Scientific Journal of
Neurology & Neurosurgery

Review Article

Intradural Intramedullary Primary Spinal Melanoma: A Case Report and Review of the Literature-

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Submitted: 17 December 2019; **Approved:** 26 December 2019; **Published:** 27 December 2019

Cite this article: Majeed K, Hussain I, Pisapia DJ, Song W, Magge R, et al. Intradural Intramedullary Primary Spinal Melanoma: A Case Report and Review of the Literature. Sci J Neurol Neurosurg. 2019;5(1): 012-018.

ISSN: 2640-5733

ABSTRACT

Background & Importance: Primary CNS melanoma of the spinal cord are rare neoplasms. They represent a spectrum of benign melanocytomas to malignant melanomas.

Clinical Presentation: A 53-year-old female had presented with several months of right thigh pain and paresthesia's. There was also midthoracic pain. MRI revealed a 1.5 cm contrast enhancing mass at T10-T11 level. It was exophytic, intradural and intramedullary. Patient underwent laminectomy, gross total excision and received radiotherapy post-operatively. Histopathology analysis showed features of malignant melanoma and molecular study revealed a *GNAQ* mutation. Full body exam and scanning did not reveal any other primary malignancy. Literature was reviewed and correlated to the current case with regards to symptoms, surgical management, adjuvant therapy, follow up and outcomes.

Conclusion: Most cases do remarkably well with gross total resection only. Post-op adjuvant therapy and long term follow up is advised in cases where gross total resection is not possible.

Keywords: Primary melanoma; Spinal cord; Thoracic; Cervical; Gross total resection; Radiotherapy; Chemotherapy

BACKGROUND AND IMPORTANCE

Melanomas can arise wherever melanocytes exist [1]. Primary melanocytic tumors of the Central Nervous System (CNS) present along a spectrum from benign melanocytomas to malignant melanoma [2]. Primary Central Nervous System Melanoma (PCNSM) arise from leptomeningeal melanocytes [3,4]. PCNSM are rare, representing only 1% of total body melanomas and 0.07% of all brain neoplasms [1,3,5,6]. Hayward proposed the first diagnostic criteria to differentiate PCNSM from metastatic tumors [7,8].

Technological advances since then have enhanced our understanding of the genetic and molecular aberrations driving their development. PCNSM frequently harbor one of the two mutually exclusive mutations, *GNAQ* or *GNA11* affecting codon 183 on exon 4 or codon 209 of exon 5, respectively, impairing enzymatic function that constitutively activates GTP-signaling cascades promoting oncogenesis [9,10].

Within PCNSM, Primary Spinal Melanoma (PSM) are even rarer with only 64 reported cases [11-16] (Supplementary Table 1). Here a unique case of a thoracic Intradural Intramedullary (IDIM) PSM, its histopathologic and genetic analyses and review of literature is presented. Whereas previous cases have reported *GNAQ* mutations in PCNSM, this is the first case to demonstrate this mutation in a solitary IDIM PSM.

CLINICAL PRESENTATION

A 53-year-old female with no known family history presented with 6 months of progressive numbness, and right anterior thigh and mid-thoracic pain. There were no other symptoms including bowel or bladder incontinence. On examination her only deficit was in thigh sensation and no upper motor neuron signs elsewhere.

Preoperative imaging

An MRI of the thoracic spine demonstrated a 14mm x 6mm gadolinium enhancing mass at the T10-T11 level (Figure 1A). There was mild cord effacement without intramedullary T2 hyperintensity (Figure 1B). There was a questionable pial enhancement versus an engorged vasculature extending superoinferior to the lesion (Figure 1A). MRI of the brain and cervical spine and preoperative angiography for tumor blush were negative. Considering an ependymoma, an astrocytoma or a hemangioblastoma surgery was recommended for decompression and definitive diagnosis.

Intraoperative findings

She underwent a T10-T11 laminectomy for tumor resection (Figure 1C). Intraoperative Somatosensory Evoked Potentials (SSEP) and Motor Evoked Potentials (MEP) were monitored. The tumor extent was determined using an intraoperative ultrasound. The mass lacked clear planes, appeared intramedullary, exophytic and invading the adjacent peripheral nerves. Laterally, the capsule was cauterized, incised, and tumor was debulked significantly but not completely due to over 50% drop in MEPs bilaterally. SSEPs remained stable though. Frozen section revealed a highly-cellular spindle cell neoplasm. A small capsule adherent to the cord was left behind (Figure 1D), hemostasis was secured and the dura, closed (Figure 2).

