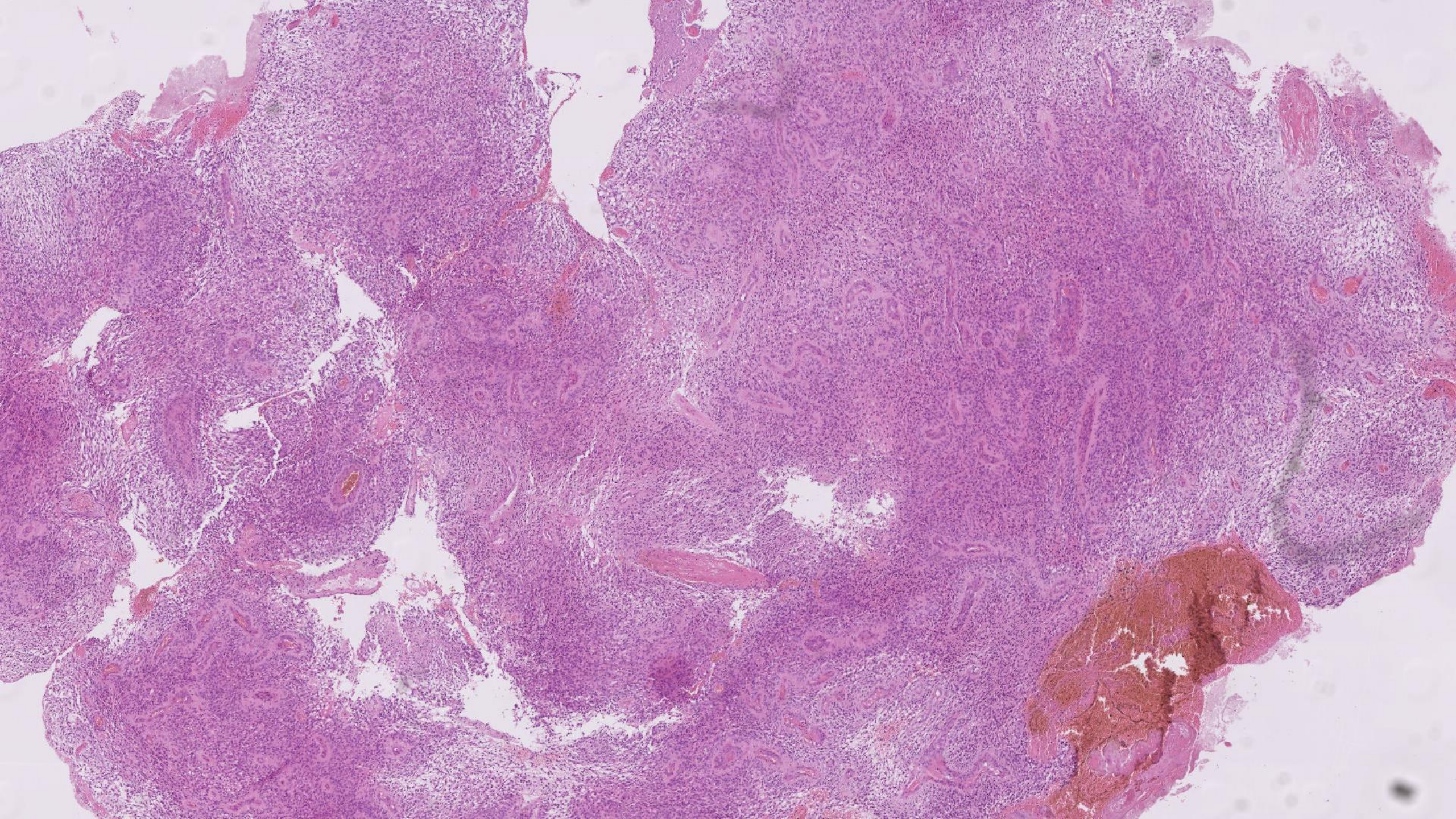
XXX. Martinský bioptický seminár SD-IAP

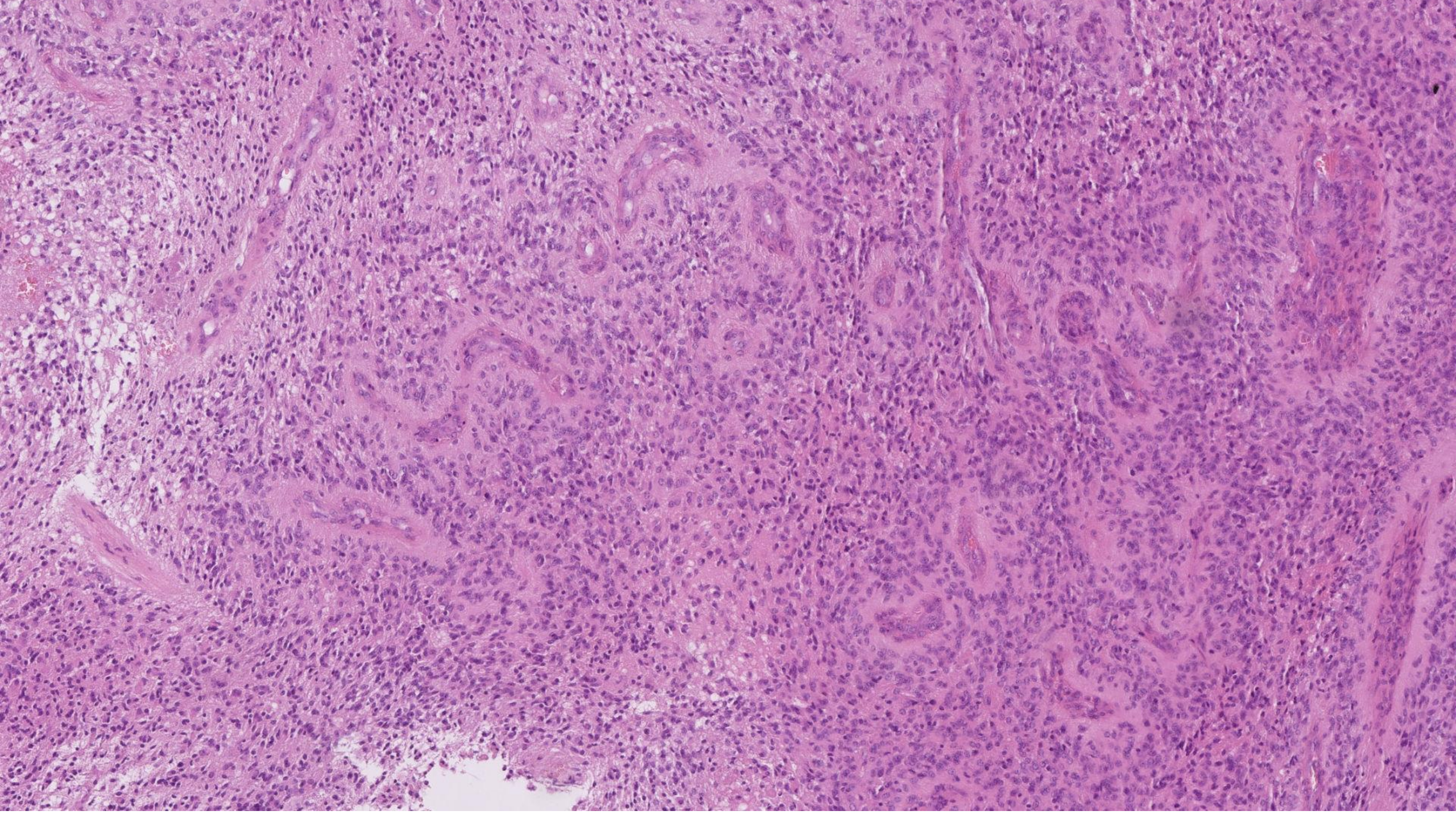
Prípad SD-IAP 854

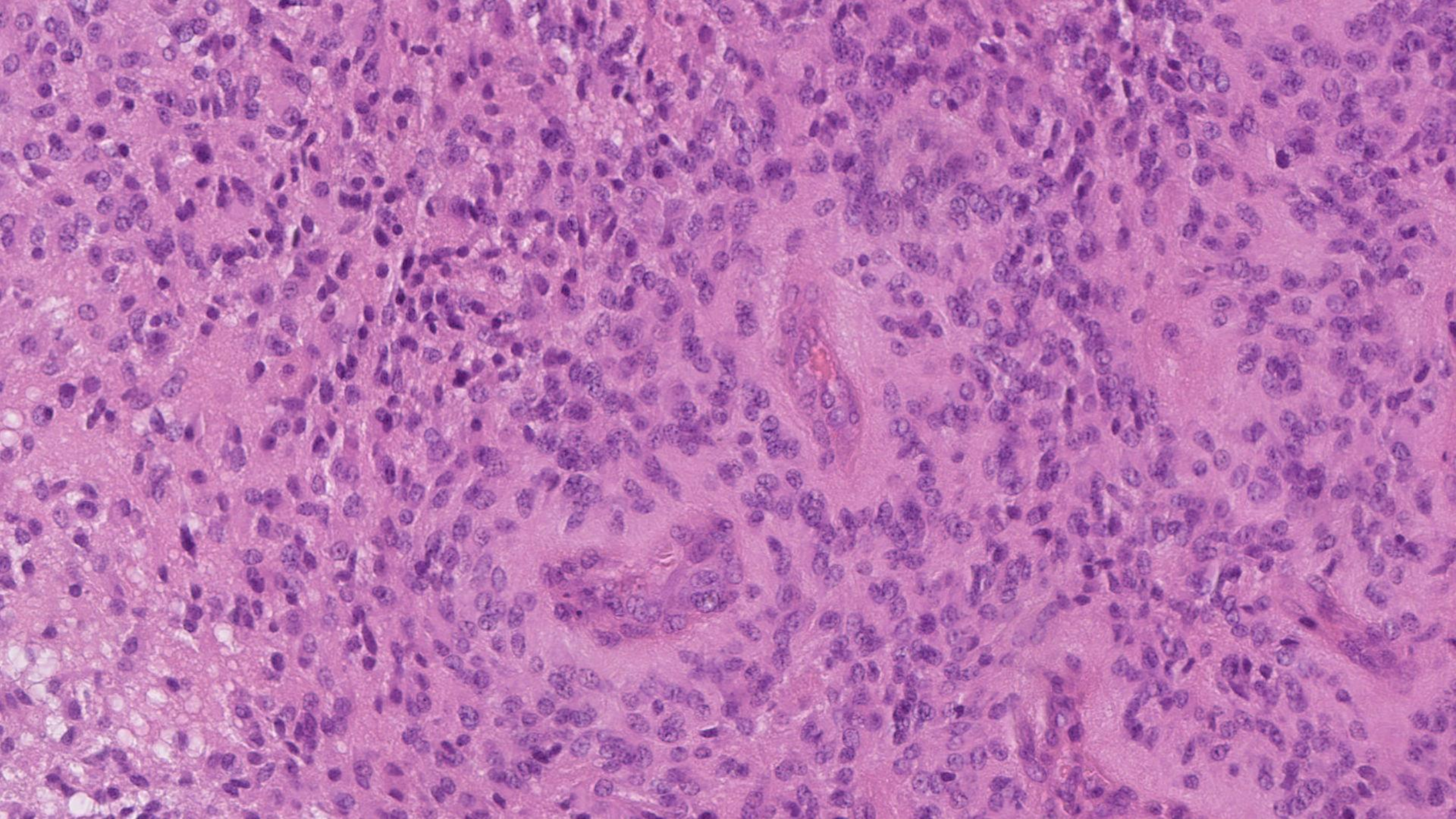
M. Švajdler

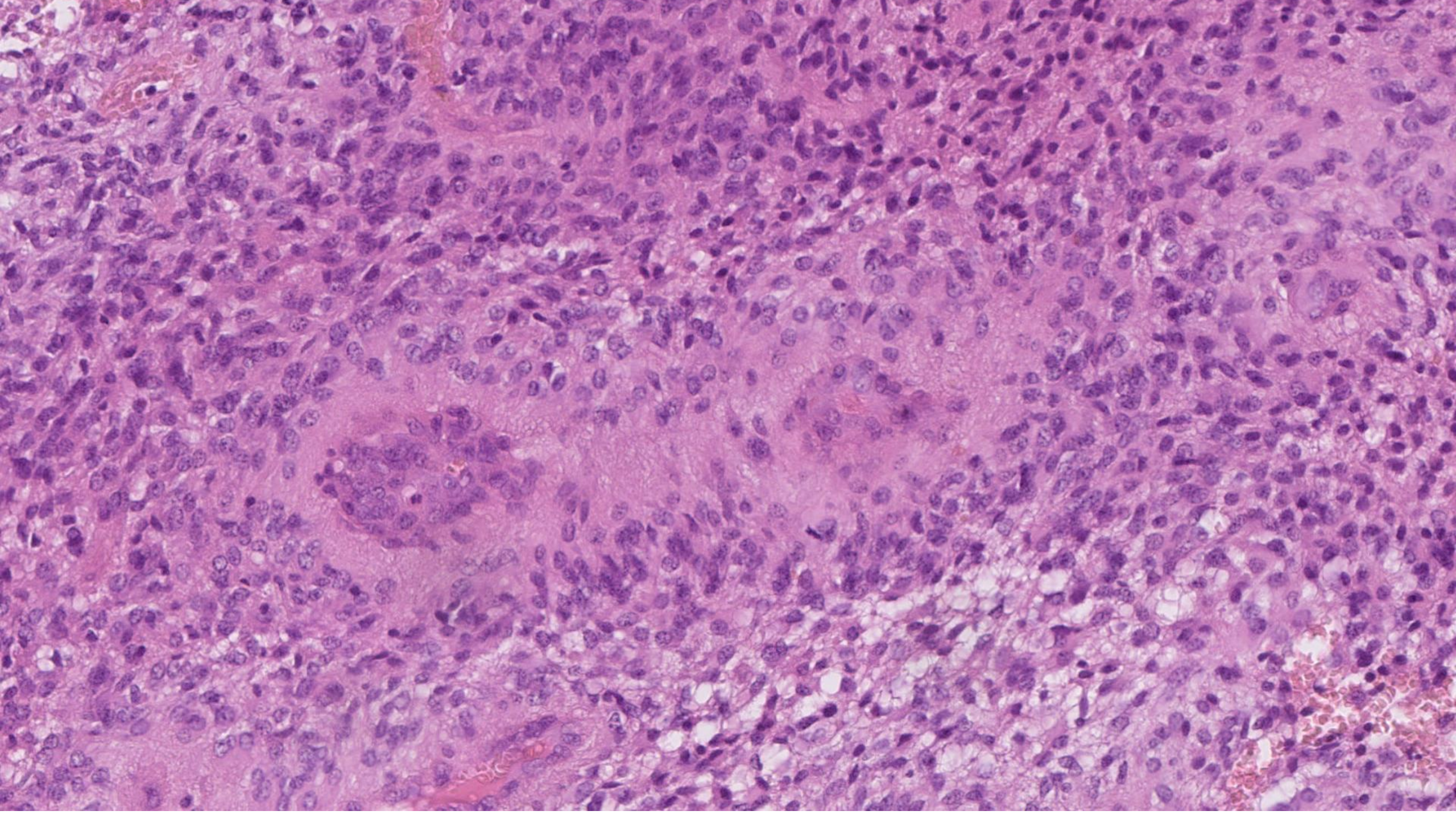
- **11-ročné dievča, tumor mozgu, konzultačné vyšetrenie - patologická diagnóza ependymóm**

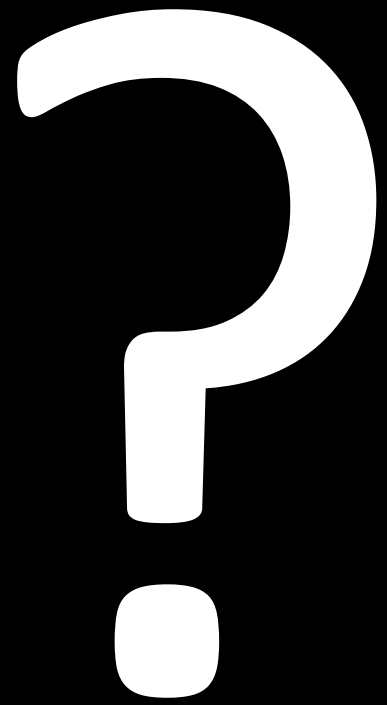
- **prípad zaslaný za účelom molekulovej subklasifikácie pomocou metylačného profilovania**



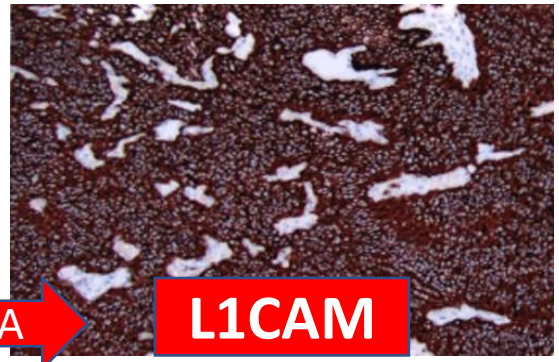




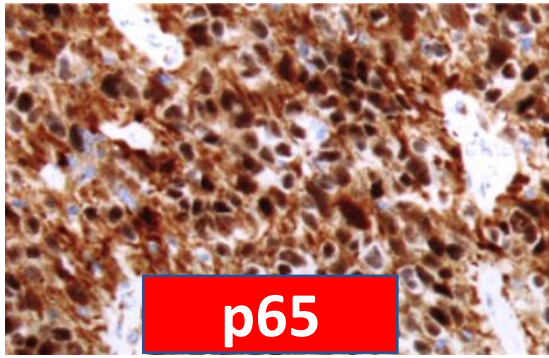




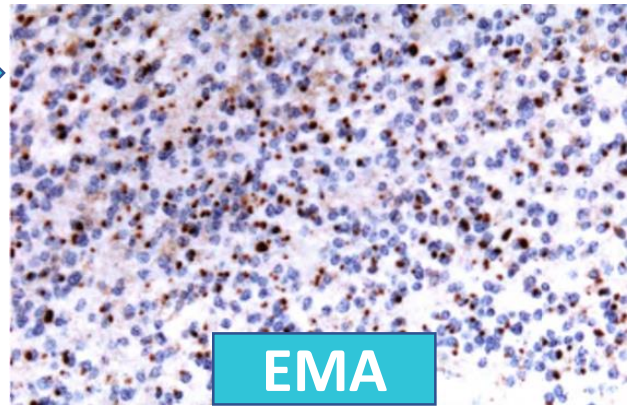
		Age	Sex	CNS WHO grade	Molecular features	Outcome
Supratentorial	ST-SE		♂ ♂ ♂ ♀	1	*Balanced genome*	
	ST-*ZFTA*		♂ ♂ ♀	2 / 3	*ZFTA fusions* *Chromothripsis* *CDKN2A and/or CDKN2B loss*	
	ST-*YAP1*		♂ ♀ ♀ ♀	2 / 3	*YAP1 fusions*	
Infratentorial	PF-SE		♂ ♂ ♂ ♀	1	*Balanced genome*	
	PFA		♂ ♂ ♀	2 / 3	*EZHIP mutations* *H3 p.K28M (K27M) mutations* *Chr. 1q gain*	
	PFB		♂ ♀	2 / 3	*Chromosomal instability*	
Spinal	SP-SE		♂ ♀	1	*Chr. 6q deletion*	
	SP-EP		♂ ♂ ♀	2 / 3	*NF2 mutations*	
	SP-MP		♂ ♀	2	*Chromosomal instability*	
	SP-*MYCN*		♂ ♀		*MYCN amplification (Chr. 2p)*	



