

Molecular profile of adult primary leptomenigeal gliomatosis aligns with glioblastoma, IDH-wildtype

Running title: Adult primary leptomenigeal gliomatosis

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Supporting information

FIGURE S1. Pathological findings of primary leptomenigeal gliomatosis in cases 3 and 4.

Leptomeningeal biopsies from the frontal lobe of case 3 and cauda/filum of case 4 are shown with H&E. Yellow arrowhead highlights a mitotic figure.

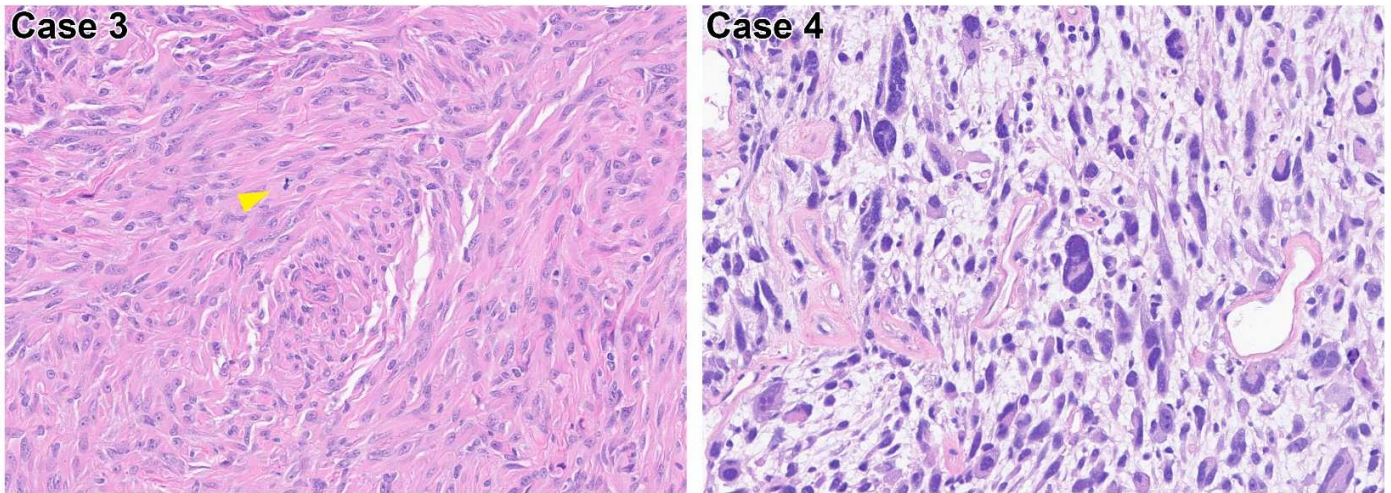


FIGURE S2. Autopsy findings of primary leptomenigeal gliomatosis in case 6.

Gross findings of the optic chiasm (A) and cauda equina nerve root (B). Histopathological findings of the cingulate cortex (C), cerebellum (D), and cauda equina nerve root (E, low magnification; F, high magnification).