Postoperative course

On her immediate post-op exam, there was anterior thigh sensory loss and decreased right foot proprioception. Motor exam remained normal. In ICU she was on high dose steroids. On the floor on postoperative day 2, she had difficulty ambulating requiring assistance. She was discharged to an acute rehabilitation center. On one-month follow-up, her only deficit was sensory. Final pathology confirmed a PCNSM. A full body workup and an FDG-PET ruled out another primary, a cutaneous or a uveal melanoma.

Histopathology and genetic analysis

Histopathologically, the tumor cells were predominantly

Table 1: Adjuvant therapies patients received in relation to the extent of surgical resection for PSM.

EOR	No Therapy	IT	CT	RT	RT & CT/IT	AT NOS	Total
GTR	17	1	8	3	3	0	32
STR	6	0	10	1	1	1	19
Surgery NOS	5	0	1	2	1	4	13
Total	28	1	19	6	5	5	64

EOR: Extent of Resection; NOS: Not Otherwise Specified; GTR: Gross Total Resection; STR: Subtotal Resection; IT: Immunotherapy; CT: Chemotherapy; RT: Radiotherapy; AT NOS: Adjuvant Therapy, Not Otherwise Specified.

spindled demonstrating a fascicular growth pattern (Figure 3A). A nodular area of epithelioid features, increased nuclear atypia and prominent nucleoli (Figure 3B) revealed mitotic activity (2 mitotic figures in a single 600X field) and increased MIB-1 (Ki67) index of about 10 to 15% (Figure 3C). The neoplasm involved peripheral nerve axons splaying them apart as apparent on neurofilament staining (Figure 3D). Melanin containing cells were rare. Immunostaining was diffusely and strongly positive for SOX10 and A103 along with strong GFAP, S-100, and CK labelling, and diffuse yet weak labeling for S-100 and HMB45 in some foci (Figure 3E). Stains for EMA, PR, ERG, and CD45 were only focally weak or negative, and H3K27-me3 expression was preserved. PLD1 levels were 0%.

Therefore, melanotic schwannoma with focal atypical features, metastatic melanoma and PMM of the CNS were considered. Only upon 143 gene targeted next generation sequencing assay, Oncomine v2 (ThermoFisher) [17], a *GNAQ* Q209L mutation was confirmed (Figure 3F) without any other variants. *GNAQ-Q209L* is characteristic

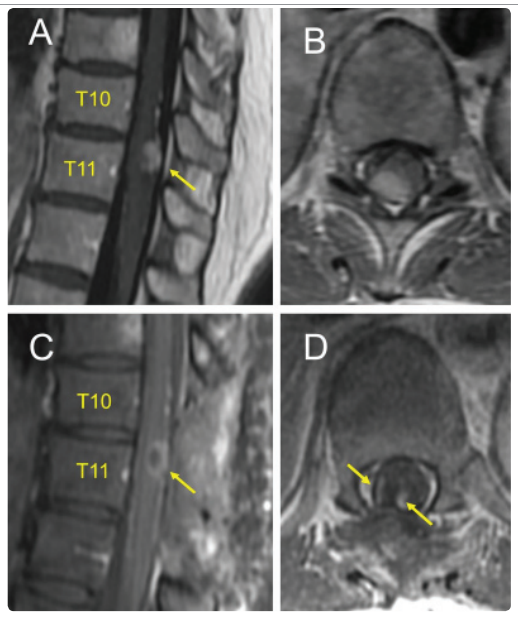

Figure 1: Sagittal and axial MRI scans of IDIM PSM taken pre-operatively (1A & 1B) and post-operatively (1C & 1D). A questionable pial enhancement vs an engorged blood vessel is seen (1A & 1C) extending above and below the lesion. Residual contrast enhancing tumor is demarcated by yellow arrows (1D).