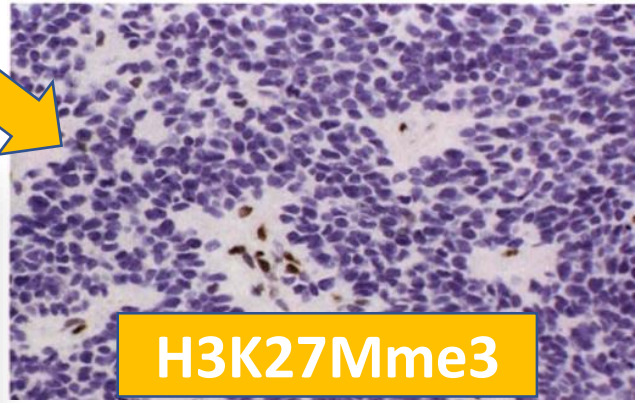
ZFTA

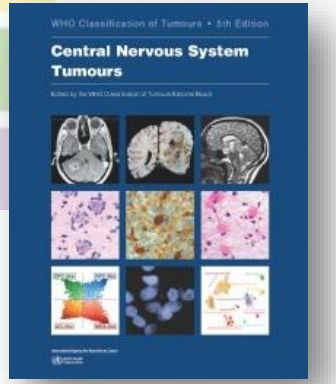


YAP1

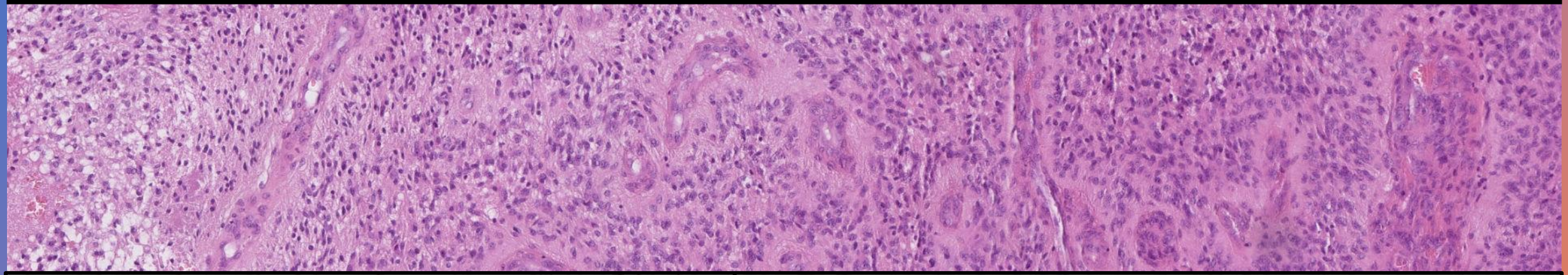


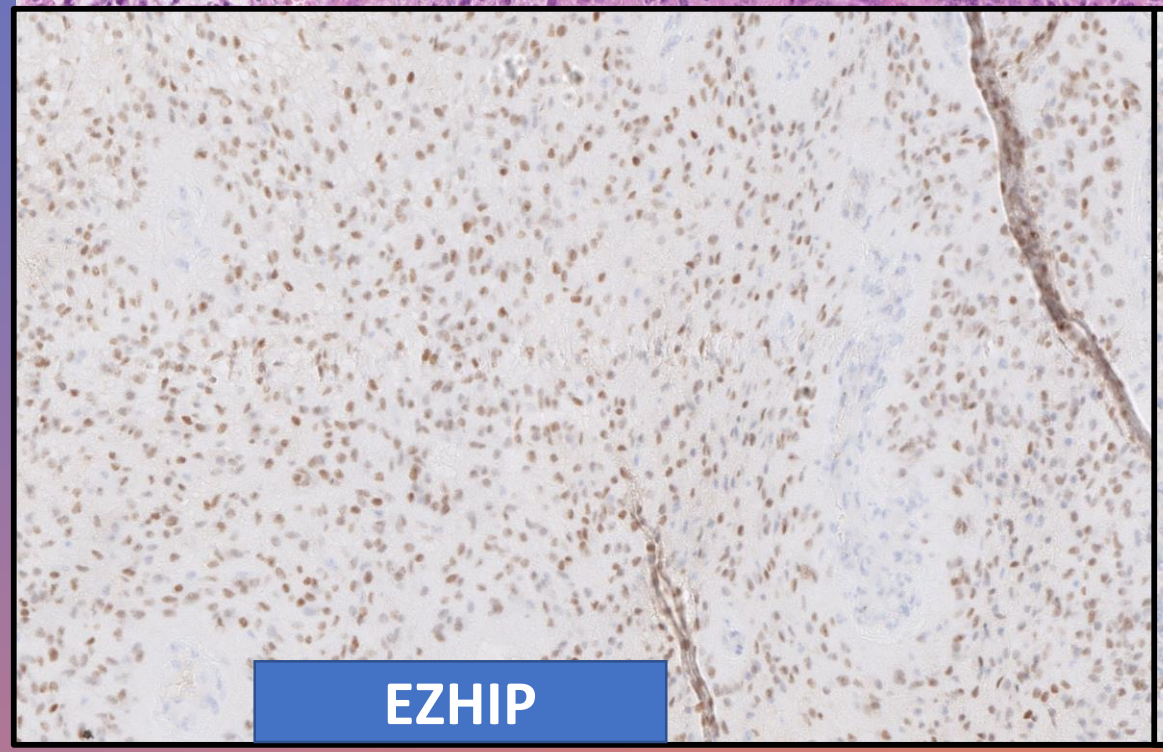
PFA

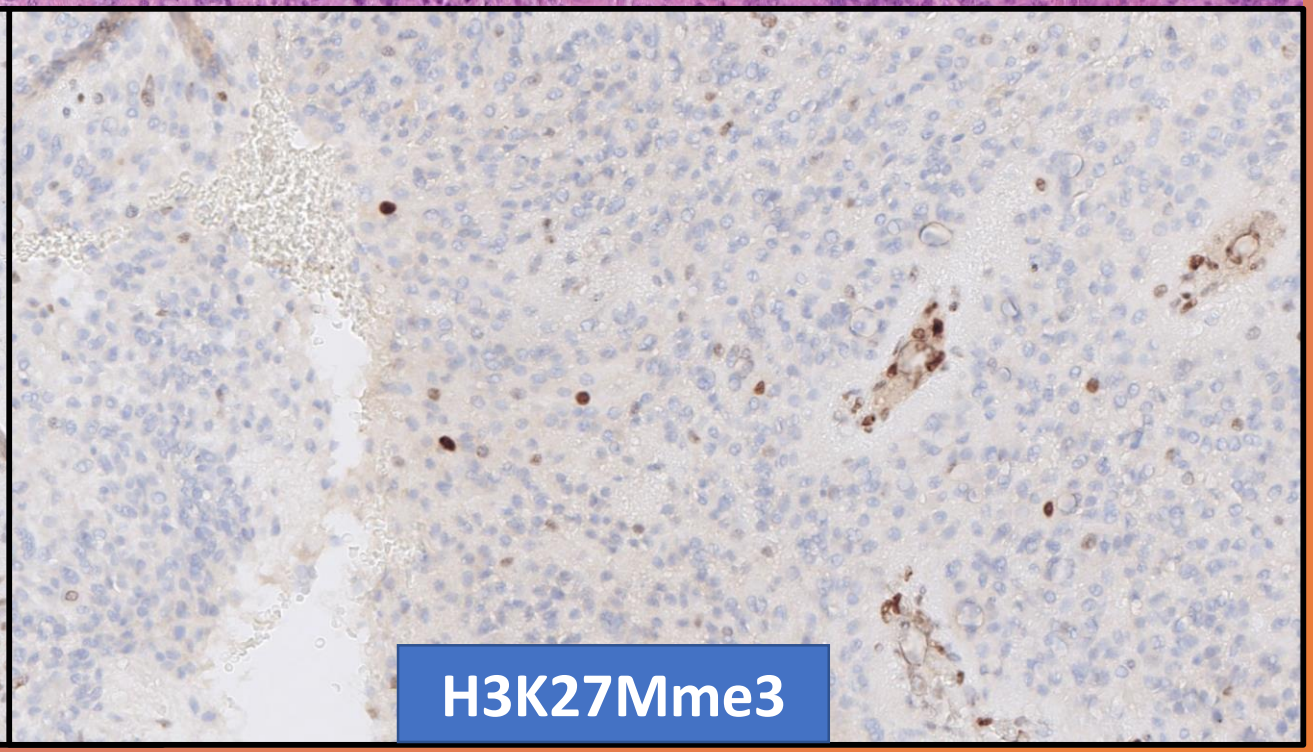




11-ročné dievča, ependymóm



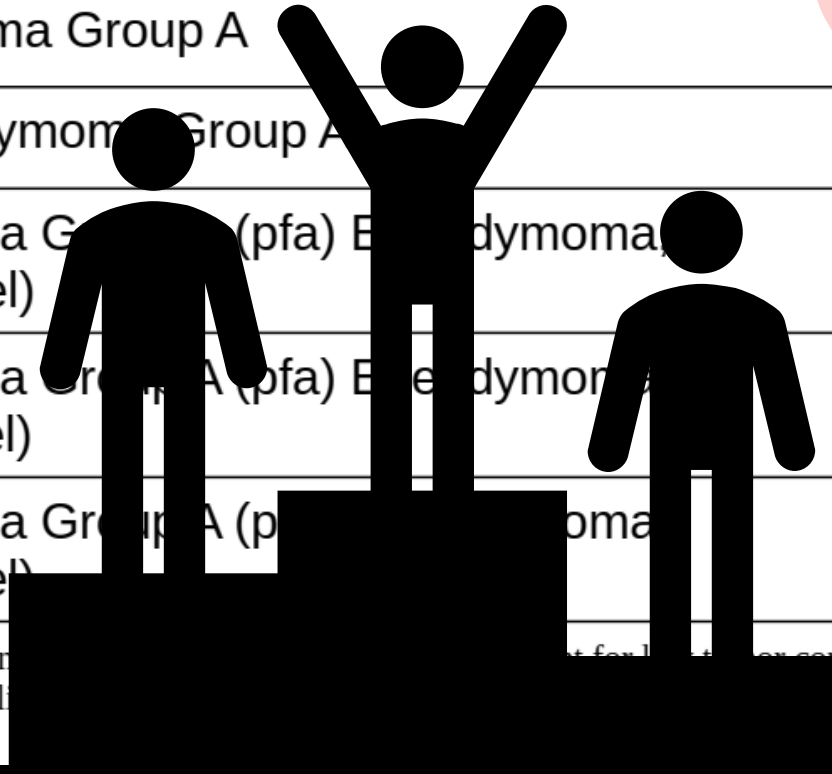




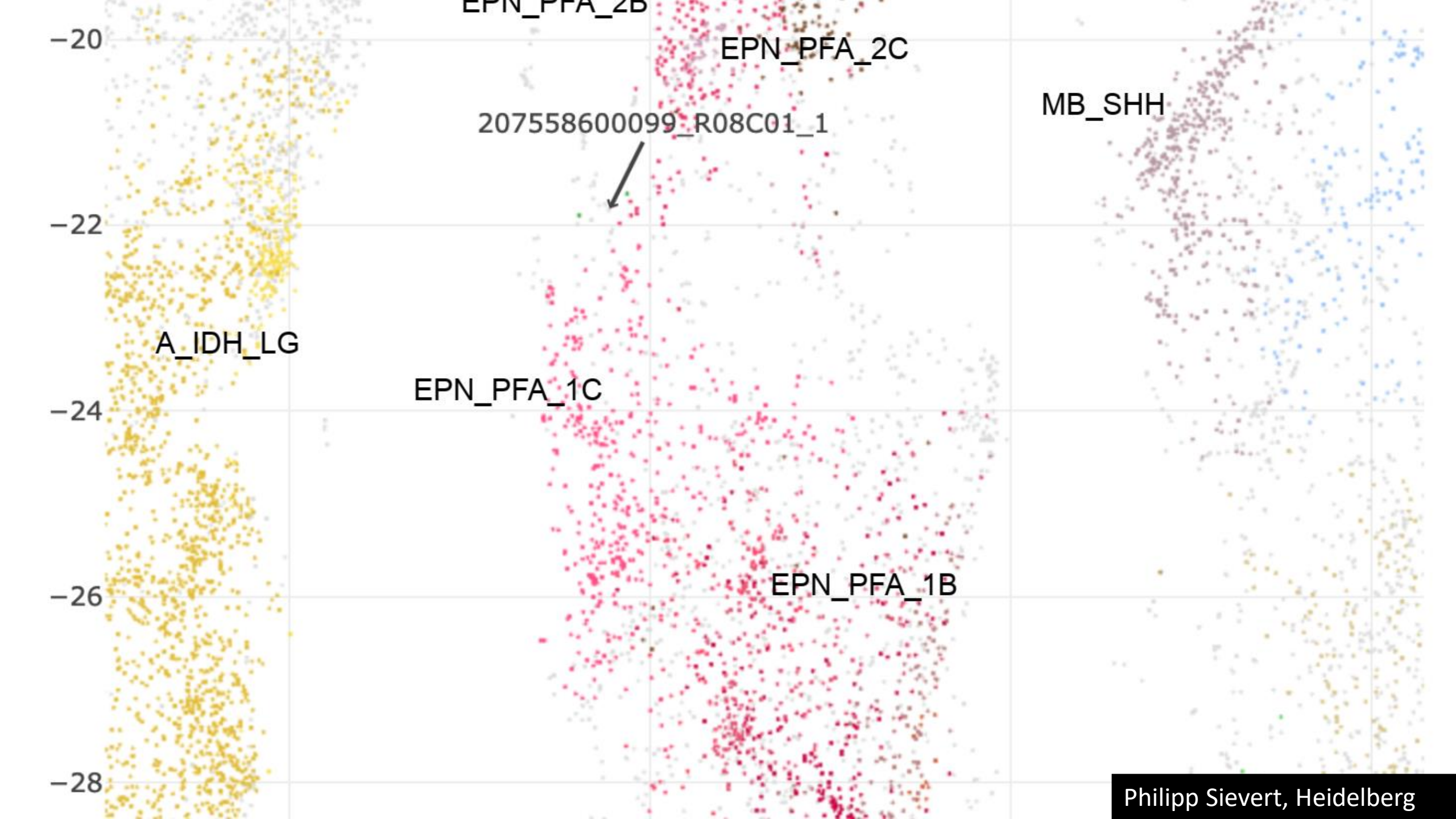
Brain tumor classifier results (12.5)

Methylation classes (Highest level >= 0.3, lower levels >= 0.1, all of lowest level)	Calibrated score	Interpretation	
Ependymal Tumours	0.85	no match	✗
Posterior Fossa Ependymoma Group A	0.78	no match	✗
Posterior Fossa Ependymom Group A	0.68	no match	✗
Mc Posterior Fossa G (pfa) E dymoma, Subclass 2b (novel)	0.67	no match	✗
Mc Posterior Fossa Gr A (pfa) E dymom Subclass 2c (novel)	0.00	no match	✗
Mc Posterior Fossa Gr A (p oma Subclass 2a (novel)	0.00	no match	✗