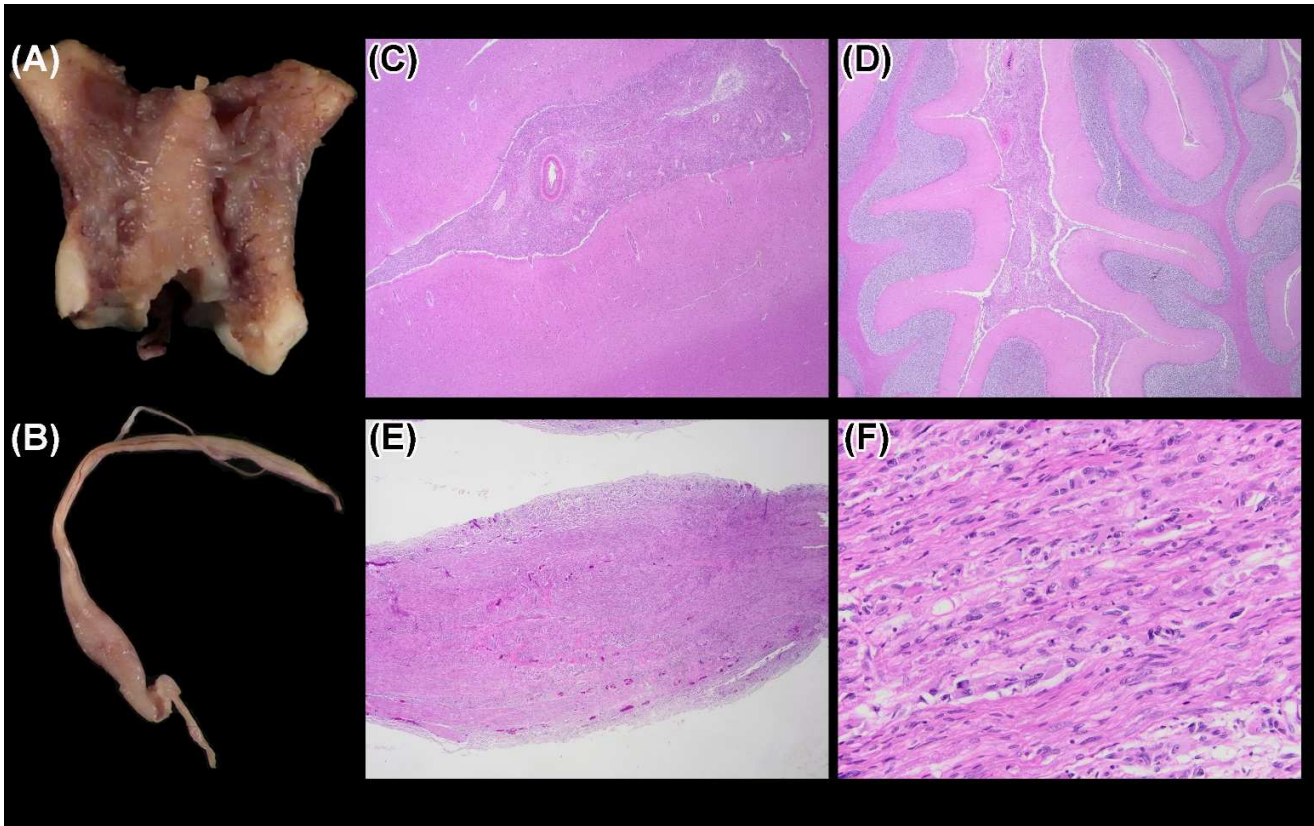


TABLE S1 Summary of reported PLG cases

	Year	First author	PMID	Age/ year	Sex	Imaging	CSF	Biopsy/resection site	Pathological diagnosis on biopsy/resection	Pathological diagnosis on autopsy	Genetic analysis	Survival
1	1954	Moore[1]	13118379	60	F	N/A	N/A	N/A	N/A	Untyped	N/A	Died 15 months after onset of symptoms
2	1974	Bhrany[2]	4446969	46	F	N/A	Negative for tumor cells	Right occipital lobe	Negative	Astrocytoma	N/A	Died 2 weeks after second admission
3	1981	Ho[3]	7295114	55	M	Symmetrical dilation of the ventricular system. No parenchymal lesions.	Negative for tumor cells	N/A	N/A	Astrocytoma	N/A	Died 3 month after onset of symptoms
4	1983	Kalyan-Raman[4]	6886737	61	M	Myelogram revealed total block at T2 due to intradural extramedullary mass	Negative for tumor cells	Mass resection from C7 to T3	Astrocytoma	Astrocytoma	N/A	Died 1 month after mass resection
5	1986	Blumenkopf[5]	3703199	48	M	Absence of normal smooth contour of the cervical cord from the level of the foramen magnum to mid-C2	Negative for tumor cells	Suboccipital craniectomy and C1 to C2 laminectomy	Low-grade astrocytoma with pilocytic features	N/A	N/A	Alive 5 months after surgery
6	1987	Whelan[6]	3652562	42	M	Ventricular dilation	Negative for tumor cells	Cerebellar	Negative	Astrocytoma	N/A	Died 10 days after admission
7	1990	Heye[7]	2336982	43	M	Blurring of the cortical sulci and basal cisterns, no contrast enhancement and progressive ventricular enlargement.	Negative for tumor cells	N/A	N/A	Untyped	N/A	Died 4 months after onset of symptoms
8	1993	Dietrich[8]	8360714	63	F	Contrasted/noncontrasted MRI, including the spinal cord, did not show any anomaly even on retrospect	Negative for tumor cells	Right temporal lobe	Negative	GBM, WHO grade 4	N/A	Died 40 days after admission
9	1994	Carpentier[9]	7863170	44	F	Diffuse contrast enhancement of the leptomeninges. A lesion in the left temporal region of the Sylvian fissure.	Negative for tumor cells	Left temporal lobe	Anaplastic oligoastrocytoma	N/A	N/A	Died a few days later after biopsy
10	1994	Fayet[10]	7792477	53	F	Diffuse meningeal enhancement extending to the posterior fossa and cervical spine without intraparenchymal lesion	Negative for tumor cells	N/A	N/A	Astrocytoma	N/A	Died after a progressive course of 6 months
11	1994	Fayet[10]	7792477	55	F	Diffuse, bilateral meningeal enhancement.	Negative for tumor cells	Right temporal lobe	Negative	Astrocytoma	N/A	Died 40 days after onset of symptoms
12	1994	Ashworth[11]	8163998	69	F	Slight dilation of the lateral ventricles	Negative for tumor cells	N/A	N/A	Astrocytoma, WHO grade 4	N/A	N/A
13	1995	Giordana[12]	7754854	49	F	Diffuse bilateral enhancement in the basal	Negative for tumor cells	Perispinal	Astrocytoma/GBM, WHO grade 4	Astrocytoma/GBM, WHO grade 4	N/A	Died 2 months after

