girolami to "know my neuroanatomy". Thank you all for making me the professional I am today; you all are still my compasses and Northern stars. This book was an endeavor "against all odds", and it would never come to a fruition without the hard work and support of many. Becky, you were our glue, the engine that pushed us always forward and the best teacher I could ever wish for! Ms. Hilary Gonzales and Ms. Taryn Morningstar kept our checks and balances while navigating through an ocean of figures, references and neuropathology materials. Thank you to an absolutely wonderful staff and editors at Cambridge University Press – you've believed in us from the start and your professionalism, understanding and encouragement has brought us through the finish line. Finally a huge thank you goes to my ultimate inspiration and encouragement – my husband Stan and wonderful kids Laura and Eric. Guys, I would have never made it without your support; and Eric kudos for creating an amazing cover art!

Dr. Del Bigio: I share my gratitude to the late Dr. Dwight Parkinson for introducing him to the world of neurological disorders and to his PhD supervisor Dr. Edward Bruni for teaching him the critical importance of detail. I am indebted to all of my mentors at the University of Toronto and in particular the late Dr. Laurence Becker who instilled in me a fascination of the growing nervous system and how I could have positive impacts on childhood health even when I could not interact with patients directly. I also thank all of my students and colleagues at the University of Manitoba who facilitated my work in the area of developmental neuropathology. Through the thick and thin of education and a research career, my wife Janice has always been supportive of my pursuits. Amid a lifetime of travel and sporting activities together, we have managed to raise two great children.

Dr. Sanda Alexandrescu: I am thankful to my family for being my biggest cheerleader in whatever path I decide to pursue, including academic writing.

Dr. Steven Moore would like to thank Mr. Joel Carl for assistance with the assembly of several figures.

Abbreviations

AAS	atomic absorption spectroscopy
ADHD	attention-deficit/hyperactivity disorder
AES	atomic emission spectroscopy
AFP	alpha-fetoprotein
AIF	apoptosis-inducing factor
AMC	arthrogryposis multiplex congenita
AP	anteroposterior
APCI	atmospheric pressure chemical ionization
APP	amyloid precursor protein
ASAP	atmospheric solid analysis probe
BBB	blood-brain barrier
BC	biochemistry
BDG	beta-D-glucan
BDNF	brain-derived neurotrophic factor
BESS	benign enlargement of the subarachnoid space
BFPP	bilateral frontoparietal polymicrogyria
BPD	biparietal diameter
BPP	biophysical profiling
CA	cornu ammonis
CAGE	cap analysis gene expression
CDT	carbohydrate-deficient transferrin
CE	capillary electrophoresis
CEDIA	cloned enzyme donor immunoassay
CFTD	congenital fiber-type disproportion myopathy
CGH	comparative genomic hybridization
CHN	congenital hypomyelinating neuropathy
CK	creatine kinase
CLIA	chemiluminescence immunoassays
CMAP	compound muscle action potential
CMS	congenital myasthenic syndromes
CMT	Charcot-Marie-Tooth disease
CNS	central nervous system
CP	cortical plate
CPT	choroid plexus tumors
CSF	cerebrospinal fluid
CST	corticospinal tract
CT	computed tomography
CVS	chorionic villus sampling
CZE	capillary zone electrophoresis
DA	distal arthrogryposis
DART	direct analysis in real time
DESI	desorption electrospray ionization
DG	dentate gyrus
DHAPAT	dihydroxyacetone-phosphate acyltransferase
DI	direct injection
DIOS	desorption/ionization on porous silicon
DS	Down syndrome
DSD	Dejerine-Sottas disease
DTI	diffusion tensor imaging
DWMG	diffuse cerebral white matter gliosis
EGL	external granule cell layer
EIA	enzyme immunoassays
ELISA	enzyme-linked immunosorbent assay
EM	electron microscopy
EMG	electromyography
EMIT	enzyme multiplied immunoassay technique
ER	endoplasmic reticulum
ERT	enzyme replacement therapy
ESI	electrospray ionization
FAOD	fatty acid oxidation disorders
FASD	fetal alcohol spectrum disorder
FCD	focal cortical dysplasia
FFPE	formalin fixation and paraffin embedding
FGF	fibroblast growth factor
FISH	fluorescent in situ hybridization
FLAIR	fluid-attenuated inversion recovery
FXMRP	fragile X mental retardation protein
FXPOI	fragile X-associated primary ovarian insufficiency
FXS	fragile X syndrome
FXTAS	fragile X-associated tremor ataxia syndrome
GAD	glutamic acid decarboxylase
GC	gas chromatography
GFAP	glial fibrillary acidic protein
GHB	gamma-hydroxybutyric acid
GI	gastrointestinal
GMH	germinal matrix hemorrhage
GSDs	glycogen storage disorders
GU	genitourinary
GW	gestational week
H&E	hematoxylin and eoxin
HC	head circumference
hCG	human chorionic gonadotropin
HGF	hepatocyte growth factor
HIE	hypoxic-ischemic encephalopathy
HKHG	hypoketotic hypoglycemia
HMSN	hereditary motor and sensory neuropathy
HPE	holoprosencephaly
HPLC	high-performance liquid chromatography
HSCT	hematopoietic stem cell transplant
ICD	inner canthal distance
IEM	inborn errors of metabolism
ILAE	International League against Epilepsy
IR	infrared
ISCA	International Standard Cytogenomic Array
iSDA	isothermal strand displacement amplification
ISOL	in situ oligonucleotide ligation
ISSD	infantile free sialic acid storage disease
IVH	intraventricular hemorrhage
IZ	intermediate zone
LAL	limulus amoebocyte lysate
LC	liquid chromatography