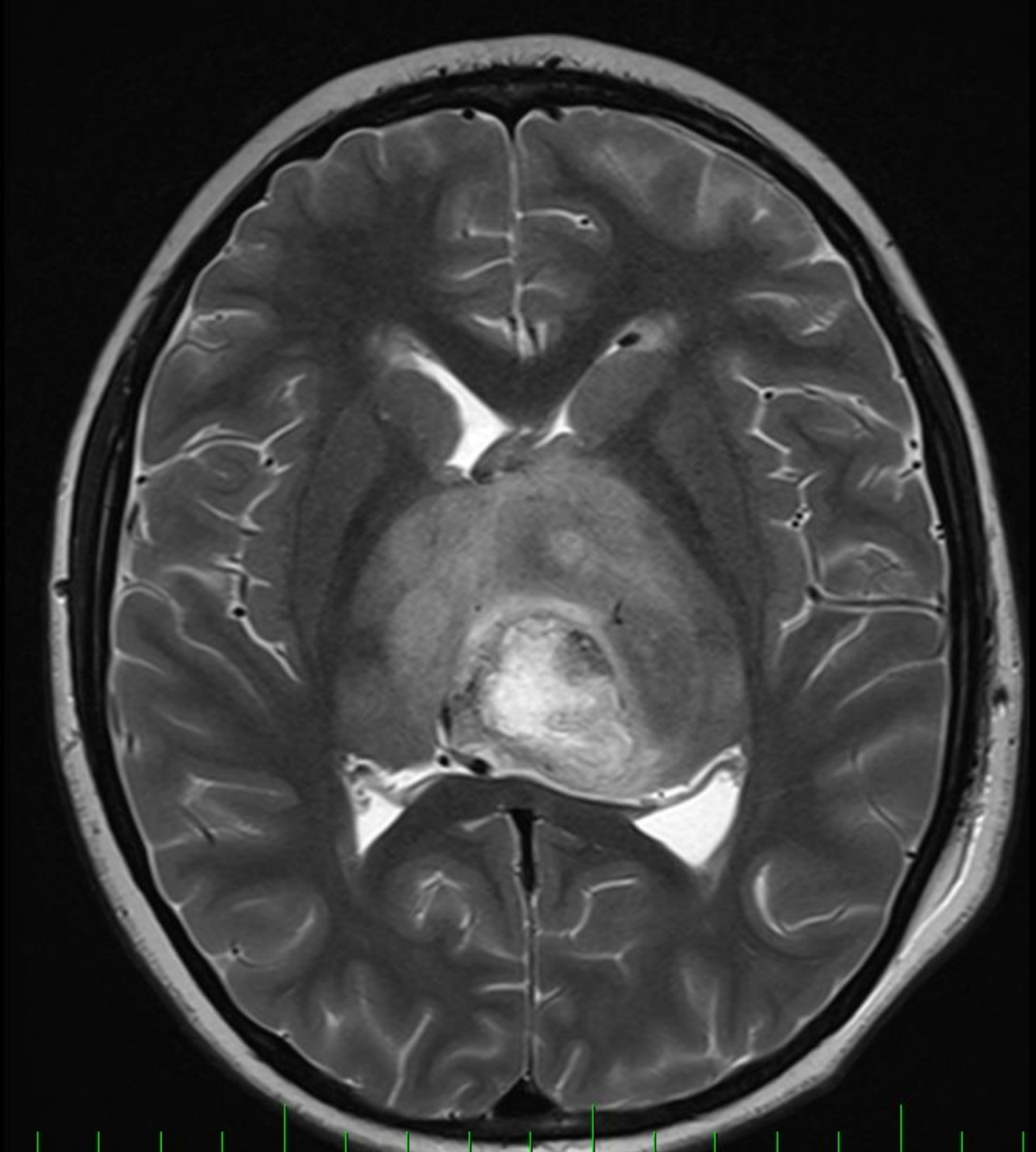
Legend: ✓ Match (score >= 0.9) ✗ No r t for l t or content and low DNA quali ● Match to MC family member (score >= 0.5)



Dx.: ependymóm, morfologicky klasického typu, s expresiou EZHIP a stratou expresie H3K27Mme3 a metylačným profilom konzistentným s ependymómom posterior fossa type A



Philipp Sievert, Heidelberg



Klinicky strednočiarový bitalamický tumor

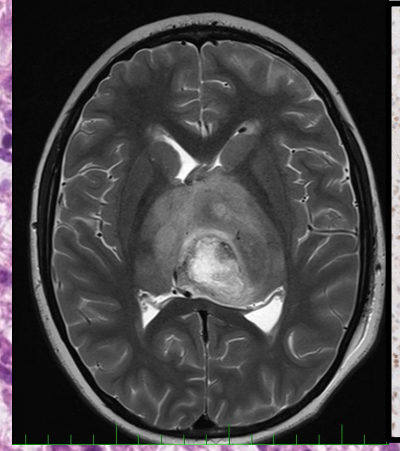
Žiadny tumor v zadnej jame

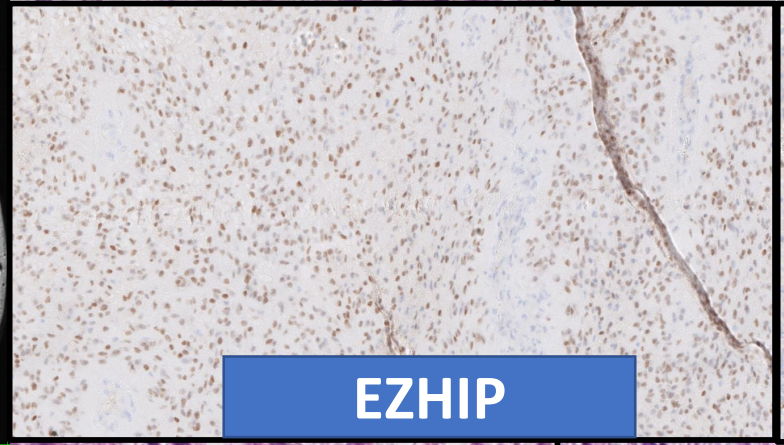
Zdravotnícke zariadenie: Národný ústav detských chorôb

Predmet vyšetrenia a lokalizácia:

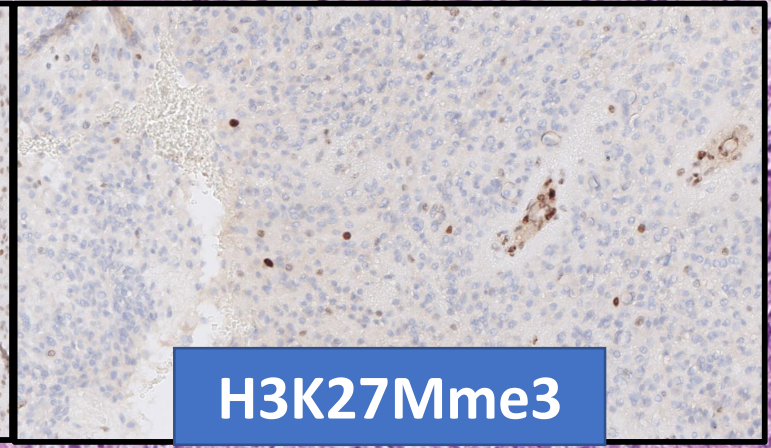
CITO!

1. kapsula tumoru-zadná časť
2. vnútorná časť tumoru - zadná časť (susp nekróza)
3. vnútorná časť tumoru - predná časť (tu robená endohistologia-LGG)

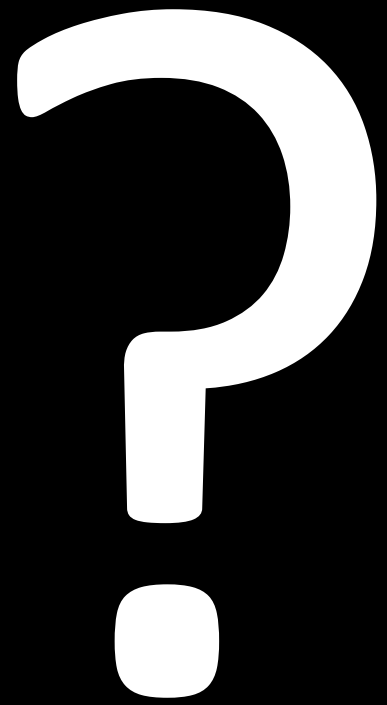


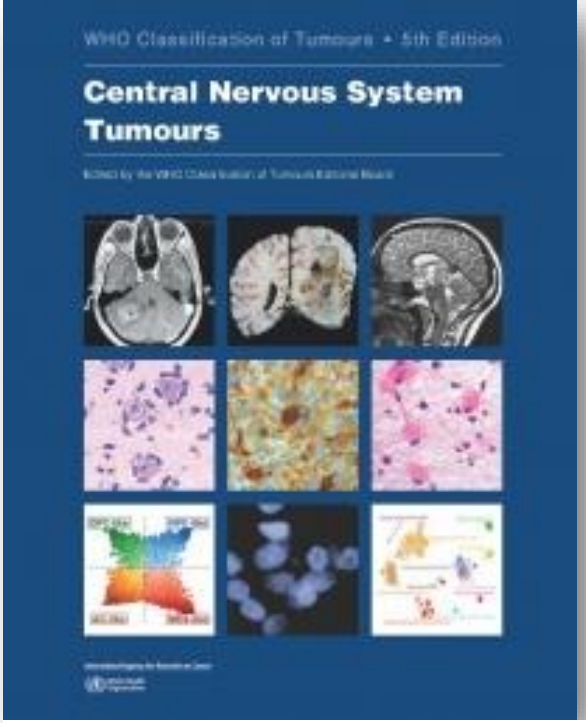


EZHIP



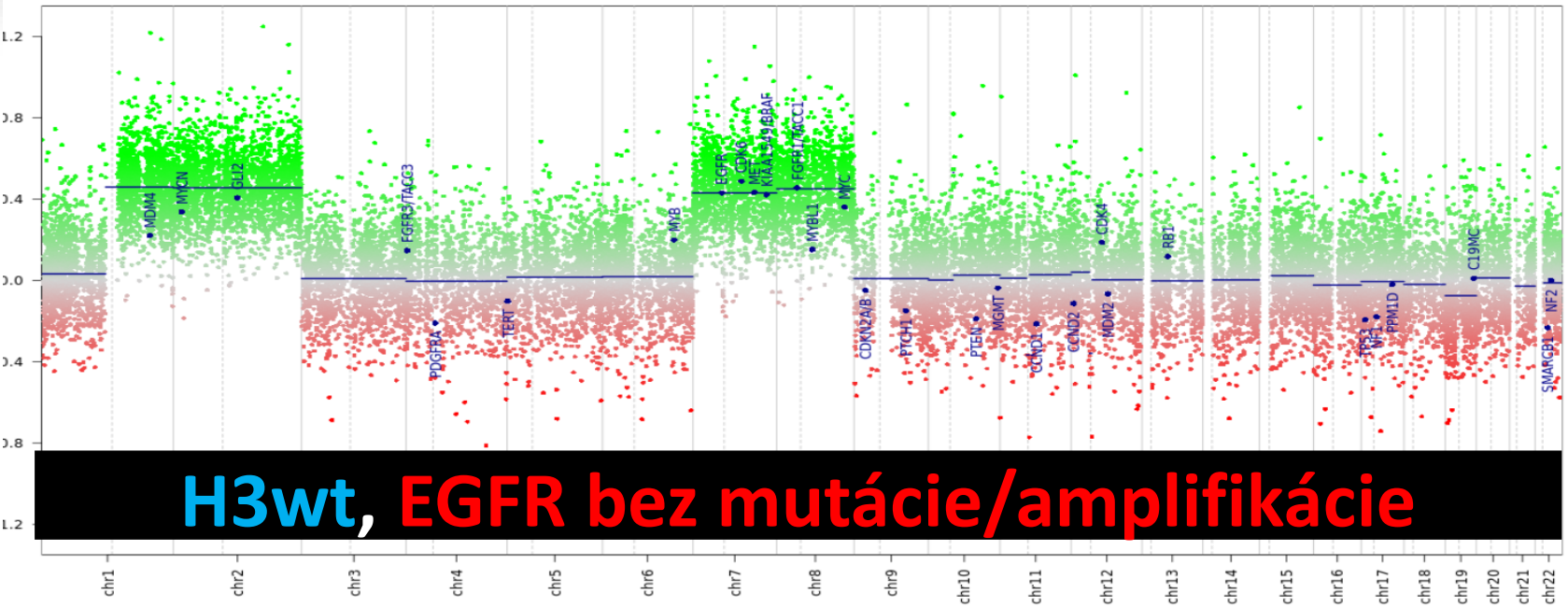
H3K27Mme3





Definition

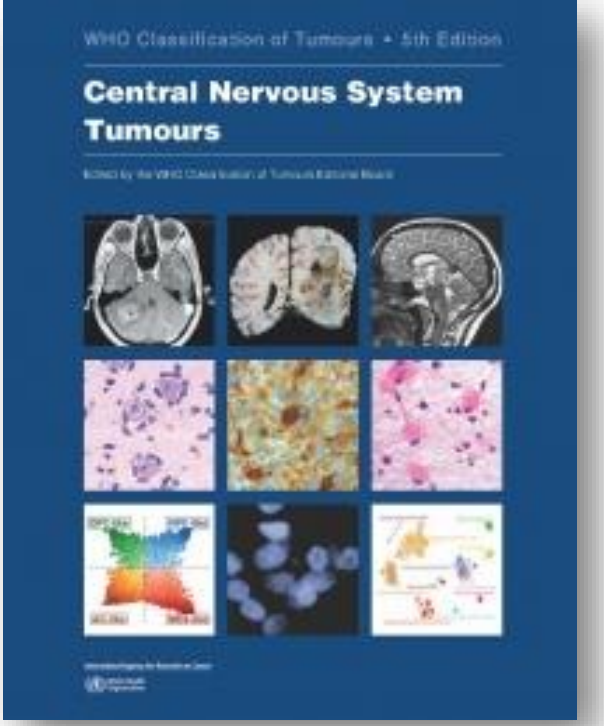
Diffuse midline glioma, H3 K27–altered, is an infiltrative midline glioma with loss of H3 p.K28me3 (K27me3) and usually either an H3 c.83A>T p.K28M (K27M) substitution in one of the histone H3 isoforms, aberrant overexpression of EZHIP, or an *EGFR* mutation (CNS WHO grade 4).



H3wt, EGFR bez mutácie/amplifikácie

PROKAZUJEME klinicky významnou mutaci genu:

- **BCOR** c.1550_1551del p.(Asn517ArgfsTer39) AF: 38%; **- popísané v DMG aj EPE**
- **BCORL1** c.1825C>T p.(Arg609Ter) AF: 46%;
- **ACVR1** c.617G>A p.(Arg206His) AF: 27%; **- popísané v DMG**
- **LZTR1** c.1321C>T p.(Gln441Ter) AF: 95%.