						and perisellar cisterns and perispinal space						pathological diagnosis
14	1996	Kobayashi[13]	8738401	60	M	Holocord leptomeningeal gliomatosis without a definite intraparenchymal lesion	Negative for tumor cells	T3	Astrocytoma, WHO grade 3	N/A	N/A	Died 11 months after operation
15	1998	Singh[14]	9817460	47	M	Diffuse meningeal enhancement, especially in the posterior fossa and spine, enlargement of the right cerebellar tonsil, and a mass in the canal of Magendie	"Atypical" lymphocytes	Suboccipital craniotomy with biopsy of the right cerebellar tonsil, obex, and leptomeninges	Anaplastic astrocytoma, subependymoma	Anaplastic astrocytoma, subependymoma	N/A	Died 2 weeks after biopsy and 8 weeks after the onset of symptoms
16	1999	Pradat[15]	10619500	44	M	Convexity and spine enhancement	Not specified	Corticomeningeal	Anaplastic oligoastrocytoma	N/A	N/A	Died 4 weeks from presentation
17	2000	Corsten[16]	11303666	44	M	Mild ventricular enlargement consistent with communicating hydrocephalus and enhancement of the basal meninges but no evidence of intra-parenchymal lesions or hemorrhage	Negative for tumor cells	T12 and L1	GBM, WHO grade 4	N/A	N/A	Rapid decline
18	2000	Sell[17]	14606585	62	M	Enhancing right cerebellar lesion with areas of central necrosis and abnormal enhancement of the leptomeninges.	Positive for anaplastic cells	N/A	N/A	Astrocytoma, high grade	N/A	Died 5 weeks after stopping radiation.
19	2000	Trivedi[18]	11154809	81	M	Extensive subependymal and brainstem enhancement, in addition to the signal at the left trigone	Negative for tumor cells	Frontal pole of the right lateral ventricle	GBM, WHO grade 4	N/A	N/A	Died 4 weeks after admission
20	2001	Rees[19]	11118261	51	M	Communicating hydrocephalus and conspicuous contrast enhancement around the basal cisterns	Occasional atypical cell	N/A	N/A	Astrocytoma, WHO grade 3	N/A	Died 2 days after starting systemic chemotherapy
21	2001	Baborie[20]	11160482	71	M	No leptomeningeal enhancement	Negative for tumor cells	N/A	N/A	Astrocytoma	N/A	Died 7 months after onset of symptoms
22	2005	Franceschi[21]	15980977	40	F	Leptomeningeal enhancement and hydrocephalus	Negative for tumor cells	Intrapeduncular cistern	Astrocytoma	N/A	N/A	Died 17 months after diagnosis
23	2005	Riva[22]	15995830	62	F	Extra-axial contrast enhancement in the absence of mass lesions	Negative for tumor cells	N/A	N/A	Untyped	N/A	Died 3 weeks after presentation
24	2007	Ishige[23]	17645245	45	M	Diffuse leptomeningeal enhancement throughout the central nervous system without intra-axial mass accompanied with the	Negative for tumor cells	Right frontal lobe	GBM, WHO grade 4	N/A	N/A	Died 3 months after the biopsy and 18 months after