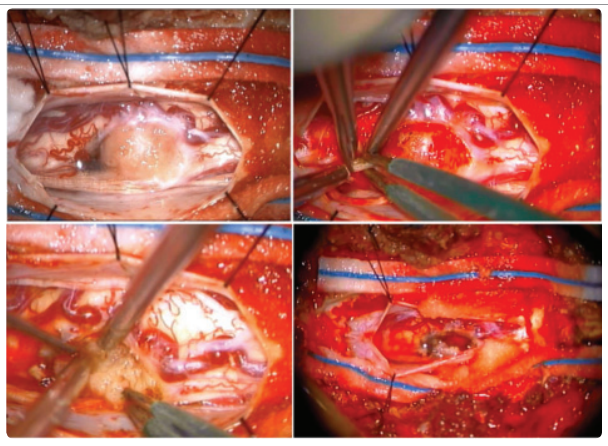

Figure 2: Intraoperative images of the IDIM PSM tumor showing before and after subtotal resection.

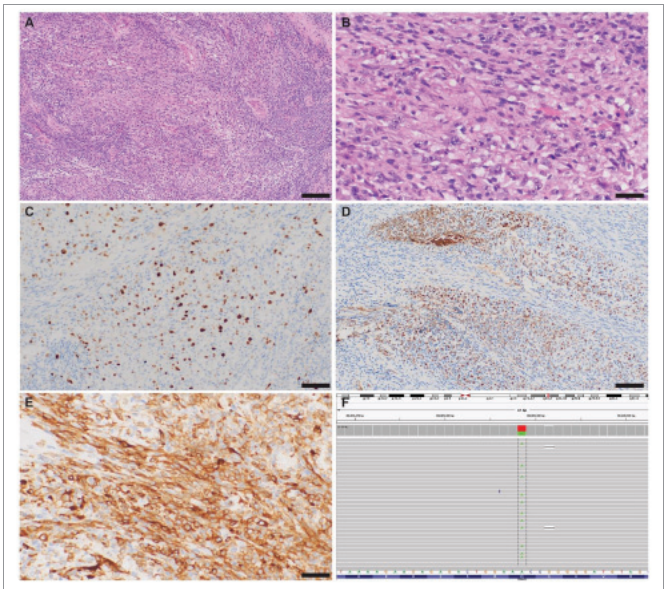

Figure 3: Histopathological and molecular analysis. A. Hematoxylin and Eosin (H&E) stained section demonstrating a highly cellular spindle cell neoplasm with a fascicular growth pattern. B. H&E stained nodular focus with increased cytological atypia including prominent nucleoli. C. Immunohistochemical staining (IHC) for MIB-1 (Ki67) shows increased labeling in the focus shown in panel B. D. Neurofilament staining (in brown) shows native peripheral nerve axonal elements splayed apart by tumor cells (counterstained with hematoxylin to show nuclei). E. A subset of cells demonstrates positive labeling for HMB-45. F. Next generation sequencing showed a GNAQ, c.616 A > T p.Q209L mutation is shown (using the Integrative Genomics Viewer). Scale bars: 200μm (A,D); 100μm (C); 50μm (B,E).

of PCNSM as well as uveal melanomas thereby ruling out metastatic cutaneous melanoma or a melanotic schwannoma.

Treatment

At 2-month follow-up, MRI revealed stable residual disease and no postoperative complication. With negative PDL1, a *GNAQ* mutation, and elevated MIB index, ipilimumab plus nivolumab combination toxicity appeared to outweigh benefits, like uveal melanomas where immunotherapy fails [18]. Therefore, only radiotherapy, of 5400 cGY over 30 fractions was given without any adverse sequalae. One-month post-radiation MRI failed to discern radiation effects from persistent tumor. Her surveillance MRIs every 3 months are pending. On her last 6 months follow-up, she remained clinically stable.

Literature review

Methods: Literature was searched for "primary CNS melanoma", "primary melanoma of the spinal cord" and "primary malignant melanomas of the spinal cord."

Results: The search yielded 201 articles in total. After removing 20 duplicates, metastatic and non-spinal cord melanomas, 65 articles remained. Fifty-five of these were case reports, 7, case series and 3, retrospective reviews. Four non-English articles were further excluded. Forty-five articles were available for final review (Figure 4).