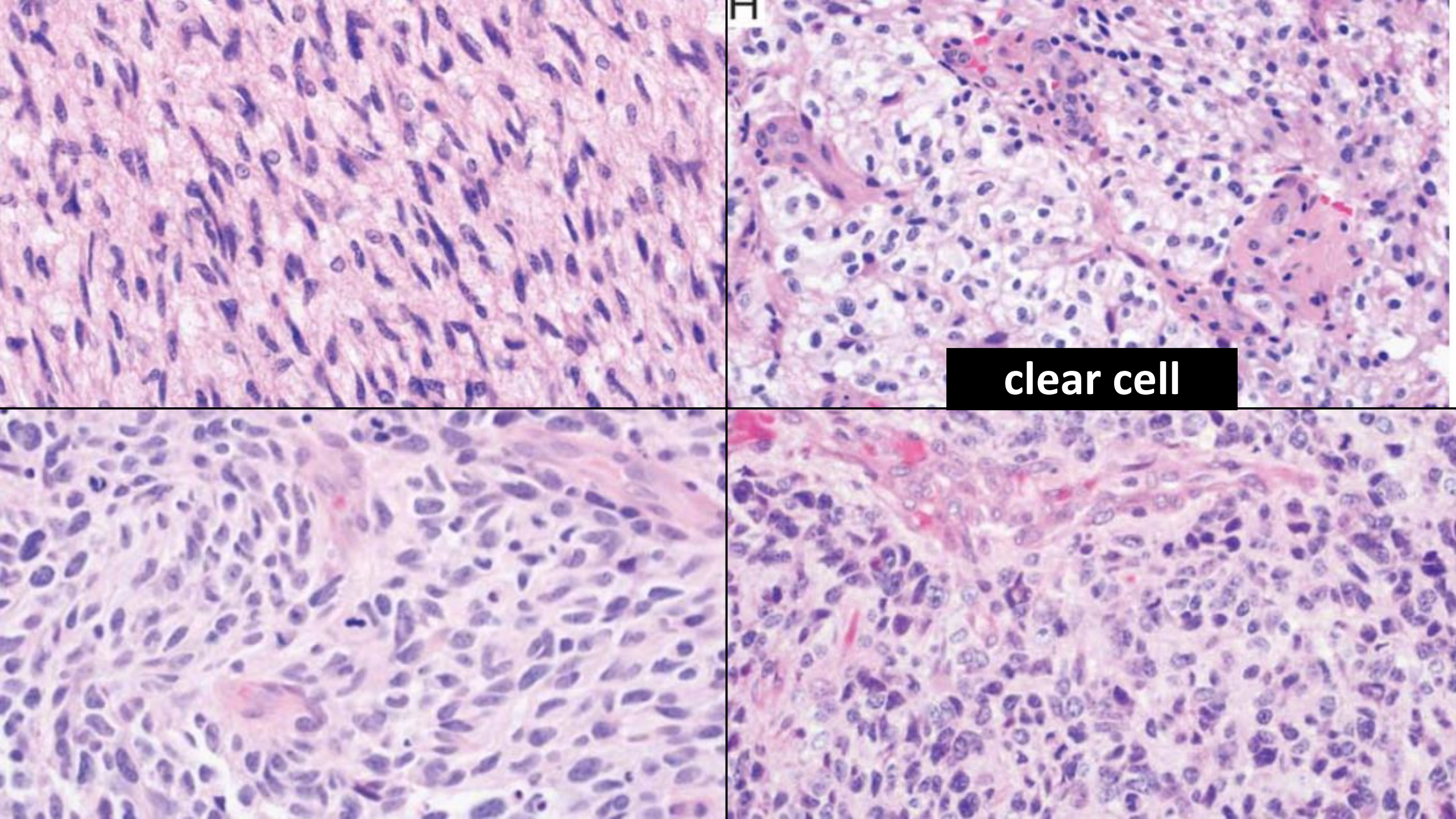


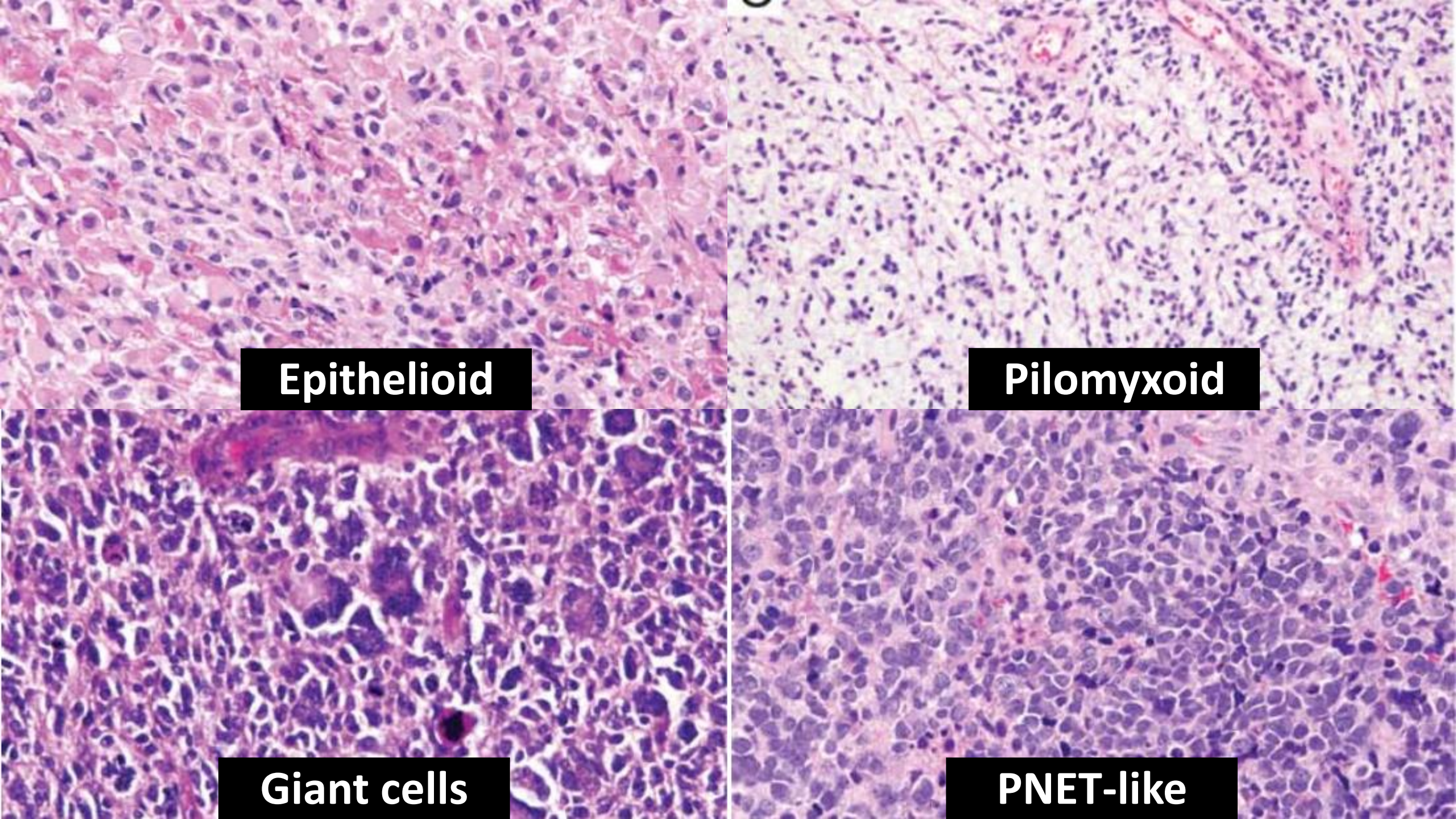
In posterior fossa group A **(PFA) ependymomas**, H3 p.K28 (K27) mutations are extremely rare, but loss of H3 p.K28me3 (K27me3) or EZHIP overexpression occurs; **these tumours can be distinguished from DMGs on a morphological basis.**

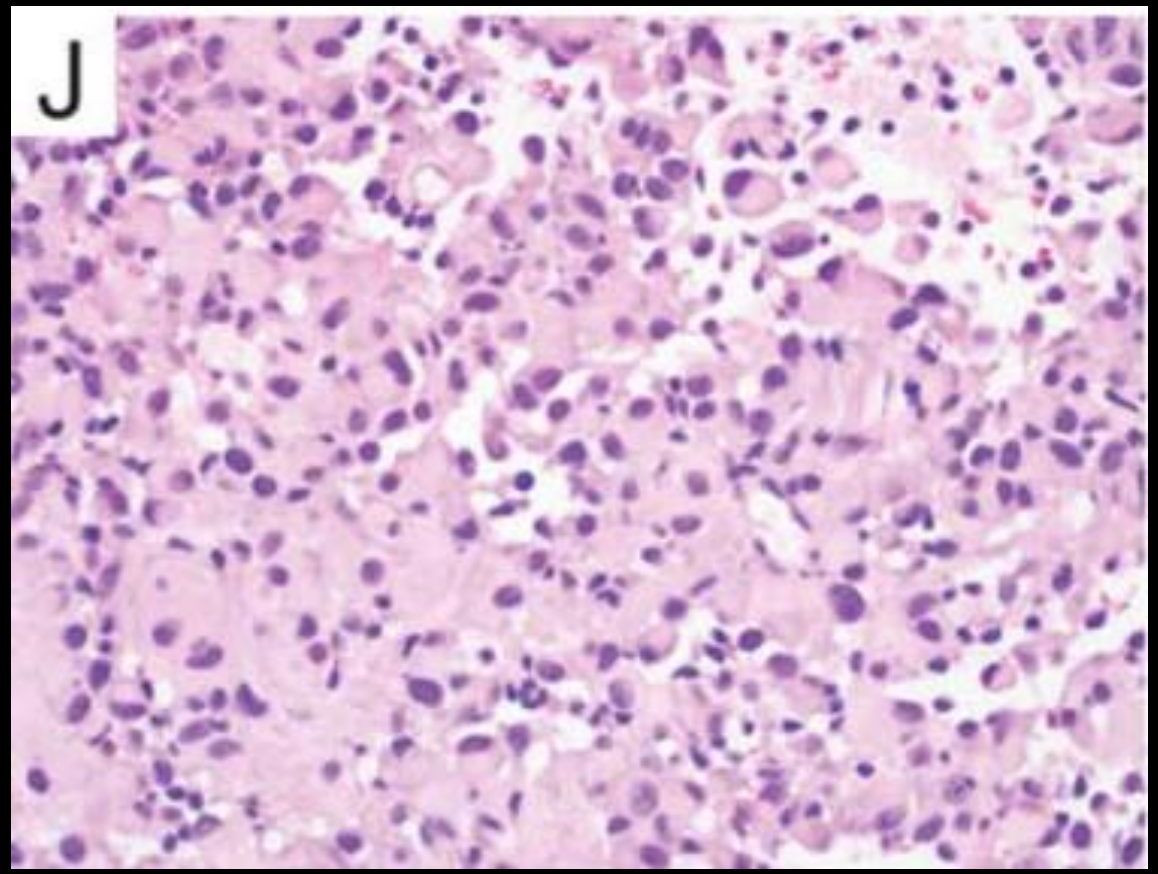
Diffuse Midline Gliomas with Histone H3-K27M Mutation: A Series of 47 Cases Assessing the Spectrum of Morphologic Variation and Associated Genetic Alterations

David A. Solomon[1]; Matthew D. Wood[1]; Tarik Tihan[1]; Andrew W. Bollen[1]; Nalin Gupta[2,3]; Joanna J. J. Phillips[1,2]; Arie Perry[1,2]

Brain Pathol. 2016 Sep;26(5):569-80.


clear cell


Epithelioid
Pilomyxoid
Giant cells
PNET-like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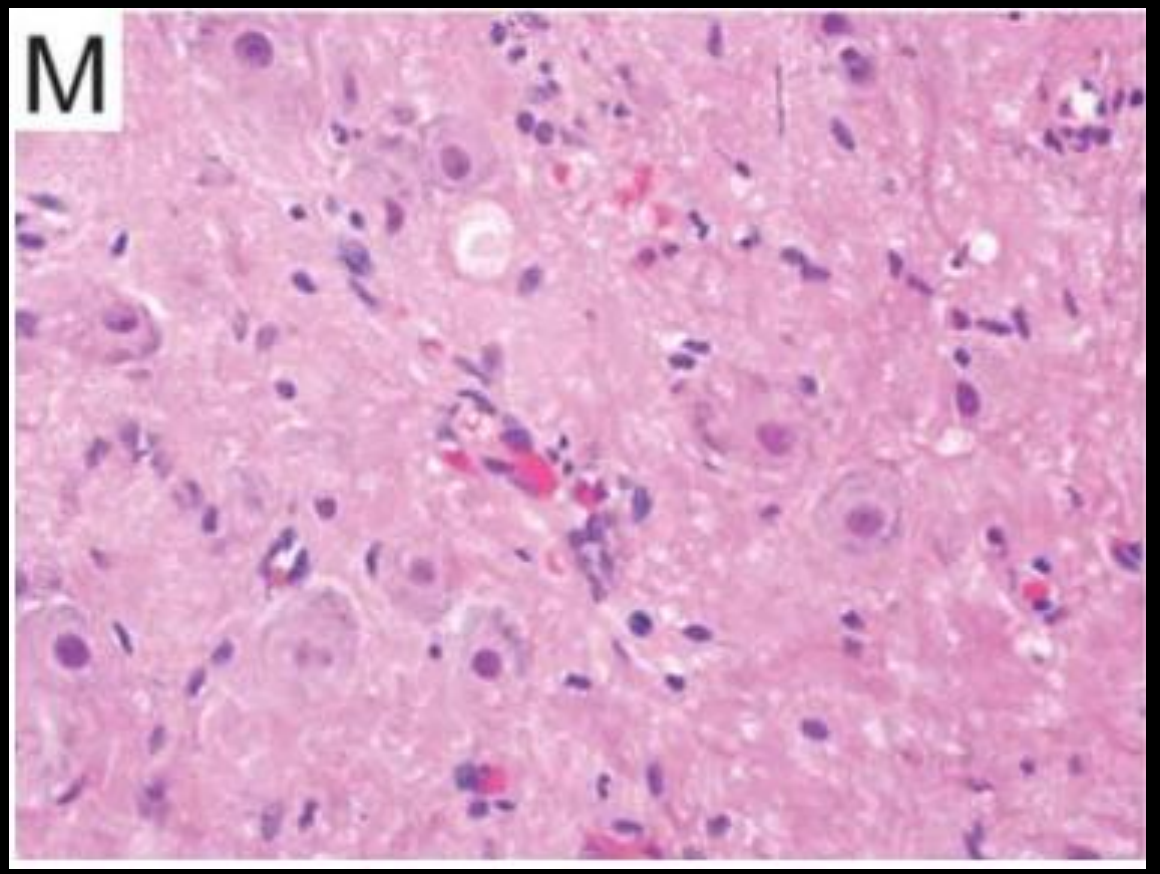
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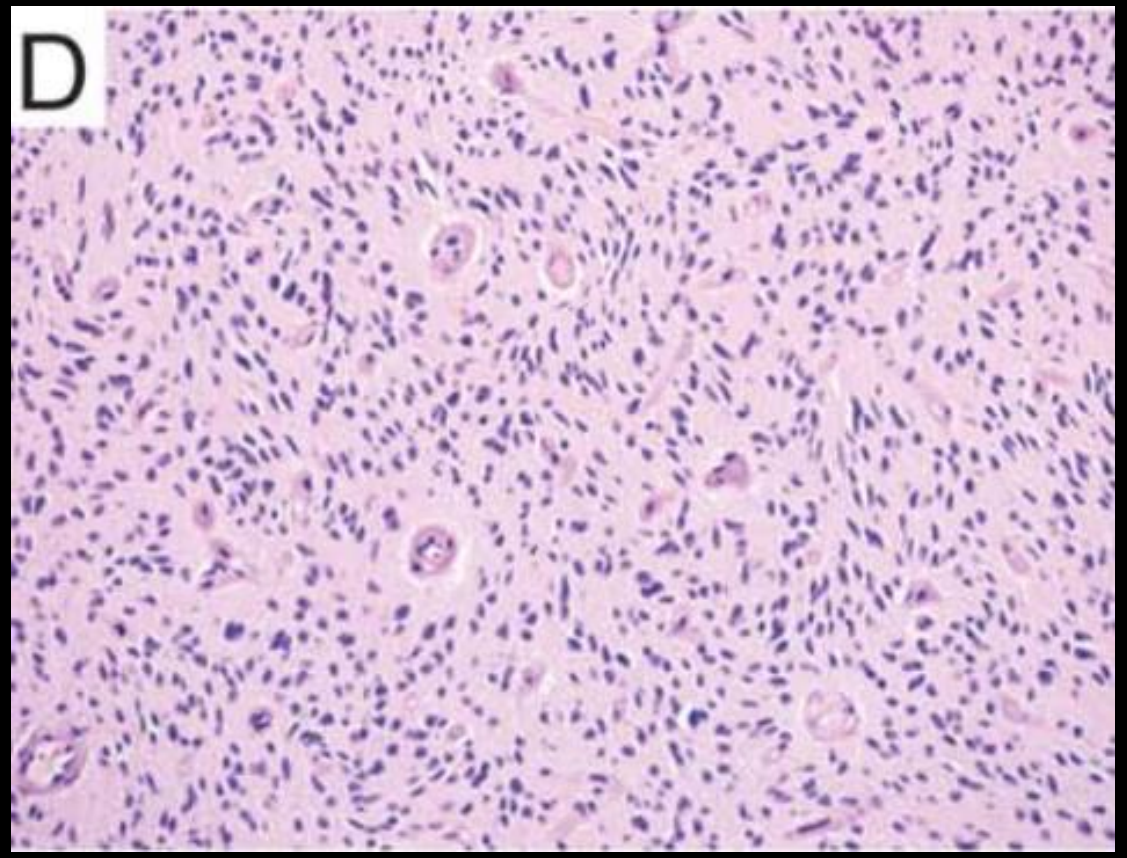
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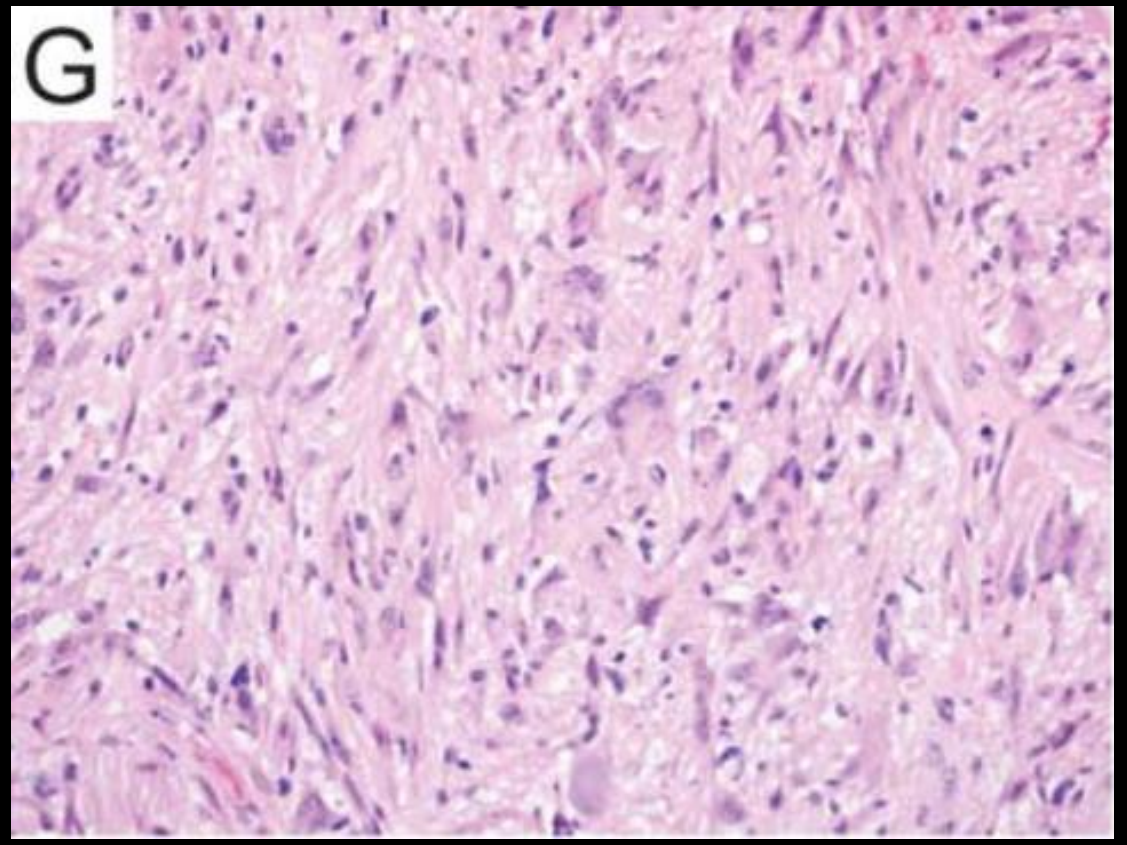
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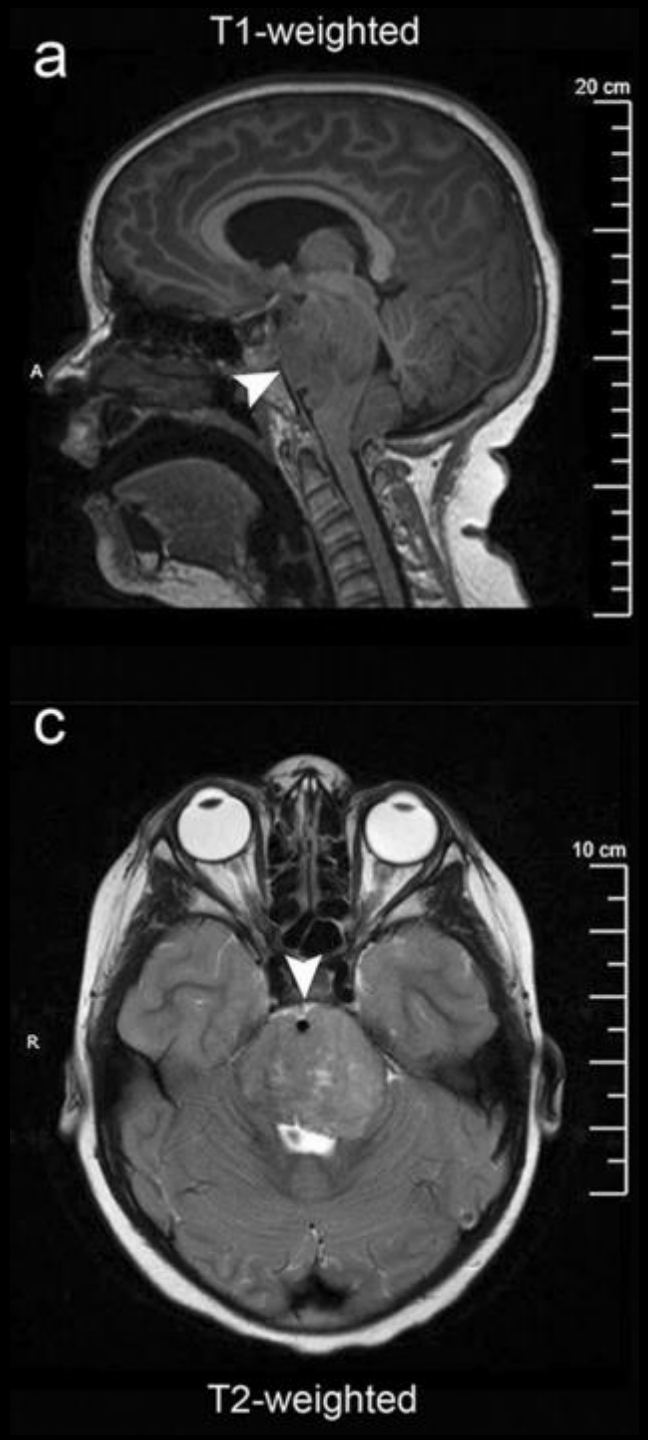
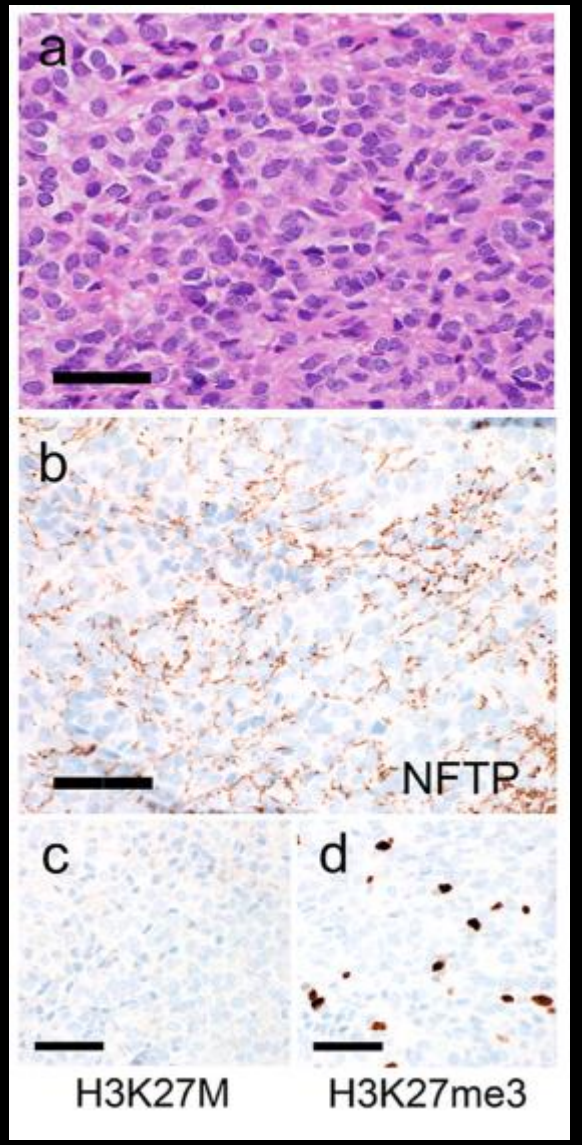
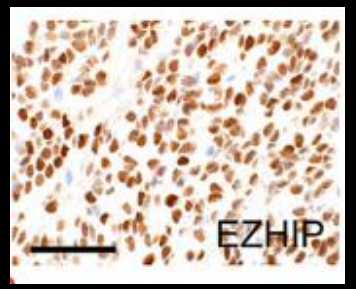