						dilatation of ventricles and focally enlarged cerebral sulci						onset on symptoms
25	2007	Yomo[24]	17031563	52	M	Diffuse leptomeningeal enhancement without any source of intraparenchymal lesion	Negative for tumor cells	1st right frontal, 2nd right frontotemporal	1st non-specific, 2nd anaplastic astrocytoma	Astrocytoma/GBM, WHO grade 4	N/A	Died 3 months after presentation
26	2008	Watanabe[25]	17628746	48	F	Diffuse meningeal thickening and enhancement without a definite intraparenchymal lesion	Atypical anaplastic cells, GFAP+, S100+	Left frontotemporal lobe	Gliosarcoma	Gliosarcoma	N/A	Died 11 months after admission
27	2009	Mathews[26]	19290482	50	F	Diffuse enhancement of leptomeninges throughout brain and spine, prominent over the basilar region.	Negative for tumor cells	Left frontotemporal lobe	Oligodendroglioma	N/A	Negative for 1p19q codeletion	Died 4 days after hospice care.
28	2009	Michotte[27]	19751941	61	M	Diffuse leptomeningeal enhancement without intraparenchymal extension, most pronounced in the right parietotemporal region	N/A	Right parietal lobe	Anaplastic Oligodendroglioma, WHO grade 3	N/A	FISH: 1p36 19q13 co-deletion	Alive more than 2 years after diagnosis
29	2010	Bhatia[28]	19898776	52	F	Enhancing cervicothoracic lesion confined to the leptomeninges	Negative for tumor cells	T2	Astrocytoma, WHO grade 3	N/A	N/A	Died 8.5 months after pathological diagnosis
30	2010	Somja[29]	21305863	76	M	Diffuse and nodular leptomeningeal contrast enhancement predominant at the skull base and several osteolytic lesions in the right parietal bone	Atypical large lymphocytes and monocytes	Right parietal lobe	Negative	GBM, WHO grade 4	FISH: inclusive due to fixation artefacts	Died 35 days after admission
31	2011	Hansen[30]	22024443	53	M	Numerous spinal and cranial enhancing nodules in the meninges	Atypical cells	L2-L3	Astrocytoma, WHO grade 3	N/A	N/A	Died 22 months after diagnosis
32	2011	Keith[31]	21316246	73	F	Meningeal enhancement with patchy nodularity extending to the spine	Negative for tumor cells	Left occipital lobe	Untyped	N/A	N/A	Died 10 days after pathological diagnosis, 6 month after initial presentation
33	2011	Dimou[32]	21356591	84	F	A large lesion within the sphenoid sinus and sella resulting in chiasmal compression, and diffuse cranial and spinal leptomeningeal enhancement	Negative for tumor cells	Sphenoid/sellar	Gliosarcoma	N/A	N/A	N/A
34	2012	Heijink[33]	22274977	50	F	Dural thickening starting from the craniocervical junction to the level of C4 without any parenchymal lesions	Negative for tumor cells	C1	Astrocytoma and oligodendroglioma, WHO grade 3	N/A	N/A	N/A