DISCUSSION

Melanoma represents the 3rd most common metastatic tumor to the CNS, behind breast and lung [6]. In contrast, the incidence of PCNSM is only 0.005 cases per 100,000 [7]. PSM is even rarer, with only 64 reported cases (Supplementary table 1). While many studies have reported solitary IDEM tumors in the cervical or thoracic spine

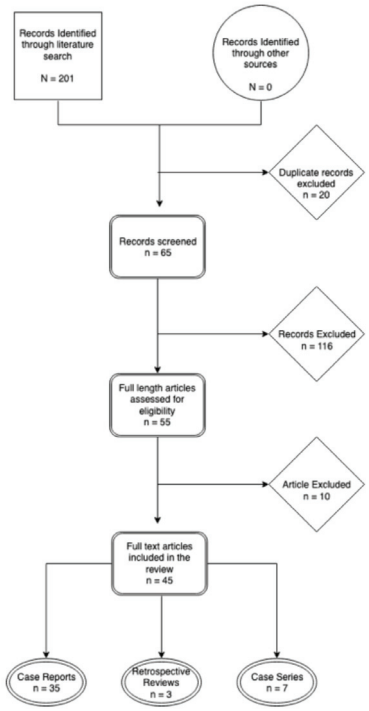

Figure 4: Flow diagram showing literature search and PSM cases selection.

[5,19,20], the incidence of IDIM PSM is far rarer [21], as seen in this case.

The peak incidence of PSM is in the fifth decade of life (52.4 15.5) with ages ranging from 15 to 80 years (Supplementary table 1) [5,20,22]. Motor weakness along with dysesthesias, abnormal reflexes, loss of bowel and bladder function, or pain are the most common presenting signs and symptoms [19,23,24]. MRI is the imaging modality for visualization [3,8,25], with tumors appearing hyperintense on T1 weighted imaging and hypo- to isointense on T2 weighted imaging with uniform contrast enhancement [1,5,8,25,26]. Confirmatory diagnosis with histology is required with genetic features aiding in ambiguous situations. Immunostaining characteristically demonstrates S-100 and HMB-45 immunoreactivity, markers of melanogenesis [8]. Additionally, *GNAQ Q209L* mutation is characteristic of PCNSM as well as uveal melanoma [9,10,27].

PSM must be differentiated from the metastatic cutaneous melanoma [1,19]. The 5-year survival rate for local melanoma is 98%, however it drops to 23% with widespread metastases [28]. The preferred treatment for PSM is complete surgical resection whenever possible followed by radiotherapy [1,5,20]. In cases where Gross Total Resection (GTR) was achieved, survival reached around 88%, compared to 78% in cases of Subtotal Resection (STR). Adjuvant radiation with 4700 cGy in subtotal resections has been reported, however, given the relatively small number of these cases, its effectiveness remains unclear [5,25]. The efficacy of adjuvant chemotherapeutic agents, used for PSM, like dacarbazine, vincristine, bleomycin, and cisplatin also needs to be ascertained [15,21,22,26,29,30] (Table 1).

CONCLUSION

PCNSM are rare tumors associated with *GNAQ Q209L* mutation. Since most previously reported cases are intracranial, data regarding IDIM PSM management is sparse. We report the first such case carrying this signature mutation. Thorough neurologic examination and imaging of the entire neuraxis along with dermatologic and ophthalmologic evaluations is recommended every 3-6 months. Adjuvant radiation is advised when there is residual tumor. Further studies are ongoing regarding their optimal treatment including an active clinical trial involving intravenous and intrathecal nivolumab (NCT03025256).

REFERENCES

1. Farrokh D, Fransen P, Faverly D. MR findings of a primary intramedullary malignant melanoma: Case report and literature review. AJNR Am J Neuroradiol. 2001; 22: 1864-1866. **PubMed:** https://www.ncbi.nlm.nih.gov/pubmed/11733317

2. Brat DJ, Giannini C, Scheithauer BW, Burger PC. Primary melanocytic neoplasms of the central nervous systems. Am J Surg Pathol. 1999; 23: 745-754. **PubMed:** https://www.ncbi.nlm.nih.gov/pubmed/10403296

3. Lee NK, Lee BH, Hwang YJ, Sohn MJ, Chang S, Kim YH, et al. Findings from CT, MRI, and PET/CT of a primary malignant melanoma arising in a spinal nerve root. Eur Spine J. 2010; 19: 174-178. **PubMed:** https://www.ncbi.nlm.nih.gov/pubmed/20127497

4. Pappenheim E, Bhattacharji SK. Primary melanoma of the central nervous system. Clinical-pathological report of a case, with survey and discussion of the literature. Arch Neurol. 1962; 7: 101-113. **PubMed:** https://www.ncbi.nlm.nih.gov/pubmed/14483757

5. Kim MS, Yoon DH, Shin DA. Primary spinal cord melanoma. J Korean Neurosurg Soc. 2010; 48: 157-161. **PubMed:** https://www.ncbi.nlm.nih.gov/pubmed/20856666/