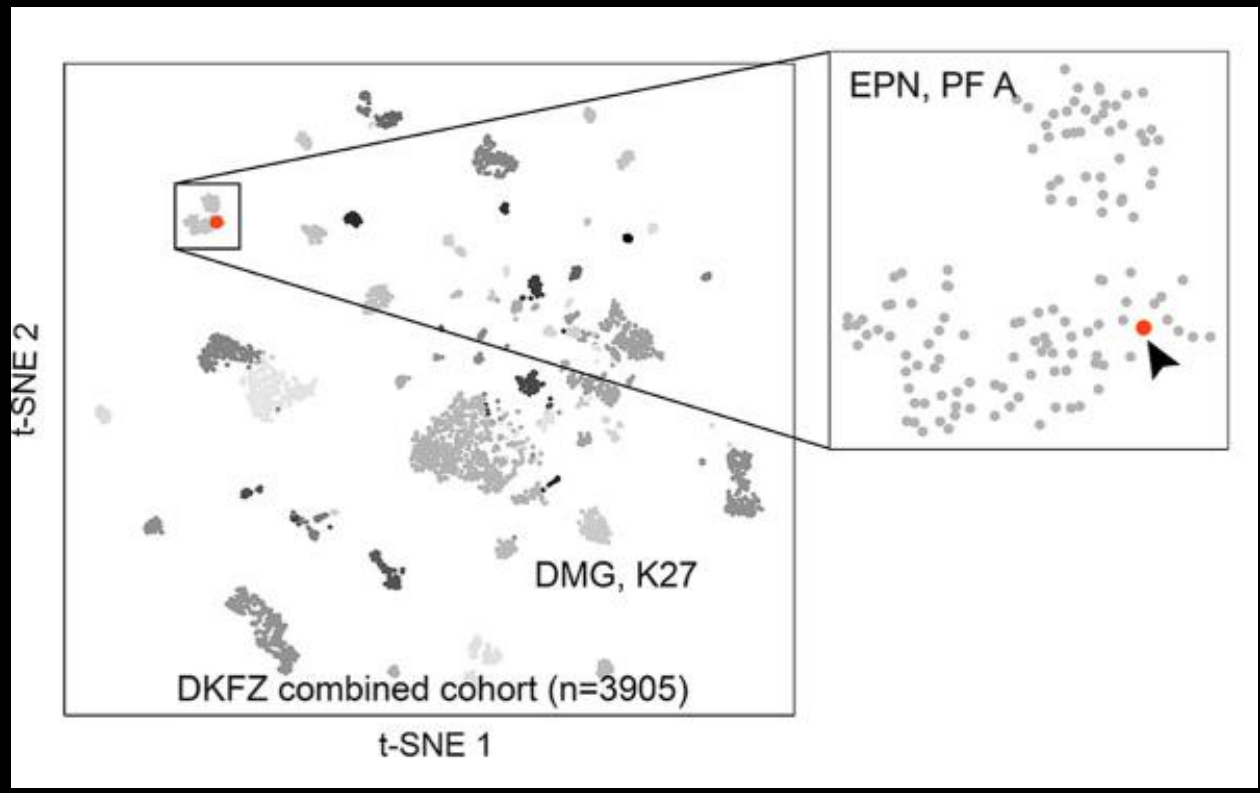




LETTER TO THE EDITOR

Diffuse intrinsic pontine glioma-like tumor with EZHIP expression and molecular features of PFA ependymoma

Pratt et al. Acta Neuropathologica Communications (2020) 8:37



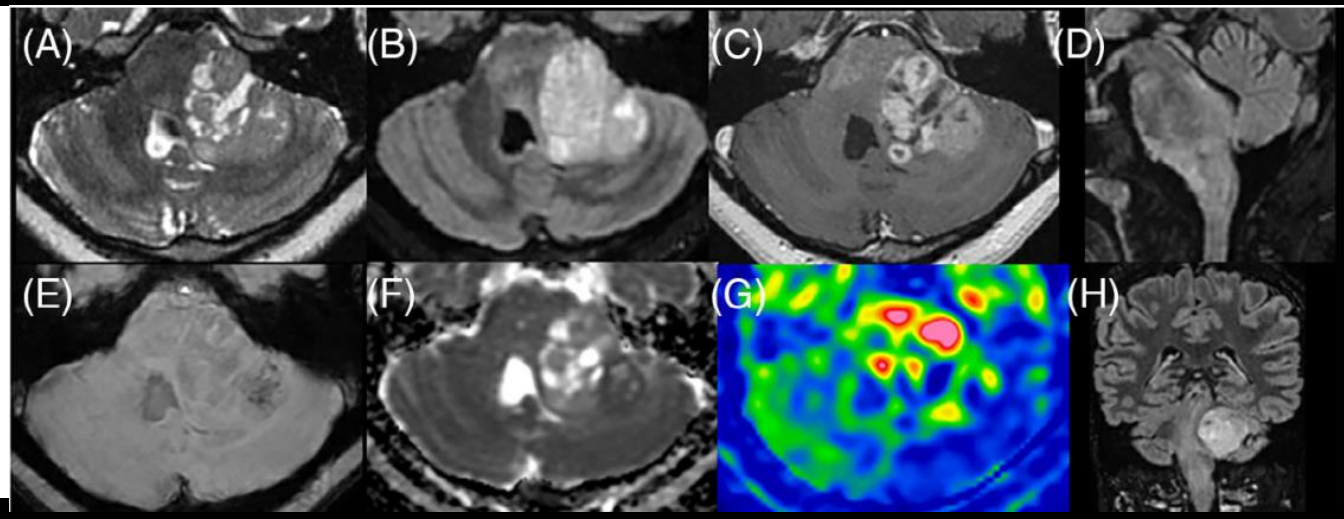
Received: 28 March 2023 | Accepted: 7 June 2023
DOI: 10.1111/bpa.13181

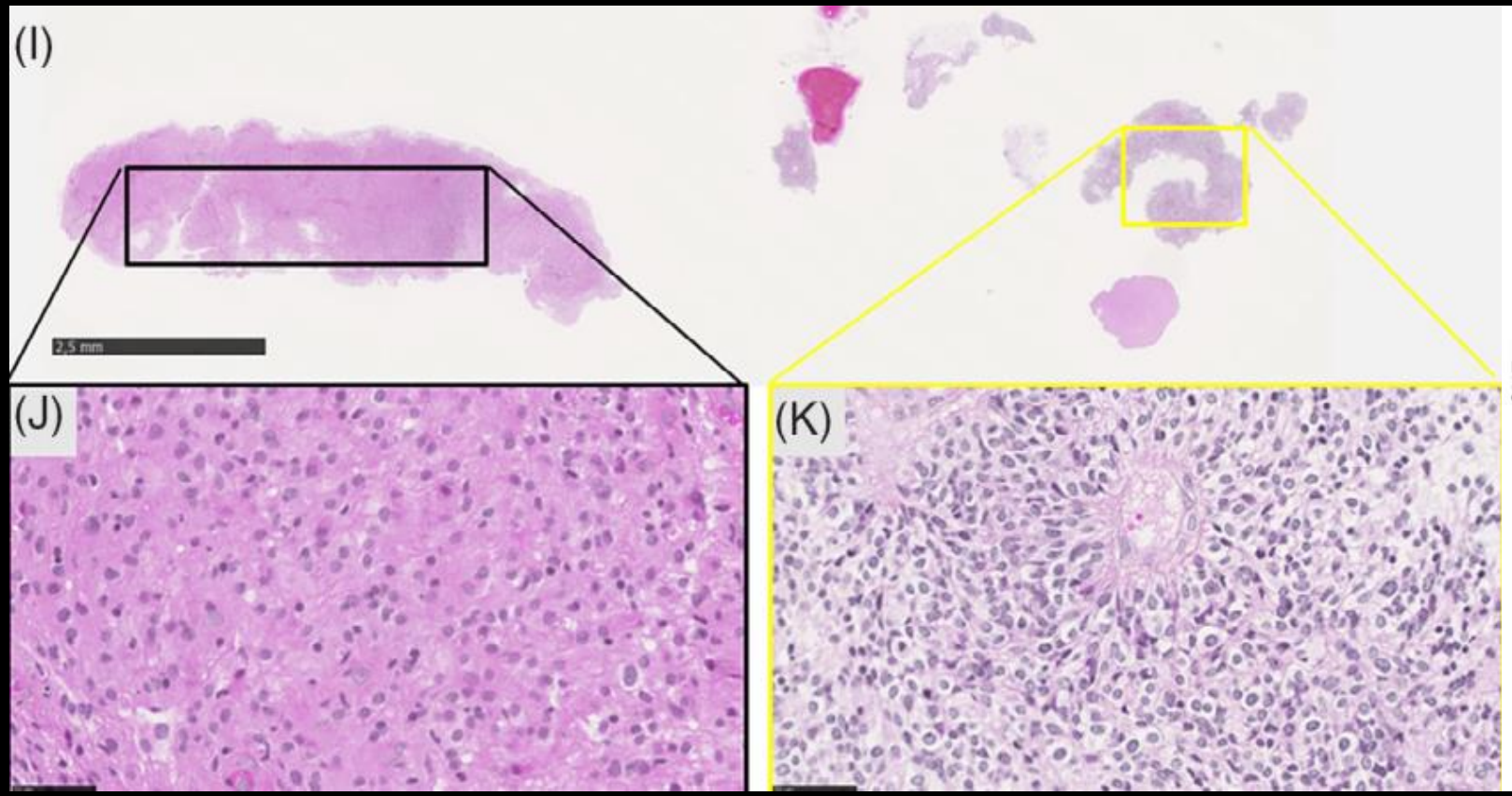
Brain Pathology

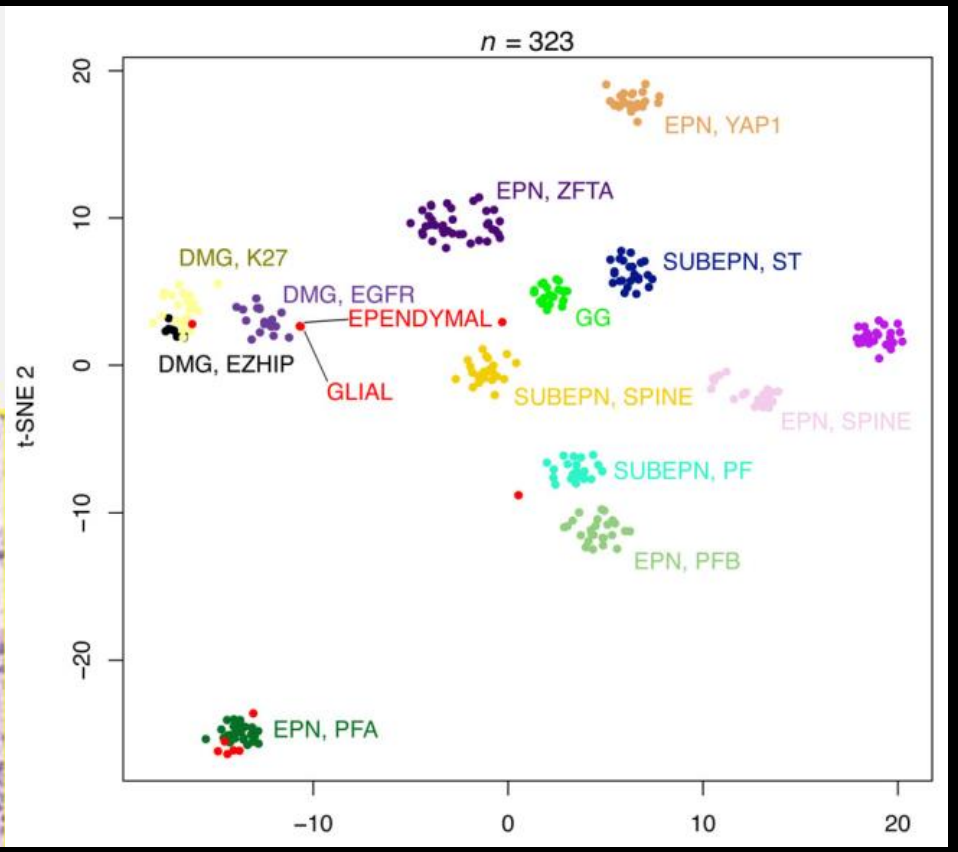
RESEARCH LETTER

The pontine diffuse midline glioma, *EGFR*-subtype with ependymal features: Yet another face of diffuse midline glioma, H3K27-altered

Arnault Tauziède-Espariat[1,2] | Alice Métais[1,2] | Cassandra Mariet[1] | David Castel[3] | Jacques Grill[3,4] | Raphaël Saffroy[5] | Lauren Hasty[1] | Volodia Dangouloff-Ros[6,7] | Nathalie Boddaert[6,7] | Sandro Benichi[8] | Fabrice Chrétien[1] | Pascale Varlet[1,2]







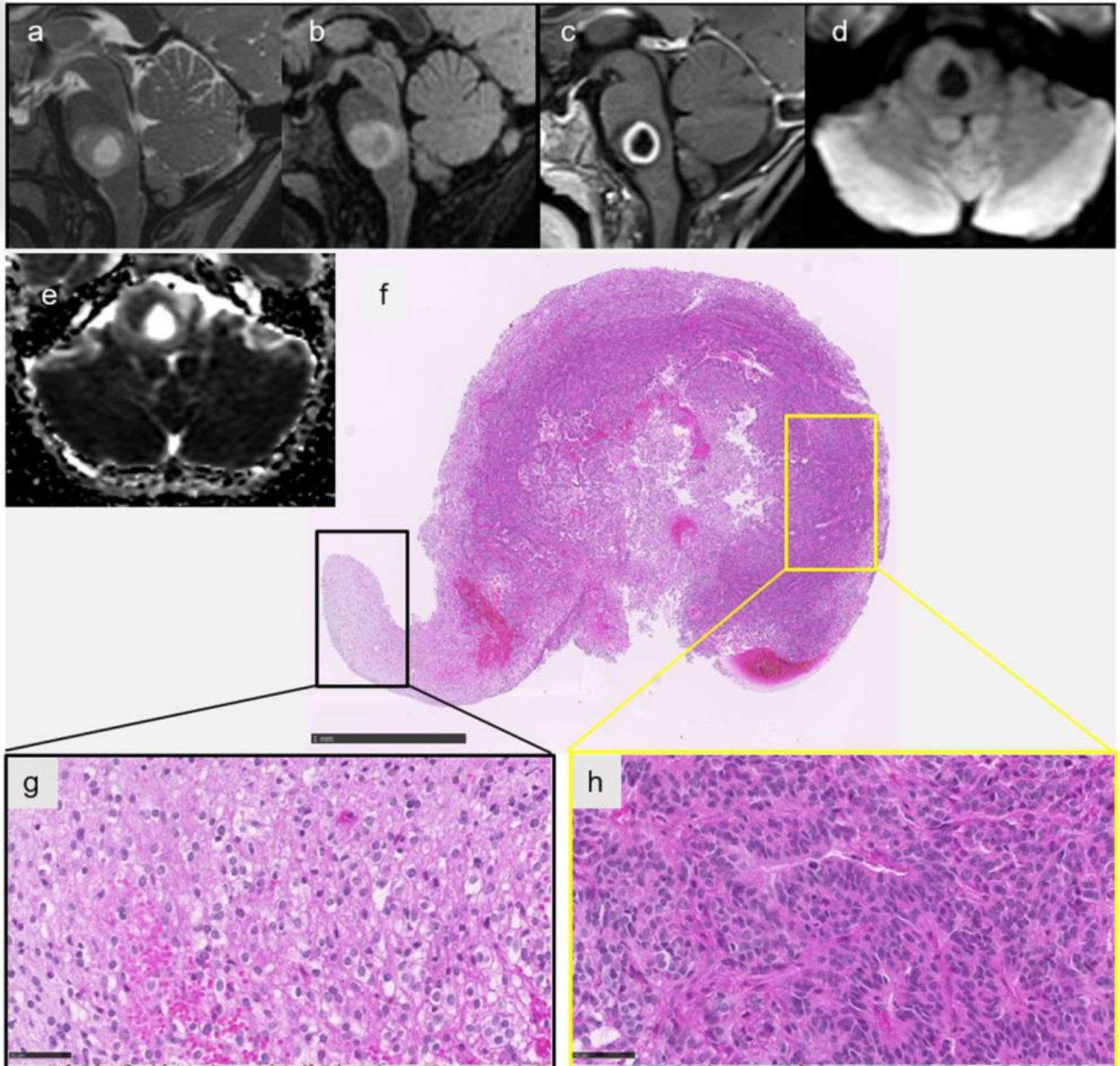
Posterior fossa ependymoma H3 K27-mutant: an integrated radiological and histomolecular tumor analysis