35	2012	Rodriguez[34]	22941225	46	F	Small non-enhancing mass at the edge of the frontal lobe 3-4 years previously; recent MRI dissemination in ventricles and spinal cord (enhancement)	N/A	Not specified	Oligodendroglial-like tumor	Not specified	Not specified	Not specified
36	2013	Leep Hunderfund[35]	23914328	54	F	Optic chiasm enlargement, diffuse nodular leptomeningeal enhancement with communicating hydrocephalus, and nodular enhancement of the cauda equina	Negative for tumor cells	1st lumbar, 2nd lumbar and cauda equina, 3rd right frontal lobe	1st, 2nd negative, 3rd anaplastic oligodendroglioma	N/A	FISH: 1p19q codeletion	Died several weeks after pathological diagnosis
37	2014	Yamasaki[36]	24473978	60	M	Diffuse leptomeningeal thickening and enhancement throughout the brain and spinal cord without any intraaxial involvement.	Suggestive, but not conclusive for malignancy	Left frontal	GBM, WHO grade 4	N/A	Sanger sequencing: TERTp mutation C228T. Methylation-specific PCR: MGMTp methylation positive	Died 8 months after initial presentation
38	2014	Louapre[37]	25246603	79	F	Spinal cord meningeal enhancement. No intracranial meningeal enhancement. .	Atypical large cells, strongly suggesting malignancy, GFAP+, S100+	N/A	N/A	N/A	N/A	Died 7 months after initial neurological symptoms
39	2015	Cho[38]	24770606	62	M	Leptomeningeal thickening with enhancement and minor superficial parenchymal lesion.	N/A	Cerebellum, resection	DL-GNT	N/A	N/A	Died 1 month after resection
40	2015	Fernandez-Vega[39]	26086054	64	F	Leptomeningeal enhancement involving the whole brain, M1 segment of the right middle cerebral artery, and upper part of the spinal cord	N/A	Frontal lobe (twice)	Not specified	Untyped, WHO grade 3	N/A	Died 6 months after first admission
41	2015	Moon[40]	25977905	68	M	Diffuse leptomeningeal enhancement without a definite intraparenchymal lesion	N/A	Temporal	Gliosarcoma	N/A	Methylation-specific PCR: MGMTp methylation positive, FISH: intact 1p19q	Died 5 months after presentation
42	2016	Ahmad[41]	27891270	43	F	Diffuse thickening of the leptomeninges	Negative for tumor cells	Lower thoracic dura	Untyped	N/A	N/A	Died 5 months after presentation
43	2016	Tauziede-Espariat[42]	26397750	50	M	Diffuse nodular enhancement of	Negative for tumor cells	L2	Astrocytoma, WHO grade 3	Astrocytoma, WHO grade 3	FISH: intact 1p19q	Died 7 months after

						the leptomeninges of the cerebral hemispheres, cerebellum, spinal cord, and cauda equina						pathological diagnosis
44	2016	Sivak[43]	26944049	56	F	Meninges were enhanced in frontoparietal regions	Negative for tumor cells	N/A	N/A	GBM, WHO grade 4	N/A	Died 10 months after first report of neurological pain
45	2016	Tauziede-Espariat[42]	26397750	56	F	Diffuse leptomeningeal enhancement around the cerebellum, the cauda equina, and the spinal cord	Negative for tumor cells	Cervical enhancement area (three times)	1st and 2nd biopsies: inconclusive, 3rd biopsy: Oligodendroglioma, WHO grade 3	N/A	FISH: Isolated 19q deletion, H3K27M mutated, H3K27me3 loss	Alive with stable disease 23 month after diagnosis
46	2016	Tauziede-Espariat[42]	26397750	58	M	Compressive intramedullary hypersignal from T8 to T11, associated with a diffuse leptomeningeal enhancement of the cervicothoracolumbar spine, cauda equina, and infra- and supratentorial meninges	Negative for tumor cells	Temporal lobe (twice)	1st: negative, 2nd: Astrocytoma, WHO grade 2	N/A	FISH: intact 1p19q	Died 2 month after diagnosis
47	2017	Lepreux[44]	28332472	68	M	Lateral ventricles dilatation with wall thickening as well as high intensity of the right leptomeninges. No intraparenchymatous tumor was noted	Scattered atypical cells	N/A	N/A	Untyped	N/A	Died 1 month after admission
48	2018	Champeaux[45]	29752148	40	F	Multiple leptomeningeal lesions with no intra parenchymal involvement	Negative for tumor cells	L2	Untyped	N/A	H3K27M mutation	Death 18.5 weeks after initial diagnosis
49	2023	Gatzert[46]	31752539	52	M	Diffuse leptomeningeal thickening and enhancement without definitive evidence of an intraparenchymal lesion	Negative for tumor cells	Left temporal lobe	Oligodendroglioma, WHO grade 3	N/A	FISH: Isolated 1p deletion	Died 59 days after initial presentation, 44 days after pathological diagnosis
50	2024	Sol[47]	39225924	74	M	Leptomeningeal contrast enhancement around the brainstem, cerebellum, and surrounding the cranial nerves in the absence of intraparenchymal lesions	Negative for tumor cells	N/A	N/A	GBM, WHO grade 4	cfDNA NGS: TERTp mutation. CNV: <i>PDGFRA</i> and <i>MDM4</i> gain and <i>CDKN2A/B</i> loss. DNA methylation: GBM-MID	Rapidly worsened

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