6. Kounin GK, Romansky KV, Traykov LD, Shotekov PM, Stoilova DZ. Primary spinal melanoma with bilateral papilledema. Clin Neurol Neurosurg. 2005; 107: 525-527. **PubMed:** https://www.ncbi.nlm.nih.gov/pubmed/16202828

7. Hayward RD. Malignant melanoma and the central nervous system. A guide for classification based on the clinical findings. J Neurol Neurosurg Psychiatry. 1976; 39: 526-530. **PubMed:** https://www.ncbi.nlm.nih.gov/pubmed/950562/

8. Wadasadawala T, Trivedi S, Gupta T, Epari S, Jalali R. The diagnostic dilemma of primary central nervous system melanoma. J Clin Neurosci. 2010; 17: 1014-1017. **PubMed:** https://www.ncbi.nlm.nih.gov/pubmed/20627582

9. Van Raamsdonk CD, Barsh GS, Wakamatsu K, Ito S. Independent regulation of hair and skin color by two G protein-coupled pathways. Pigment Cell Melanoma Res. 2009; 22: 819-826. **PubMed:** https://www.ncbi.nlm.nih.gov/pubmed/19627560

10. Van Raamsdonk CD, Griewank KG, Crosby MB, Garrido MC, Vemula S, Wiesner T, et al. Mutations in GNA11 in uveal melanoma. N Engl J Med. 2010; 363: 2191-2199. **PubMed:** https://www.ncbi.nlm.nih.gov/pubmed/21083380

11. Chatterjee R, Nascimento FA, Heck KA, Ropper AE, Sabichi AL. Primary spinal cord melanoma - an uncommon entity. Can J Neurol Sci. 2019; 46: 348-350. **PubMed:** https://www.ncbi.nlm.nih.gov/pubmed/31084668

12. Hering K, Bresch A, Lobsien D, Mueller W, Kortmann RD, Seidel C. Primary intradural extramedullary spinal melanoma in the lower thoracic spine. Case Rep Oncol Med. 2016; 2016: 3815280. **PubMed:** https://www.ncbi.nlm.nih.gov/pubmed/27127667

13. Iga T, Iwanami A, Funakoshi T, Mikami S, Tsuji O, Nagoshi N, et al. Multifocal primary melanoma of the cervical spinal cord successfully treated by tumorectomy: A case report. Spinal Cord Ser Cases. 2018; 4: 24. **PubMed:** https://www.ncbi.nlm.nih.gov/pubmed/29581891

14. Wu L, Xu Y. Primary spinal intramedullary malignant melanoma involving the medulla oblongata. Spine J. 2016; 16: 499-500. **PubMed:** https://www.ncbi.nlm.nih.gov/pubmed/26806813

15. Zhang M, Liu R, Xiang Y, Mao J, Li G, Ma R, et al. Primary spinal cord melanoma: a case report and a systemic review of overall survival. World

Neurosurg. 2018; 114: 408-420. **PubMed:** https://www.ncbi.nlm.nih.gov/pubmed/29614357

16. Zhang Z, Gong H, Zhao C, Wang D, Qian M, Wu Z, et al. Prognostic factors of patients with spinal malignant melanoma after surgical intervention: a case series of 21 patients and literature review. J Neurooncol. 2019; 142: 119-127. **PubMed:** https://www.ncbi.nlm.nih.gov/pubmed/30607707

17. Robinson JT, Thorvaldsdottir H, Wenger AM, Zehir A, Mesirov JP. Variant review with the integrative genomics viewer. Cancer Res. 2017; 77: 31-34. **PubMed:** https://www.ncbi.nlm.nih.gov/pubmed/29092934

18. Karivedu V, Eldessouki I, Taftaf A, Zhu Z, Makramalla A, Karim NA. Nivolumab and ipilimumab in the treatment of metastatic uveal melanoma: A single-center experience. Case Rep Oncol Med. 2019; 2019: 3560640. **PubMed:** https://www.ncbi.nlm.nih.gov/pubmed/31179139

19. Fuld AD, Speck ME, Harris BT, Simmons NE, Corless CL, Tsongalis GJ, et al. Primary melanoma of the spinal cord: A case report, molecular footprint, and review of the literature. J Clin Oncol. 2011; 29: 499-502. **PubMed:** https://www.ncbi.nlm.nih.gov/pubmed/21444862