Cassandra Mariet[1], David Castel[2], Jacques Grill[1,2], Raphaël Saffroy[3], Volodia Dangouloff-Ros[4,5], Nathalie Boddaert[4,5], Francisco Llamas-Guttierrez[6], Céline Chappé[7], Stéphanie Puget[8], Lauren Hasty[9], Fabrice Chrétien[9], Alice Métais[9,10], Pascale Varlet[9,10] and Arnault Tauziède-Espariat[9,10*]

Acta Neuropathol Commun. 2022 Sep 14;10(1):137

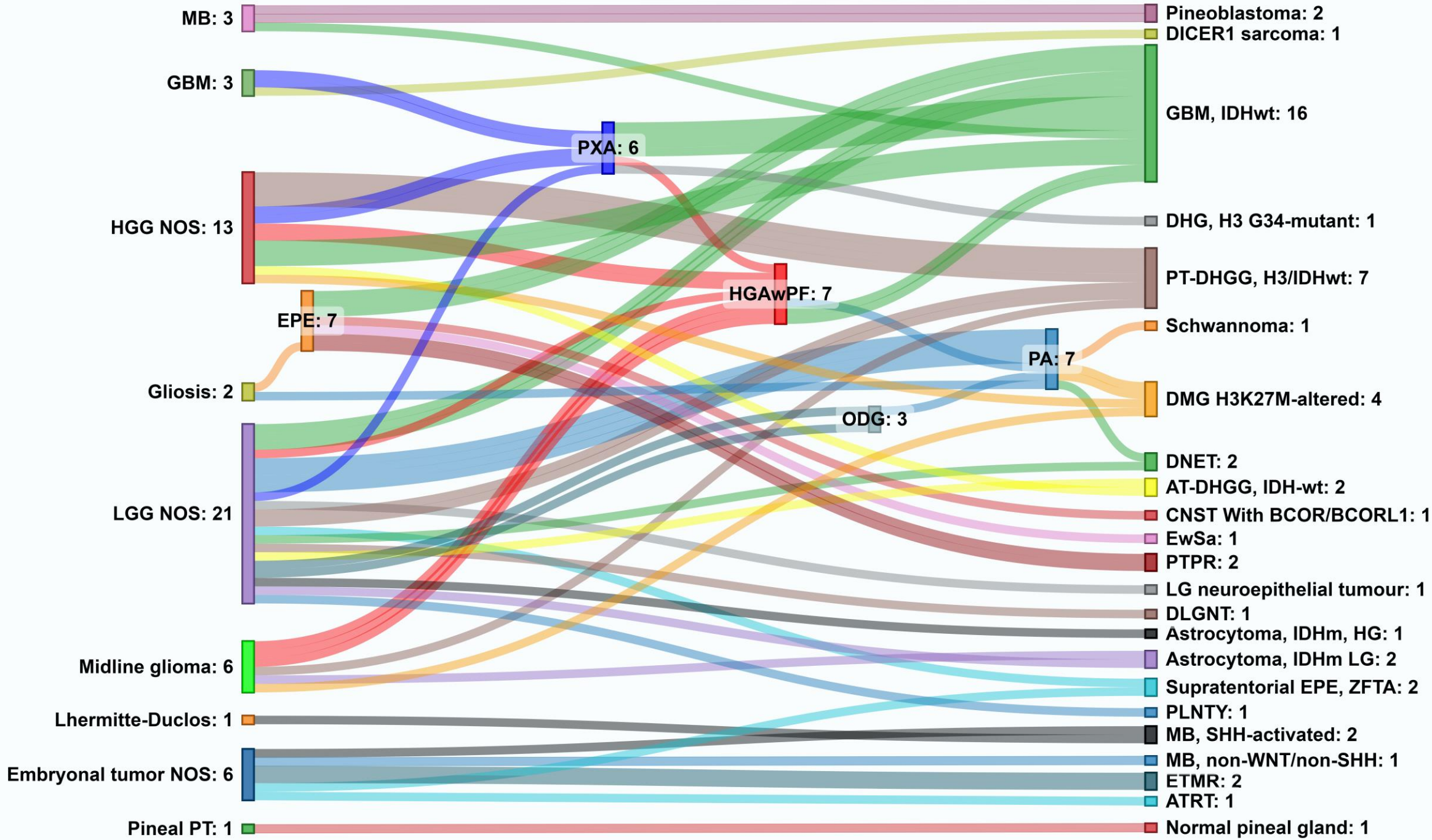
- Seven tumors clustered within EPN_PFA by DNA-methylation analysis
- Among the two remaining cases, one was reclassified as a DMG and the last was unclassified

- The diagnosis of EPN_PFA must include tumor location, growth pattern, Olig2 expression, and DNA-methylation profiling before it can be differentiated from DMG, H3 K27-altered

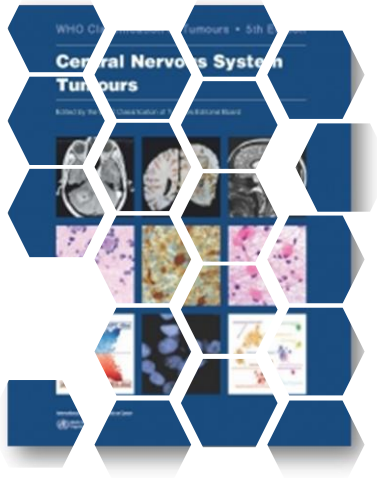


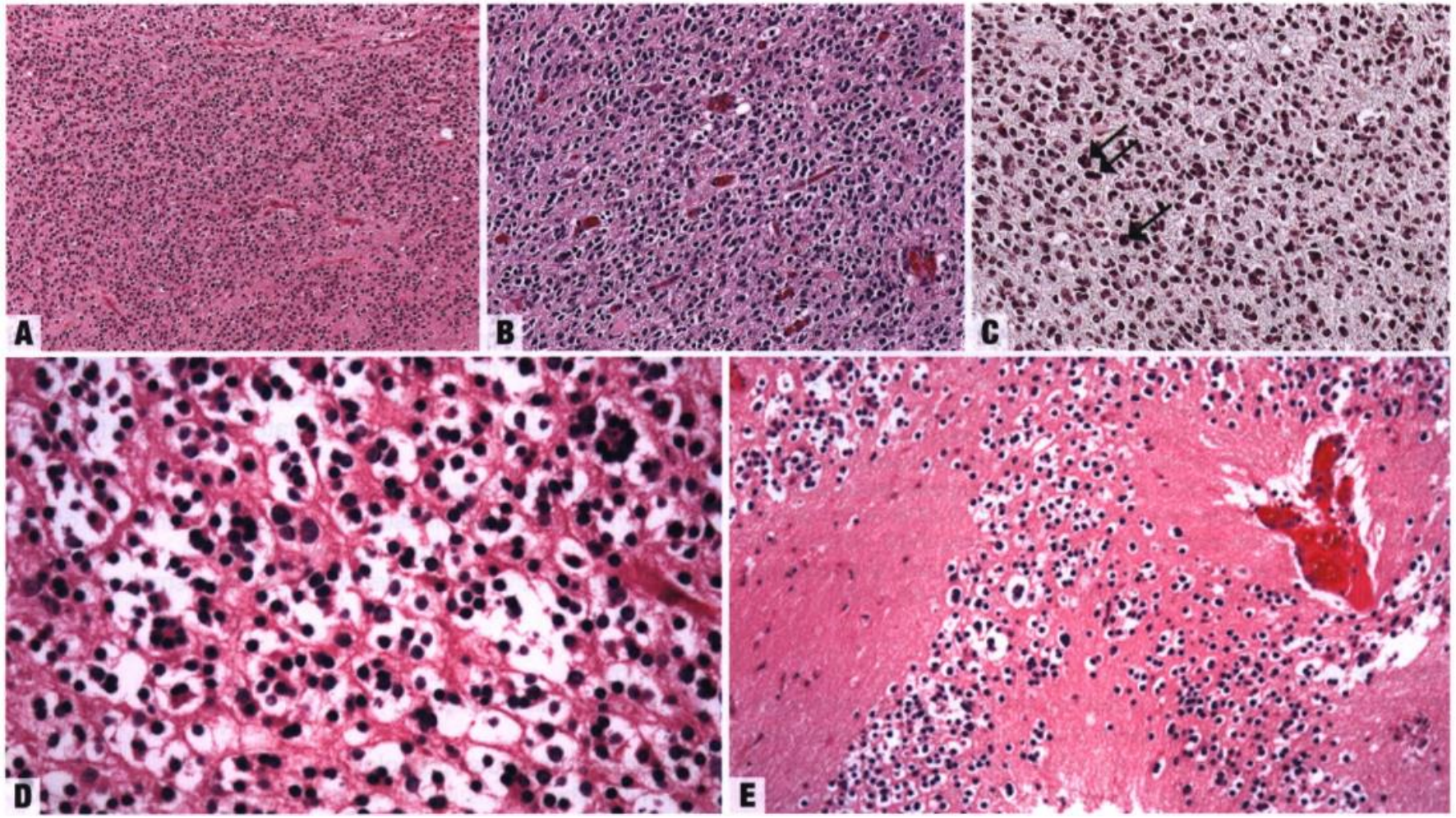
Naše skúsenosti s metylačným profilovaním za 2,5 roka: 216 nádorov CNS 206 analyzovateľných, metylóm užitočný v 78.2% prípadov

Diagnóza pomocou metylómu/významná zmena diagnózy	**N=58 (28.2%)**	Including 3 cases with CS ≥0.3 and < 0.5, and MC supporting final diagnosis
Vyriešenie diferenciálnej diagnózy	**N=20 (9.7%)**	Including 1 case with CS ≥ 0.3 and < 0.5, and MC supporting final diagnosis
Potvrdenie preferovanej diagnózy	**N=29 (14.1%)**	including 4 cases with CS ≥ 0.3 and < 0.5, and MC supporting final diagnosis
Úspešná molekulová subklasifikácia (MB, EPE)	**N=54 (26.2%)**	41 medulloblastomas, 10 ependymomas, 2 meningiomas, 1 AT/RT
Nediagnostický / nejednoznačný/neprínosný výsledok	**N=44 (21,3%)**	no CS greater 0.3 (N=6), CS ≥3 and < 0.5 and no other supportive findings (N=19), 9 cases with CS ≥ 0.5 < 0.84 and 10 cases with CS ≥ 0.84
Zavádzajúci výsledok	**N=1 (0.5%)**	

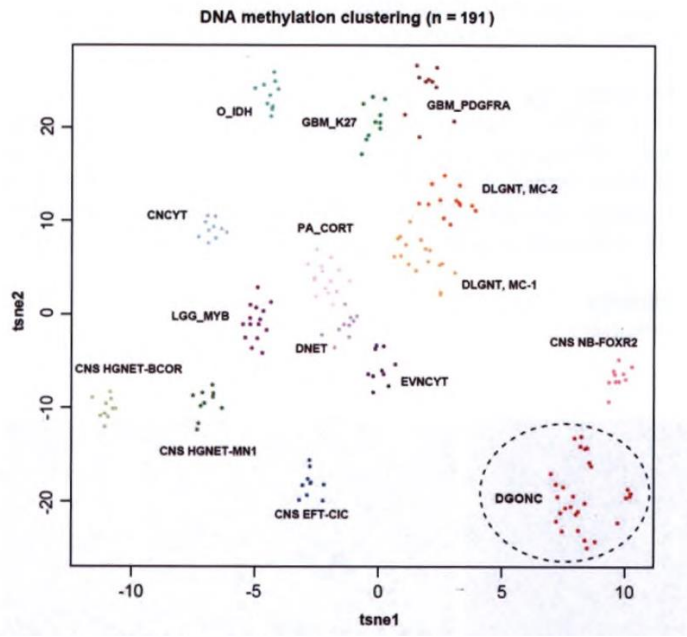

MB: 3
GBM: 3
HGG NOS: 13
EPE: 7
Gliosis: 2
LGG NOS: 21
Midline glioma: 6
Lhermitte-Duclos: 1
Embryonal tumor NOS: 6
Pineal PT: 1
PXA: 6
HGAwPF: 7
PA: 7
ODG: 3
Pineoblastoma: 2
DICER1 sarcoma: 1
GBM, IDHwt: 16
DHG, H3 G34-mutant: 1
PT-DHGG, H3/IDHwt: 7
Schwannoma: 1
DMG H3K27M-altered: 4
DNET: 2
AT-DHGG, IDH-wt: 2
CNST With BCOR/BCORL1: 1
EwSa: 1
PTPR: 2
LG neuroepithelial tumour: 1
DLGNT: 1
Astrocytoma, IDHm, HG: 1
Astrocytoma, IDHm LG: 2
Supratentorial EPE, ZFTA: 2
PLNTY: 1
MB, SHH-activated: 2
MB, non-WNT/non-SHH: 1
ETMR: 2
ATRT: 1
Normal pineal gland: 1

Diffuse glioneuronal tumor with ODG-like features and nuclear clusters(DGONC)