List of Abbreviations

LCD	linker cell-type death
LCHAD	long-chain 3-hydroxyacyl-CoA dehydrogenase
LCMV	lymphocytic choriomeningitis mammarenavirus
LFA	lateral flow assays
LFB	luxol fast blue
LGN	lateral geniculate nucleus
LM	light microscopy
LMP	lysosomal membrane protein
LSD	lysosomal storage disorder
LVI	large volume injection
MAG	myelin-associated glycoprotein
MALDI	matrix-assisted laser desorption/ionization
MBP	myelin basic protein
MCAD	medium-chain acyl CoA dehydrogenase
MCC	multiple congenital contractures
MCP	middle cerebellar peduncle
MDDG	muscular dystrophy-dystroglycanopathy
MIF	migration inhibitory factor
MLD	metachromatic leukodystrophy
MPC	multipotent muscle progenitor cell
MPS	mucopolysaccharidoses
MR	magnetic resonance
MRF	myogenic regulatory factor
MRI	magnetic resonance imaging
MS	mass spectrometry
MSUD	maple syrup urine disease
MVUP	maternal vascular underperfusion
MZ	marginal zone
NAAT	nucleic acid amplification test
NBS	newborn screening
NC	notochord
NCCD	Nomenclature Committee on Cell Death
NCM	neurocutaneous melanosis
NFAT	nuclear factor of activated T-cells
NGS	next-generation sequencing
NIPT	non-invasive prenatal tests
NK	natural killer
NMD	neuronal migration disorder
NMJ	neuromuscular junction
NMps	neuromesodermal progenitors
NT	neural tube
OCD	outer canthal distance
OPC	oligodendroglial progenitor cell
OR	operating room
PAA	plasma amino acids
PAC	plasma acylcarnitine
PCR	polymerase chain reaction
PFA	paraformaldehyde
PKU	phenylketonuria
PLP	proteolipid protein
POI	primary ovarian insufficiency
PP	preplate
PPE	personal protective equipment
PS	Patau syndrome
PVH	periventricular hemorrhage
PVHI	periventricular hemorrhagic infarction
PVL	periventricular leukomalacia
PWML	punctate white matter lesions
qPCR	quantitative or real-time polymerase chain reaction chemistries
RBC	red blood cells
RCA	Ricinus communis agglutinin
Rh	Rhesus factor
RIA	radioimmunoassay
ROS	reactive oxygen species
RRF	ragged red fibers
SAF	subcortical association fibers
SALDI	surface-assisted laser desorption/ionization
SAS	subarachnoid space
SBH	subcortical band heterotopia
SD	standard deviation
SDA	strand displacement amplification
SDH	subdural hemorrhage
SEGA	subependymal giant cell astrocytomas
SELDI	surface-enhanced laser desorption/ionization
SEN	subependymal nodules
SEND	surface-enhanced neat desorption
SG	subpial granular layer
Shh	sonic hedgehog
SIDS	sudden infant death syndrome
SIM	selected ion monitoring
SMP	spinal muscular atrophy
SNP	single nucleotide polymorphism
SP	subplate zone
SPE	solid-phase extraction
SRT	substrate reduction therapy
STR	small tandem repeats
SUID	sudden unexpected infant deaths
SVZ	subventricular zone
SWS	Sturge-Weber syndrome
TBI	traumatic brain injury
TLC	thin layer chromatography
TNF	tumor necrosis factor
TSC	tuberous sclerosis complex
UHPLC	ultra-high-performance liquid chromatography
UOA	urine organic acids
UTR	untranslated region
VEGF	vascular endothelial growth factor
VLCAD	very-long-chain 3-hydroxyacyl-CoA dehydrogenase
VUS	variants of unknown significance
VZ	ventricular zone
VZV	varicella-zoster virus
WBC	white blood cell
WES	whole-exome sequencing
WGS	whole-genome sequencing
WM	white matter
WMI	white matter injury
ZE	zone electrophoresis