20. Liubinas SV, Maartens N, Drummond KJ. Primary melanocytic neoplasms of the central nervous system. J Clin Neurosci. 2010; 17: 1227-1232. **PubMed:** https://www.ncbi.nlm.nih.gov/pubmed/20558070

21. Wuerdeman M, Douglass S, Abda RB, Krasnokutsky M. A rare case of primary spinal cord melanoma. Radiol Case Rep. 2018; 13: 424-426. **PubMed**: https://www.ncbi.nlm.nih.gov/pubmed/29904488

22. Mallick S, Roy S, Joshi NP, Julka PK. Primary spinal melanoma treated with adjuvant radiotherapy and concurrent temozolomide: A case report and review of literature. J Cancer Res Ther. 2015; 11: 1027. **PubMed:** https://www.ncbi.nlm.nih.gov/pubmed/26881599

23. Salame K, Merimsky O, Yosipov J, Reider Groswasser I, Chaitchik S, Ouaknine GE. Primary intramedullary spinal melanoma: diagnostic and treatment problems. J Neurooncol. 1998; 36: 79-83. **PubMed:** https://www.ncbi.nlm.nih.gov/pubmed/9525829

24. Theodore C Larson III, O Wayne Houser, Burton M Onofrio, David G Piepgras. Primary spinal melanoma. J Neurosurg. 1987; 66: 47-49. https://bit.ly/2ZuIQyI

25. Somers KE, Almast J, Biemiller RA, Silberstein HJ, Johnson MD, Mohile NA. Diagnosis of primary CNS melanoma with neuroimaging. J Clin Oncol. 2013; 31: 9-11. **PubMed:** https://www.ncbi.nlm.nih.gov/pubmed/23169522

26. Yamasaki T, Kikuchi H, Yamashita J, Asato R, Fujita M. Primary spinal intramedullary malignant melanoma: case report. Neurosurgery. 1989; 25: 117-121. **PubMed:** https://www.ncbi.nlm.nih.gov/pubmed/2755570

27. Van Raamsdonk CD, Bezrookove V, Green G, Bauer J, Gaugler L, O'Brien JM, et al. Frequent somatic mutations of GNAQ in uveal melanoma and blue naevi. Nature. 2009; 457: 599-602. **PubMed:** https://www.ncbi.nlm.nih.gov/pubmed/19078957

28. Alliance MR. Melanoma Survival Rates. 2019.

29. Lee CH, Moon KY, Chung CK, Kim HJ, Chang KH, Park SH, et al. Primary intradural extramedullary melanoma of the cervical spinal cord: Case report. Spine (Phila Pa 1976). 2010; 35: 303-307. **PubMed:** https://www.ncbi.nlm.nih.gov/pubmed/20308942

30. Nishihara M, Sasayama T, Kondoh T, Tanaka K, Kohmura E, Kudo H. Long-term survival after surgical resection of primary spinal malignant melanoma. Neurol Med Chir (Tokyo). 2009; 49: 546-548. **PubMed:** https://www.ncbi.nlm.nih.gov/pubmed/19940408

Supplementary Table 1: Characteristics of PSM cases reported in literature (Adopted and modified [15,16]).