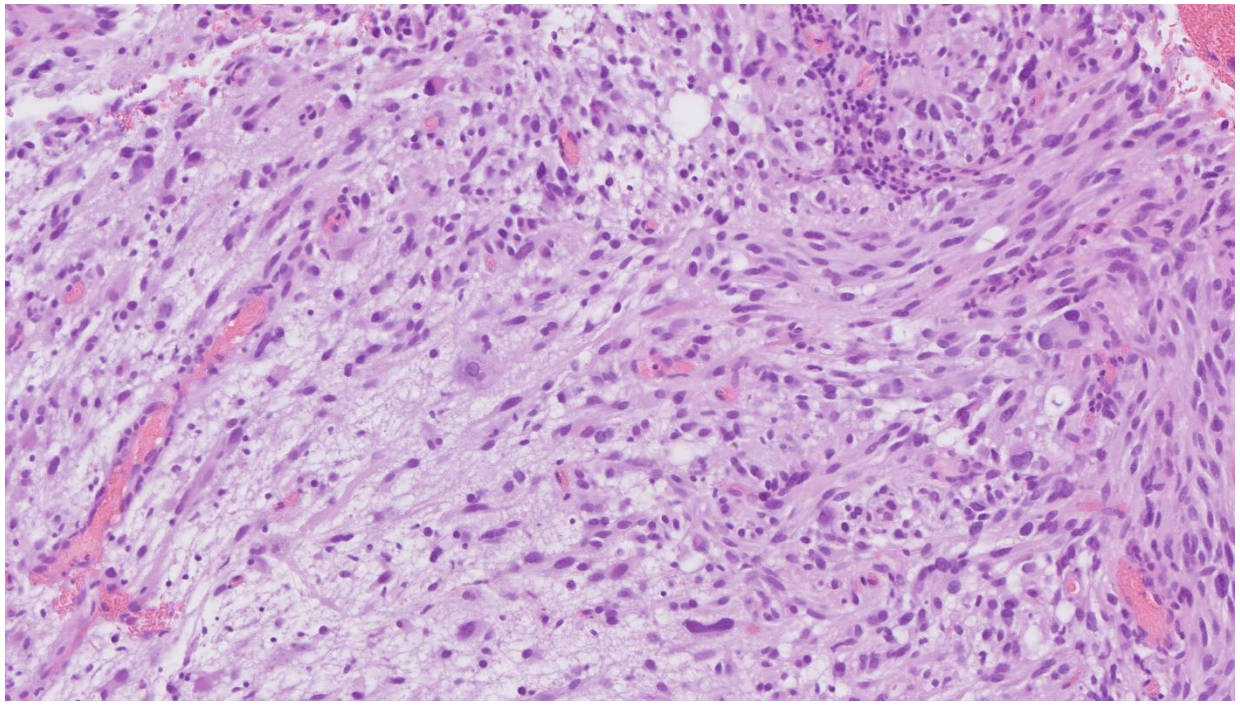


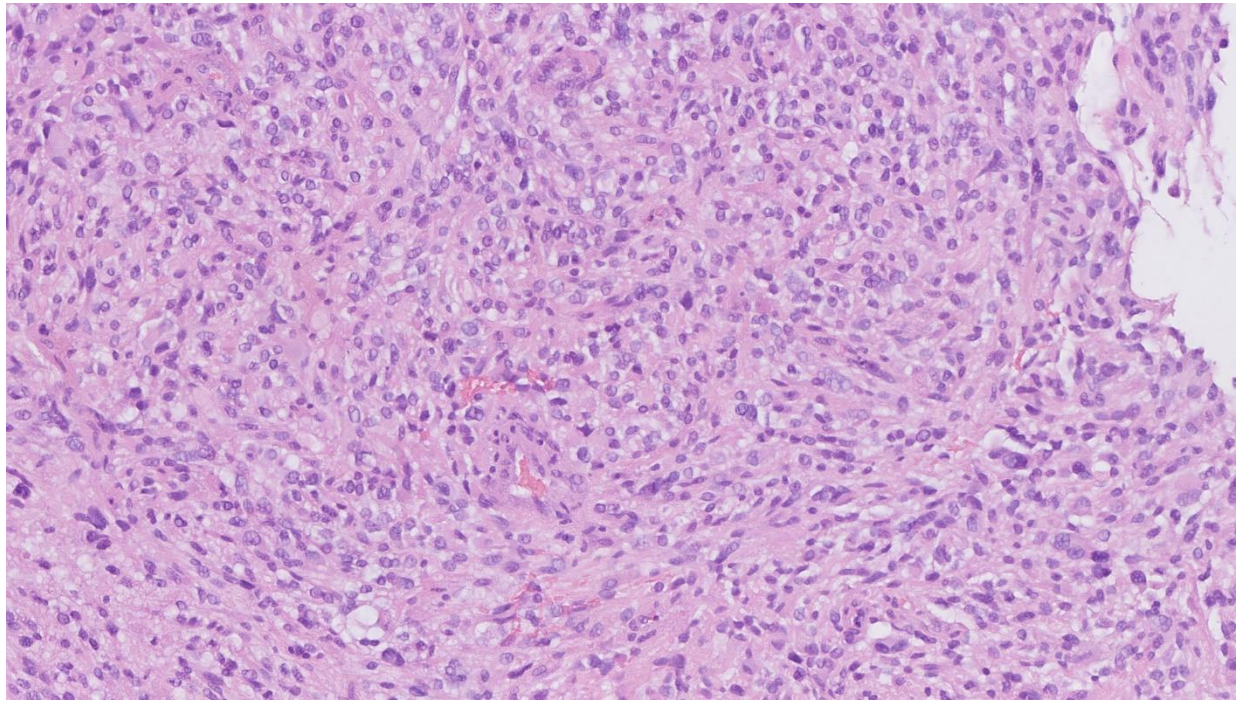


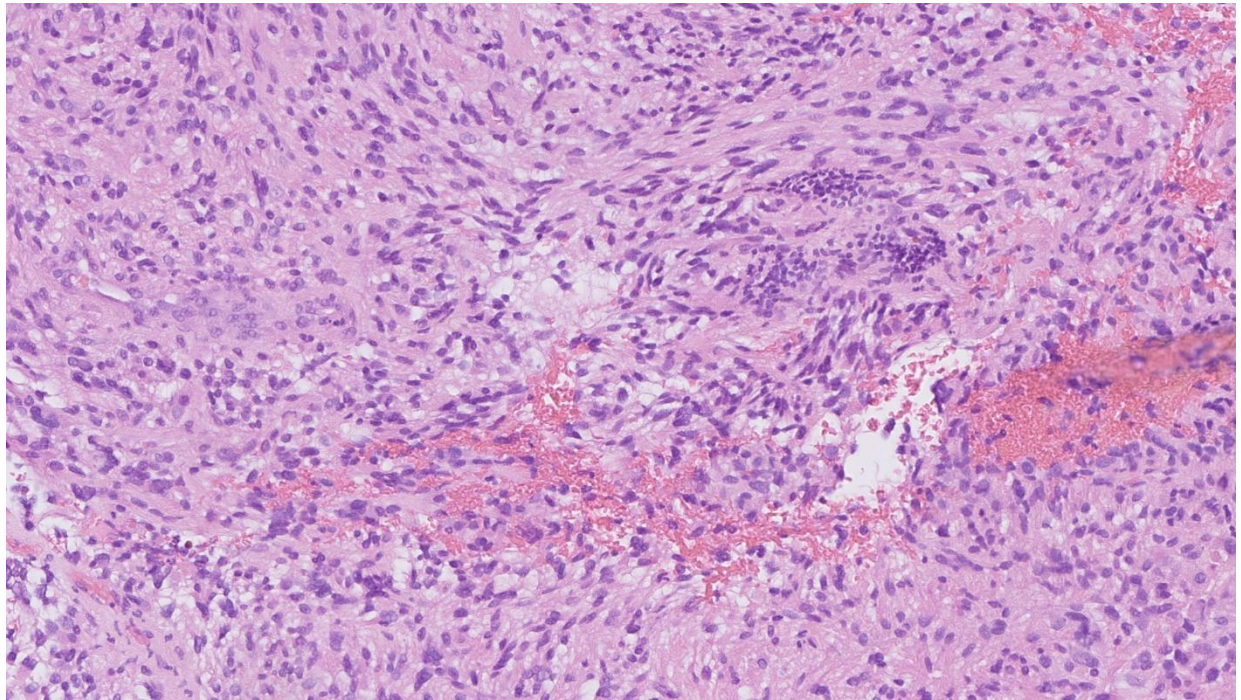
monozómia 14
žiadne ďalšie alterácie



82-ročný muž,, konzult. Slovinsko, tumor ponsu a cerebella (171148/22)







MC: High grade astrocytoma with piloid features

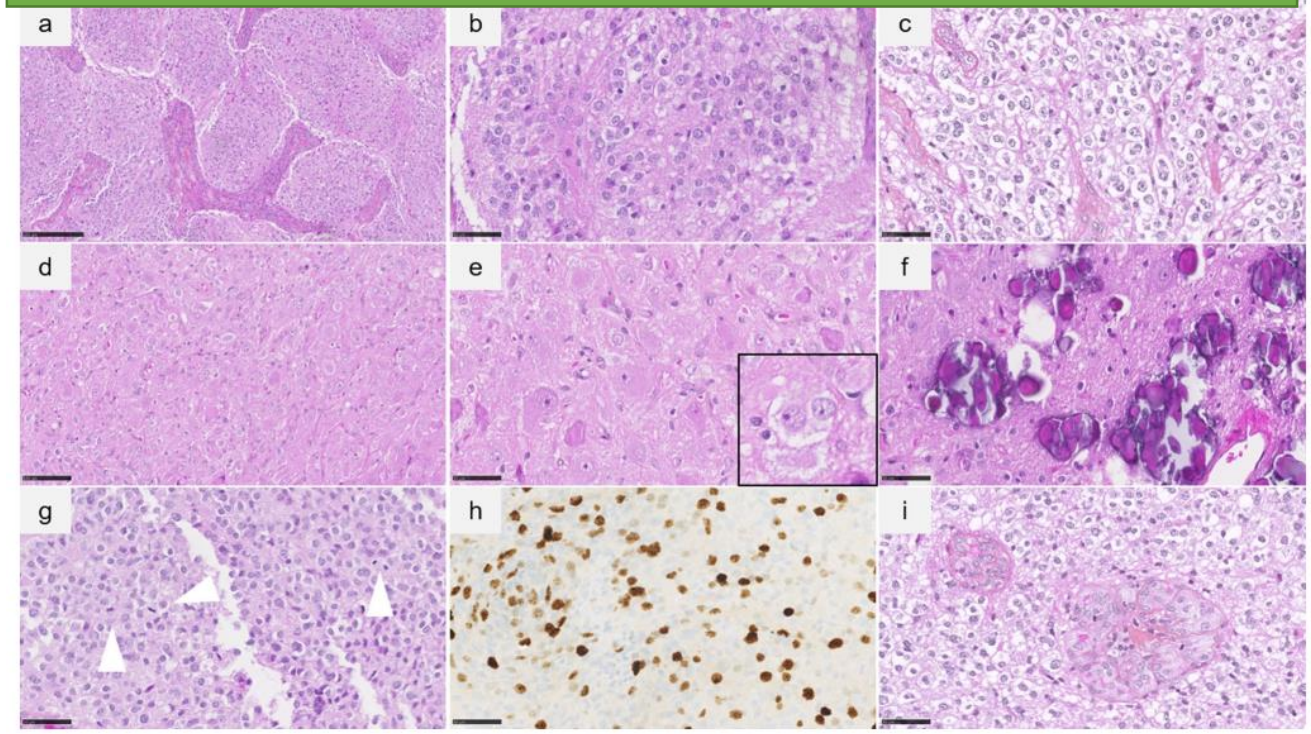
Acta Neuropathologica (2022) 144:1179–1183
https://doi.org/10.1007/s00401-022-02490-9

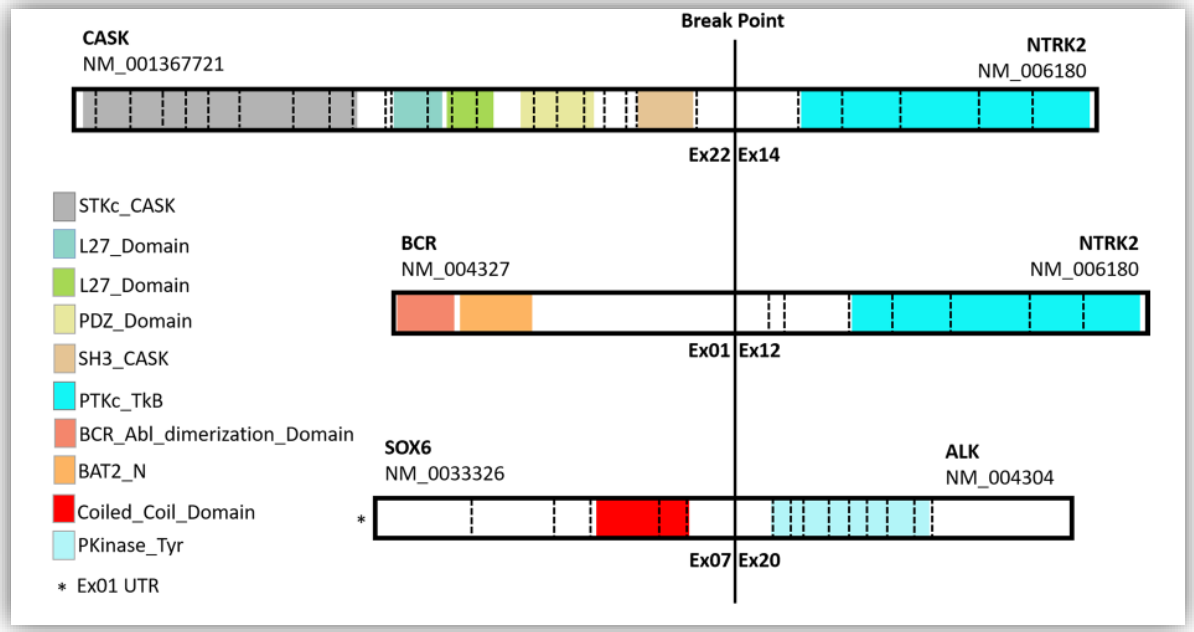
CORRESPONDENCE

Clinicopathological and molecular characterization of three cases classified by DNA-methylation profiling as "Glioneuronal Tumors, NOS, Subtype A"

Arnault Tauziède-Espariat[1,2] · Volodia-Dangouloff-Ros[3,4] · Dominique Figarella-Branger[5] · Emmanuelle Uro-Coste[6,7,8] · Yvan Nicaise[6] · Nicolas André[9,10] · Didier Scavarda[11] · Benoît Testud[12] · Nadine Girard[12] · Audrey Rousseau[13,14] · Laetitia Basset[13,14] · Guillaume Chotard[15] · Vincent Jecko[16] · François le Loarer[17,18] · Isabelle Hostein[17,18] · Marie-Christine Machet[19] · Matthias Tallegas[19] · Antoine Listrat[20] · Lauren Hasty[1] · Alice Métais[1,2] · Fabrice Chrétien[1] · Nathalie Boddaert[3,4] · Pascale Varlet[1,2] on behalf of the RENOCLIP-LOC

not included in WHO 2021





Tumor detského veku, potenciálne agresívny, ale prognóza aktuálne neistá

Identifikovateľný iba metylačným profilovaním

fúzie NTRK a ALK

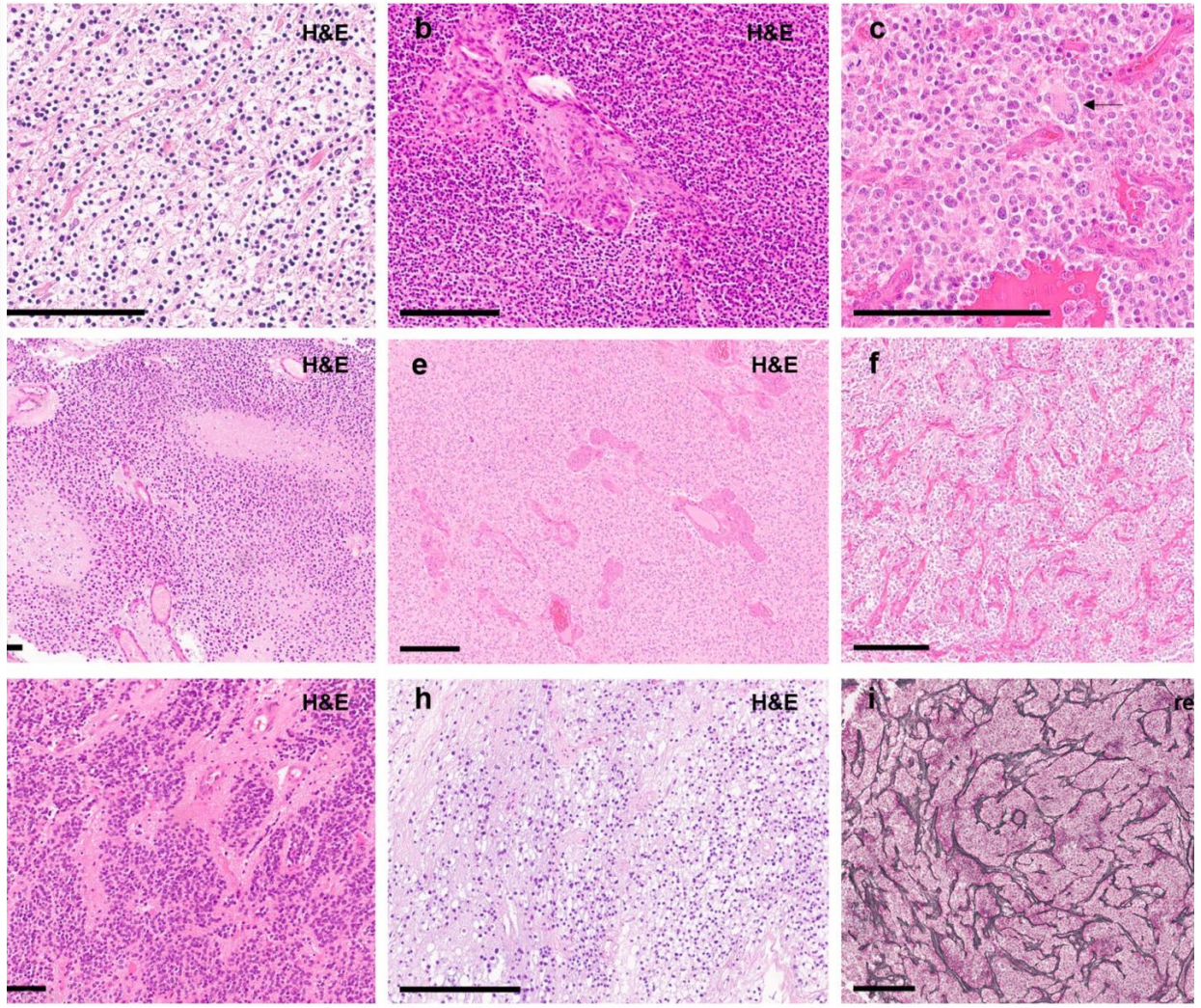
Acta Neuropathologica (2023) 145:667–680
https://doi.org/10.1007/s00401-023-02558-0

ORIGINAL PAPER

Glioneuronal tumor with *ATRX* alteration, kinase fusion and anaplastic features (GTAKA): a molecularly distinct brain tumor type with recurrent *NTRK* gene fusions

Henri Bogumil[1,2] · Martin Sill[3,4] · Daniel Schrimpf[1,2] · Britta Ismer[3,5,6] · Christina Blume[1,2] · Ramin Rahmanzade[1,2] · Felix Hinz[1,2] · Asan Cherkezov[1,2] · Rouzbeh Banan[1,2] · Dennis Friedel[1,2] · David E. Reuss[1,2] · Florian Selt[3,7,8,9] · Jonas Ecker[3,7,8,9] · Till Milde[3,7,8,9] · Kristian W. Pajtler[3,4,8] · Jens Schittenhelm[10,11,12] · Jürgen Hench[13] · Stephan Frank[13] · Henning B. Boldt[14,15] · Bjarne Winther Kristensen[14,15,16,17] · David Scheie[18] · Linea C. Melchior[18] · Viola Olesen[19] · Astrid Sehested[20] · Daniel R. Boué[21] · Zied Abdullaev[22] · Laveniya Satgunaseelan[23] · Ina Kurth[24] · Annekatrin Seidlitz[9,25,26,27,28,29,30,31] · Christine L. White[32,33,34] · Ho-Keung Ng[35,36] · Zhi-Feng Shi[36,37] · Christine Haberler[38] · Martina Deckert[39] · Marco Timmer[40] · Roland Goldbrunner[40] · Arnault Tauziède-Espariat[41,42] · Pascale Varlet[41,42] · Sebastian Brandner[43,44] · Sanda Alexandrescu[45] · Matija Snuderl[46] · Kenneth Aldape[22] · Andrey Korshunov[1,2,3] · Olaf Witt[3,7,8,9] · Christel Herold-Mende[47] · Andreas Unterberg[48] · Wolfgang Wick[49,50] · Stefan M. Pfister[3,4,8,9] · Andreas von Deimling[1,2] · David T. W. Jones[3,5] · Felix Sahm[1,2,3,9] · Philipp Sievers[1,2]

not included in WHO 2021



Supratentoriálny tumor, vek 4 – 76 rokov (median 19 rokov), potenciálne agresívny tumor, rekurencia priemerne po ~ 23 mesiacoch

