

Perinatal Neuropathology

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Mirna Lechpammer , Marc Del Bigio , Rebecca Folkerth
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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

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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 taught 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

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

List of Abbreviations

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