Sr.No	Author, Year	Age & Sex	Location	Onset, Duration	S & S	Treatment & Extent	Follow up, outcome
1	De Blasi [15,16], 1930	71, F	Thoracic	6 months	NR	Surgery	6 months, alive
2	Schnitke [15,16],1938	49, F	T8-10	30 months	Lower back paresthesia's & numbness and stiffness of BL LE	GTR + RT	6 months, succumbed
3	Forbes [15,16], 1950	57, M	Thoracic	NR	Right buttock and leg severe pain, left leg weakness	Surgery	2 months, died
4	Gibson [15,16], 1957	51, F	T10	NR	Left leg and right-hand numbness and paresthesia, and left leg stiffness	Adjuvant therapy	23 months, died
5	Zimmerman [15,16], 1958	42, M	T9-10	8 months	NR	Surgery	4 months, died
6	Hirano A [15,16], 1959	42, M	T10	4 months	Sudden onset of constant pain in left flank	Surgery, STR	6.5 months, died
7	Kiel FW [15,16], 1961	33, F	C4-5	15 years	Left shoulder and base of the neck pain	Surgery, GTR	19 months, died
8	Clifford JH [15,16], 1968	64, M	C5-6	4 months	Left shoulder arm and neck pain	Surgery, GTR	24 months, died
9	Faillace WJ [15,16], 1984	F	C-L	24 months	Hydrocephalus, no mass lesion	Radio + Chemo	4 months, died
10	Ozden [15,16], 1984	30, F	T7-10	NR	NR	Surgery + adjuvant	16 months, alive
11	Schneider SJ [15,16], 1987	68, F	L3-4	NR	Lower back pain radiating into left thigh and knee	Surgery, GTR + RT	10 months, alive
12	Larson TC [15,16,24], 1987	73, M	T6-8	6 months	LE weakness, numbness, dysesthesias, bowel and bladder incontinence	Surgery, STR, RT	84 months, alive
13	Larson TC [15,16,24], 1987	63, M	T9	96 months	Spastic paraparesis, decreased sensation, bowel & bladder incontinence, impotence	Surgery, STR + RT	13 months, died
14	Larson TC [15,16,24], 1987	67, F	T9-11	18 months	LE weakness, dysesthesias, low back pain	Surgery, STR, RT	alive
15	Larson TC [15,16,24], 1987	57, F	C1-3	3 months	Dysesthesias, triparaparesis, weight loss, incontinent bladder, neck pain	Surgery, STR, RT	30 months, alive

16	Larson TC [15,16,24], 1987	69, F	T9-10	24 months	LE weakness, decreased sensation, back, abdominal, thigh and calf pain	Surgery, STR	45 months, alive
17	Yamasaki T [15,16], 1989	31, M	T6-8	NR	NR	Chemotherapy, Partial resection	12 months, alive
18	Rastogi N [15,16],1996	57, M	L1	60 months	Choroidal melanoma of right eye, intracerebral metastasis in right fronto-parietal region	Radiotherapy	8 months, died
19	Magni [15,16], 1996	64, M	Thoracic	24 months	NS	Surgery, adjuvant	18 months, alive
20	Francois [15,16], 1998	62, M	T7-9	18 months	Progressive BL LE weakness and sensory loss and urinary dysfunction	Surgery, GTR	28 months, alive
21	Salpietro FM [15,16], 1998	62, M	C3	1 months	Neck pain, gradual weakness of left arm and leg, pins and needle sensation in left hand	Surgery, partial,radiotherapy	15 months, died
22	Salame [15,16], 1999	76, F	T9-10	6 months	Progressive LE weakness	Surgery, partial, adjuvant	`15 months, alive
23	Brat [15,16], 1999	71, F	T10	NR	NR	Surgery	14 months, alive
24	Bidzinski [15,16], 2000	36, M	C6-7	8 months	Legs and hands numbness, sometimes painful	Surgery, GTR, RT	48 months, alive
25	Farrokh D [15,16], 2001	80, F	T12-L1	A few days	Back pain, weakness in Les, bowel and bladder incontinence	Surgery, STR	9 months, alive
26	Tosaka M [15,16], 2001	20, M	CPA&T	7 months	Headache, appetite loss, progressive nausea and vomiting	Chemotherapy	5 months, died
26	Schneider [15,16], 2002	65, M	L2-4	10yr	Lumbar pain, acute sensorimotor radiculopathy	Surgery	1 months, died
28	Sanz-Trelles [15,16], 2003	26, M	L3	3 months	NR	Surgery GTR,	24 months, alive
29	Freudenstein [15,16], 2004	54, F	T10-12	8 years	NR	Surgery STR, RT, Chemo	72 months, died
30	Kwon [15,16], 2004	45, F	C6-7	4 years	NR	Surgery GTR, RT	8 months, alive
31	Montinaro [15,16], 2004	57, F	L1-2	NR	NR	Surgery GTR	3 months, alive
32	Mlaiki [15,16], 2004	51, M	C5-7	NR	NR	Surgery GTR	4.75 months, alive
33	Kounin GK [15,16], 2005	41, F	C2-4	9 months	Headache, intermittent nausea and vomiting	Surgery GTR	3 months, alive
34	Denaro L [15,16], 2007	68, M	T8-9	6 years	Disorders of LEs and gait disturbances	Surgery, GTR, RT	12 months, alive
35	Kanatas AN [15,16], 2007	76, F	C6-7	8 months	Neck pain, parasthesias, weakness in right arm with progressive myelopathy	Surgery STR, RT	6 months, alive
36	Mekni [15,16], 2007	34, M	T6-8	NR	NR	Surgery, STR	3 months, alive
37	Unal [15,16], 2007	37, F	T7	4 months	NR	Surgery, GTR, Chemo	6 months, alive
38	Kwang [15,16], 2010	68, F	T7-8	NR	NR	Surgery + adjuvant	6 months, alive
39	Jo KW [15,16], 2010	68, F	T7-8	5 days	Progressive paresis and altered sensation	Surgery GTR, RT, chemotherapy	6 months, died
40	Kolasa M [15,16], 2010	57, F	T10	2 months	Spinal pain and LE pain and progressive paresis	Surgery GTR, Chemo	12 months, alive
41	Kim MS [15,16], 2010	34, F	T4	12 months	Right leg numbness	Surgery GTR	36 months, alive
42	Lee CH [15,16], 2010	39, M	C1-6	11 months	NR	Surgery GTR, RT, Chemo	17 months, alive
43	Vij M [15,16], 2010	40, M	C2-3	6 months	Pain in right shoulder and neck	Surgery GTR	12 months alive
44	Fuld AD [15,16], 2011	62, M	C2-3	Several months	Progessive right sided weakness with ataxia and gait disturbance	Surgery GTR, RT	11 months, alive
45	Jaiswal [15,16], 2011	16, M	C1-5	NR	NR	Surgery GTR	4 months, alive
46		40, M	C1-2	NR	NR	Surgery GTR	4 months, alive
47	YU [15,16], 2012	48, M	C2-6	6 months	UE & LE numbness	Surgery STR	2 months, alive
48	Cicuendes [15,16], 2012	82, F	L2	1 months	NS	Surgery STR, Radiotherapy	2 months, Died
49	Ganiusmen O [15,16], 2012	49, F	L3	2 years	Low back and leg pain	Surgery GTR, RT, chemotherapy	48 months, alive
50	Marx S [15,16], 2014	54, F	C2-3	6 months	Intermittent dizziness, slight weakness of LEs and foot parasthesias	Surgery GTR, Chemo	24 months alive