Identifikovateľný iba metylačným profilovaním; alterácie ATRX, fúzie NTRK, FGFR1, EGFR, BRAF, MET; homozygotná delécia CDKN2A/B (50 %)

Acta Neuropathologica (2022) 145:49–69
https://doi.org/10.1007/s00401-022-02516-2

ORIGINAL PAPER

Amplification of the PLAG-family genes—*PLAGL1* and *PLAGL2*—is a key feature of the novel tumor type *CNS embryonal tumor with PLAGL amplification*

Michaela-Kristina Keck[1,2] · Martin Sill[1,3] · Andrea Wittmann[1,2] · Piyush Joshi[1] · Damian Stichel[4,5] · Pengbo Beck[1,3,6] · Konstantin Okonechnikow[1,3] · Philipp Sievers[4,5] · Annika K. Wefers[7] · Federico Roncaroli[8] · Shivaram Avula[9] · Martin G. McCabe[10] · James T. Hayden[11] · Pieter Wesseling[12,13] · Ingrid Øra[14] · Monica Nistér[15] · Mariëtte E. G. Kranendonk[12] · Bastiaan B. J. Tops[12] · Michal Zapotocky[16,17] · Josef Zamecnik[18] · Alexandre Vasiljevic[19] · Tanguy Fenouil[19] · David Meyronet[19] · Katja von Hoff[20] · Ulrich Schüller[7,21,22] · Hugues Loiseau[23] · Dominique Figarella-Branger[24] · Christof M. Kramm[25] · Dominik Sturm[1,2,26] · David Scheie[27] · Tuomas Rauramaa[28] · Jouni Pesola[29] · Johannes Gojo[30] · Christine Haberler[31] · Sebastian Brandner[32,33] · Tom Jacques[34] · Alexandra Sexton Oates[35] · Richard Saffery[35] · Ewa Koscielniak[36] · Suzanne J. Baker[37] · Stephen Yip[38] · Matija Snuderl[39] · Nasir Ud Din[40] · David Samuel[41] · Kathrin Schramm[1,2] · Mirjam Blattner-Johnson[1,2] · Florian Selt[1,42,43] · Jonas Ecker[1,42,43] · Till Milde[1,42,43] · Andreas von Deimling[4,5] · Andrey Korshunov[1,4,5] · Arie Perry[44] · Stefan M. Pfister[1,3,26] · Felix Sahm[1,4,5] · David A. Solomon[44] · David T. W. Jones[1,2]

not included in WHO 2021

najlepšie identifikovateľný metylačným profilovaním

Acta Neuropathologica
https://doi.org/10.1007/s00401-023-02643-4

CORRESPONDENCE

Check for updates

PLAG1 fusions extend the spectrum of PLAG(L)-altered CNS tumors

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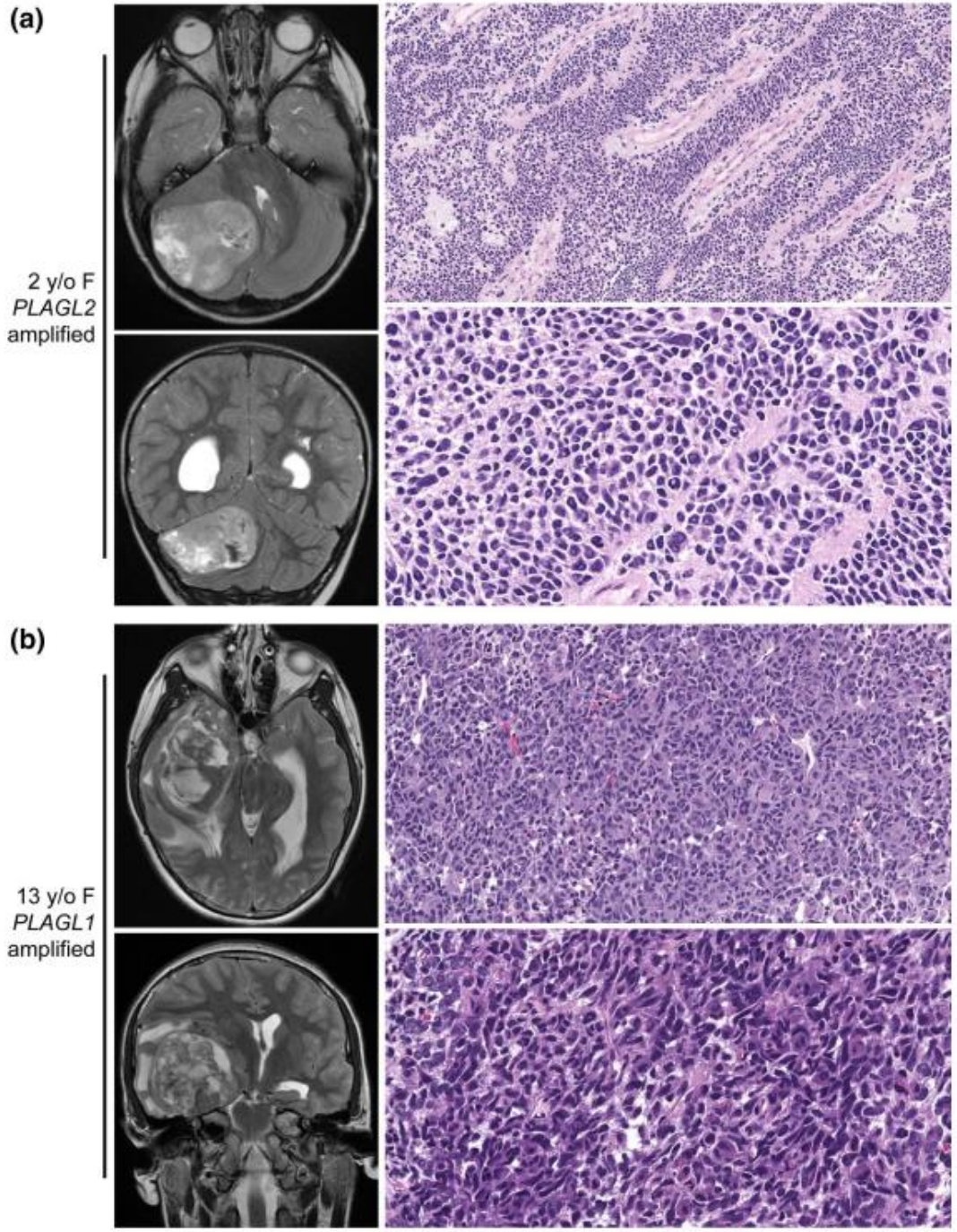
variable GFAP, MAP2, SYP, desmin
PLAGL1/2 amplification, rarely fusion



ORIGINAL PAPER

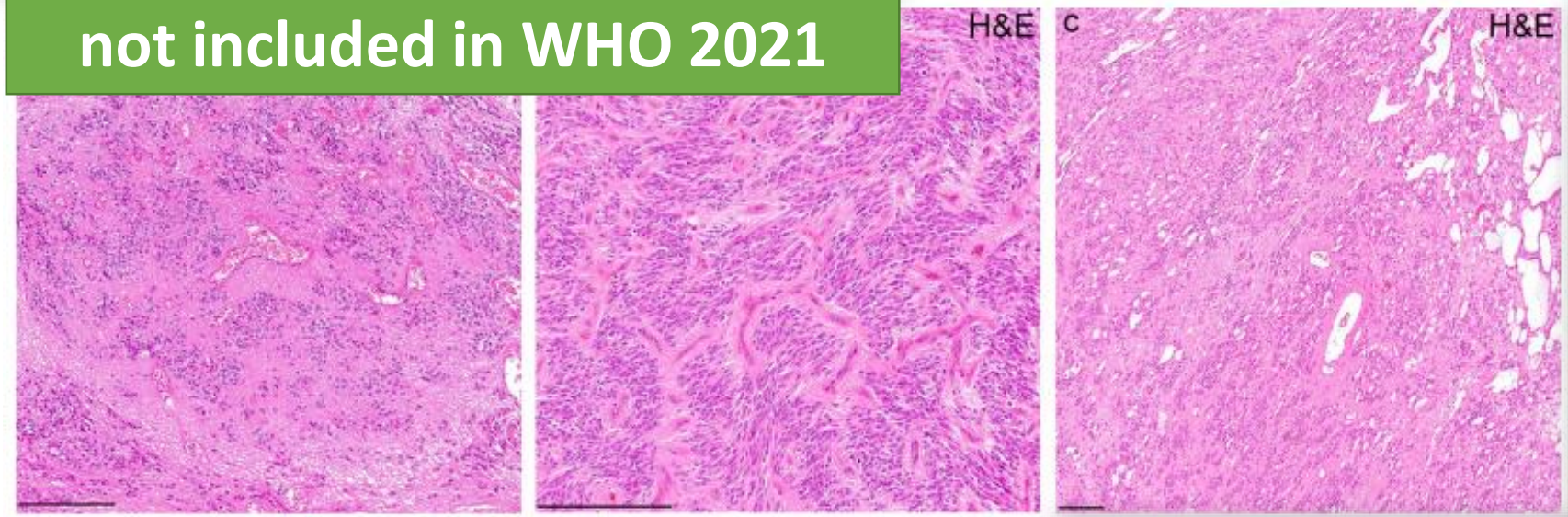
Recurrent fusions in *PLAGL1* define a distinct subset of pediatric-type supratentorial neuroepithelial tumors

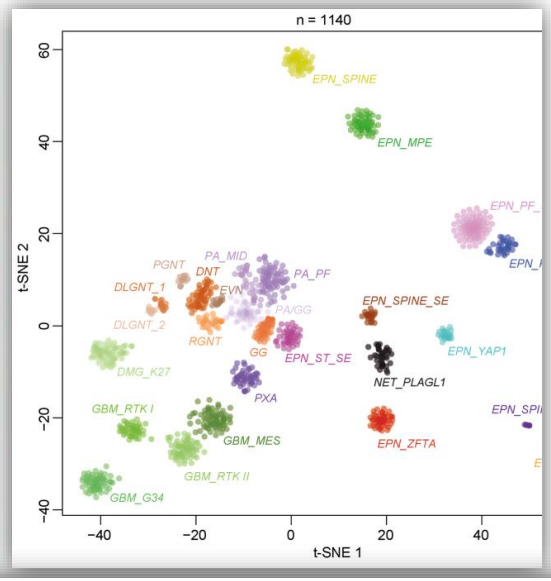
Philipp Sievers[1,2] · Sophie C. Henneken[3,4] · Christina Blume[1,2,5] · Martin Sill[3,4] · Daniel Schrimpf[1,2] · Damian Stichel[1,2] · Konstantin Okonechnikov[3,4] · David E. Reuss[1,2] · Julia Benzel[3,4] · Kendra K. Maaß[3,4,6] · Marcel Kool[3,4,7] · Dominik Sturm[3,6,8] · Tuyu Zheng[3,4,9] · David R. Ghasemi[3,4] · Patricia Kohlhof-Meinecke[10] · Ofelia Cruz[11] · Mariona Suñol[12] · Cinzia Lavarino[13] · Viktoria Ruf[14] · Henning B. Boldt[15,16] · Mélanie Pagès[17,18] · Celso Pouget[19] · Leonille Schweizer[20,21] · Mariëtte E. G. Kranendonk[7,22] · Noreen Akhtar[23,24] · Stephanie Bunkowski[25] · Christine Stadelmann[25] · Ulrich Schüller[26,27,28] · Wolf C. Mueller[29] · Hildegard Dohmen[30] · Till Acker[30] · Patrick N. Harter[31,32,33,34] · Christian Mawrin[35] · Rudi Beschorner[36] · Sebastian Brandner[37,38] · Matija Snuderl[39] · Zied Abdullaev[40] · Kenneth Aldape[40] · Mark R. Gilbert[41] · Terri S. Armstrong[41] · David W. Ellison[42] · David Capper[20,21] · Koichi Ichimura[43] · Guido Reifenberger[44,45] · Richard G. Grundy[46] · Nada Jabado[47,48,49] · Lenka Krskova[50,51] · Michal Zapotocky[50,52] · Ales Vicha[50,52] · Pascale Varlet[17] · Pieter Wesseling[7,53] · Stefan Rutkowski[27] · Andrey Korshunov[1,2,3] · Wolfgang Wick[54,55] · Stefan M. Pfister[3,4,6] · David T. W. Jones[3,8] · Andreas von Deimling[1,2] · Kristian W. Pajtler[3,4,6] · Felix Sahm[1,2,3]

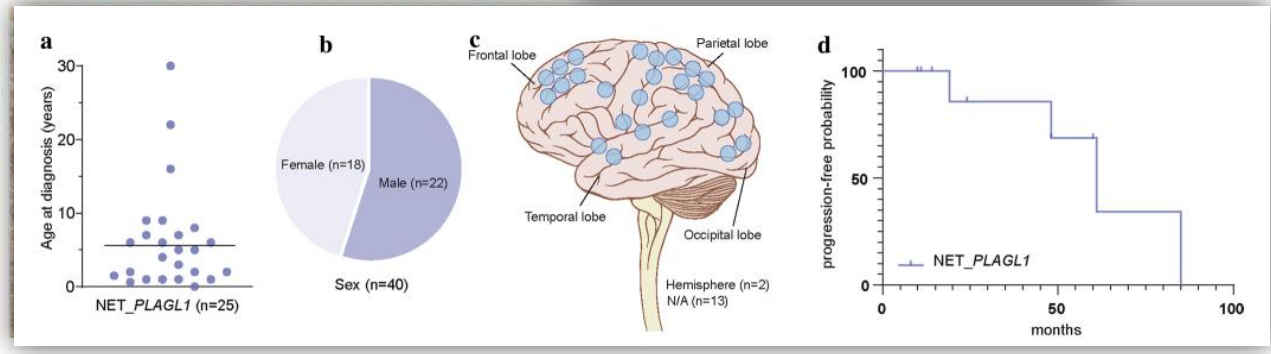
not included in WHO 2021

Tumor prevažne detského veku, pravdepodobne s ependymálnou diferenciáciou, median PFS = 35 mesiacov

Identifikovateľný iba metylačným profilovaním





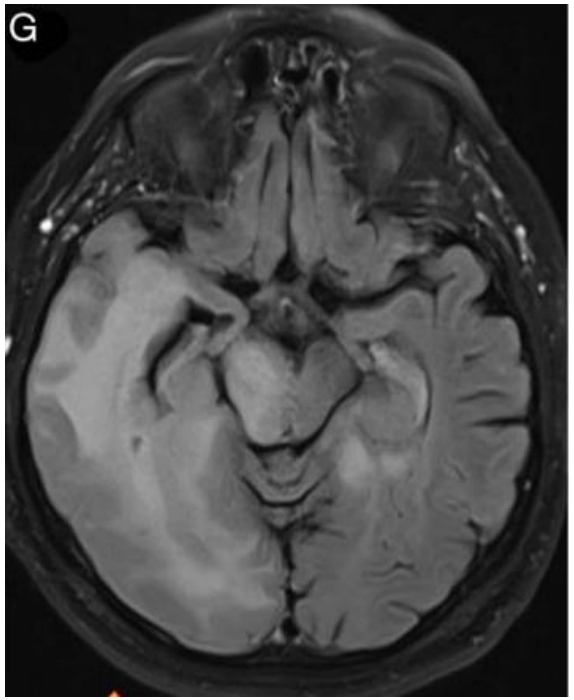


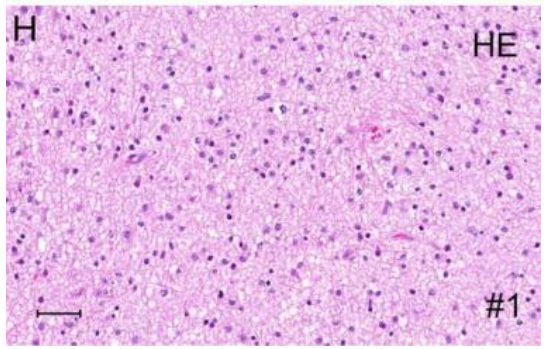
A Novel Type of IDH-wildtype Glioma Characterized by Gliomatosis Cerebri-like Growth Pattern, TERT Promoter Mutation, and Distinct Epigenetic Profile

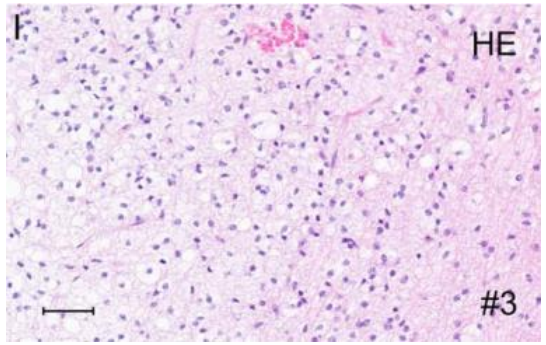
Amos Muench, MSc, Daniel Teichmann,† Dorothee Spille, MD,‡ Peter Kuzman, MD,§ Eilis Perez, MSc,† Sven-Axel May, MD,‖ Wolf C. Mueller, MD,§ Theodoros Kombos, MD,¶ Shokufe Nazari-Dehkordi, MD,¶ Julia Onken, MD,# Peter Vajkoczy, MD,# Georgios Ntoulias, MD,** Conceição Bettencourt, PhD,†† Andreas von Deimling, MD,‡‡ Werner Paulus, MD,§§ Frank L. Heppner, MD,†‖‖¶¶## Arend Koch, MD,†‖‖‖ David Capper, MD,†‖‖‖ David Kaul, MD,*** Christian Thomas, MD,§§ and Leonille Schweizer, MD*†‖‖‖†††‡‡‡*

Am J Surg Pathol 2023;47:1364–1375

not included in WHO 2021







Radiologicky často obraz podobný gliomatosis cerebri, morfologicky difúzny glióm s astrocytárnou morfológiou, bez nekrózy alebo mikrovaskulárnej proliferácie.

Prognóza signifikantne lepšia ako pri glioblastóme, IDHwt, podobná IDH-mutovaným astrocytómom

Identifikovateľný iba metylačným profilovaním

mutácie promótora TERT, PIK3R1, p53


REFLEX


Teda, to muselo dát
příšernou práci.
Přitom taková blbost, co
Zdroj: Vysoká škola života.
Katedra mikrobiológie a virológ