51	Jeong DH [15,16], 2013	42, M	T2	8 months	A seizure attack, hydrocephalus	Surgery, STR	22 months, alive
52	Sinha H [15,16], 2013	55, M	L4		Back pain, weakness of LEs, bowel and bladder incontinence	Surgery GTR	38 months, alive
53	Cetinalp NE [15,16], 2014	47, F	T9-L1	6 months	Progressive back pain, weakness in LEs	Surgery GTR,	6 months, alive
54	Chance A [15,16], 2015	46, M	T12 and L5`	1 year	LE parasthesias, urinary retention	Surgery, partial, RT	10 months, alive
55	Liu QY [15,16], 2015	39, M	T9	2 months	BL LE weakness from hip and numbness, 10 day of ataxia	Surgery GTR,	7 months, alive
56	Liu QY [15,16], 2015	47, M	C4-5	11 months	Right finger numbness	Surgery GTR	76 months, alive
57	Liu QY [15,16], 2015	76, M	L	3 weeks	LE weakness	Surgery GTR	67 months, alive
58	Mallick S [22], 2015	28, M	NR	NR	NR	Surgery, chemotherapy	24 months, alive
59	Hering K [12], 2016	57, F	T12	2 months	Progressive LE paresis and paresthesia's	Surgery, STR, RT	26 months, alive
60	Wu L [14], 2016	51, M	C2-7	1 year	BL UE & LE numbness, progressive weakness in right limbs and cough while drinking	Surgery, GTR	10 months, alive
61	Wuerderman [21], 2018	39, M	C2, C4-5	1 year	Numbness of UEs and back	Surgery GTR + antiPD-1 chemo	24 months, alive
62	Takahito [13], 2018	64, F	T9-10	NR	Dysesthesia and weak of RLE followed by RUE & LLE	Surgery STR, RT	8 years, alive
63	Zhang M [15], 2018	52, F	T10-11	3 years	Numbness in LEs & urinary incontinence	Surgery GTR + Chemotherapy	3 months, alive
64	Chatterjee [11], 2019	78, M	C3-T3	2 months	R UE & LE weakness, paresthesia and urinary incontinence	Surgery, GTR	18 months, alive
65	Current case	53, F	T10-11	6 months	Midthoracic and Right thigh pain and numbness	Surgery STR + RT	2 months, alive