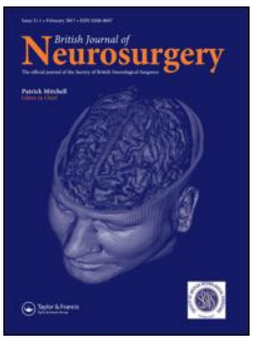

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SHORT REPORT

Glioblastoma multiforme with oculomotor nerve involvement: case report and literature review

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ABSTRACT

Gliomas involving the cranial nerves III–XIII are rare. Even rarer are glioblastomas multiforme (GBMs) with only 10 cases previously reported. Oculomotor nerve involvement was described in only 2 patients. The mechanisms proposed so far include an origin from the nerve itself or an extension within the nerve of a midbrain tumor. We report the case of a 69-year-old man who presented with an isolated left oculomotor nerve palsy. He was found to have a left temporal GBM extended to the frontal lobe. Diagnostics and intraoperative and pathological findings clearly demonstrated a massive infiltration of the cisternal portion of the left oculomotor nerve. We suppose this could be the first case of direct oculomotor nerve invasion by exophytic spread of a supratentorial GBM or by subarachnoid seeding from a temporal tumor. Less probably, it could be the first case of an oculomotor nerve GBM with a temporal lobe invasion.

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Glioblastoma; glioma; cranial nerve; oculomotor nerve; cranial nerve tumor; cranial nerve glioblastoma

Introduction

Glioblastomas (GBMs) usually grow infiltrating the adjacent cortex and are supposed to propagate along the white matter tracts.[1] Excluding cases of diffuse leptomeningeal spread, 10 GBMs with a proven neuroradiological or histopathological infiltration of a cranial nerve have been reported.[2–7] In 2 patients the tumor directly involved the oculomotor nerve, but in none of these the tumor clearly invaded the continuous lobes (Table 1)[2,7]. We here report of a 69-year old man who presented with an isolated complete left third nerve palsy. Clinical, neuroradiological, intraoperative and histopathological findings demonstrated an oculomotor nerve involvement by a tumor with a bulk extension from the left temporal and frontal lobes. To the best of our knowledge this is the third reported case of GBM directly involving this nerve. It could in fact be the case, not previously described, of an exophytic temporal GBM either directly invading this nerve or involving it by a subarachnoid/leptomeningeal spread. Vice versa, but less probably, it could also be considered the hypothesis of a so far undescribed frontal and temporal lobes invasion from a GBM primary originating in the oculomotor nerve.

Case report

History and examination

A 69-year-old man presented to our Emergency Department with a 1-week history of diplopia and left ptosis. On examination a complete left-sided oculomotor nerve palsy was found (ptosis, downward and outward displacement of the eye, fixed and dilated pupil). The remaining neurological examination was unremarkable. His past medical and family histories were silent. All blood tests resulted within the normal range.

Neuroradiological examination

Brain CT demonstrated a left-anterior hypodense area. MRI showed a left-sided enhancing mass involving the fusiform and para-hippocampal gyri, the uncus and the temporal pole, the head and the body of the hippocampus and partially the insula. The lesion appeared T2 hyperintense and T1 hypointense. Gadolinium enhancement was non homogeneous. A pseudo-nodular enhancing area extended between the uncus and involving the intra-cisternal tract of the oculomotor nerve was visible. The nerve appeared thickened with dis-homogeneous enhancing and its distal portion was not detectable. DSC MRI perfusion study showed high rCBV values within the mass and within the cisternal portion of the oculomotor nerve. No signs of midbrain invasion by the tumor were disclosed (Figure 1).

Operation

Three weeks after symptom onset, the patient underwent a left pterional craniotomy. The proximal portion of the Sylvian fissure was occupied by a soft pink-greyish tissue. The neoplasm – with typical GBM characters – appeared to involve the medial portion of the temporal pole, trespassing and invading the sub-arachnoid spaces with supraclinoid carotid and partial middle cerebral artery encasement and extension into the frontal lobe. After opening the arachnoid surface of the Sylvian fissure, the frontal and the temporal portions of the tumor, showing a necrotic core, were resected with the aid of an ultrasonic aspirator. The neoplasm was then separated from the vascular structures to which was adherent. With the temporal debulking and exposure of the supraclinoid tract of the carotid, the oculomotor nerve was seen.

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Table 1. Summary of previously reported cases of GBMs involving cranial nerves III–XII.

Author, year	Age, sex	Previous GBM	CN	Neuropathy	Duration	Location	Treatment	Duration of FU	FU
Reifenberger *et al.*[2]	70, F	No	III, L	Yes	1m	Extra-axial	S + RT	6w	Died
Wu *et al.*[3]	60, M	No	VIII, L	Yes	2m	Extra-axial	S	2m	Died
Breshears *et al.*[4]	67, M	No	V, R	Yes	8w	Extra-axial	Biopsy + RT + CT	23w	Symptoms progression
Yang *et al.*[5]	55, M	No	VIII, R	Yes	3m	Extra-axial	S	2,5m	Died
Takami *et al.*[6]	55, M	No	VIII, R	Yes	n.r.	Extra-axial	S + RT + CT	5m	Alive with stable residue
Mabray *et al.*[7]	53, F	Yes	V, VII, R	No	9m	Pons, frontal	Biopsy + RT + CT	n.r	Progression
	49, F	No	III, R	Yes	n.r.	Midbrain, frontal	biopsy + RT + CT	n.r	Progression
	22, M	Yes	V, R	No	n.r.	Pons, thalamus, frontal	n.r.	n.r	Progression
	9, M	Yes	V, R	No	n.r.	Pons, thalamus, midbrain	CT	n.r.	Progression
	24, F	No	V, VII, VII, R	Yes	n.r.	Pons	RT + CT	n.r.	Progression
Present case, 2019	69, M	No	III, L	Yes	3w	Frontal, temporal	S	2m	Died

CN: cranial nerve/s involved; S: surgery; RT: radiotherapy; CT: chemotherapy; w: weeks; m: months; n.r.: not reported.

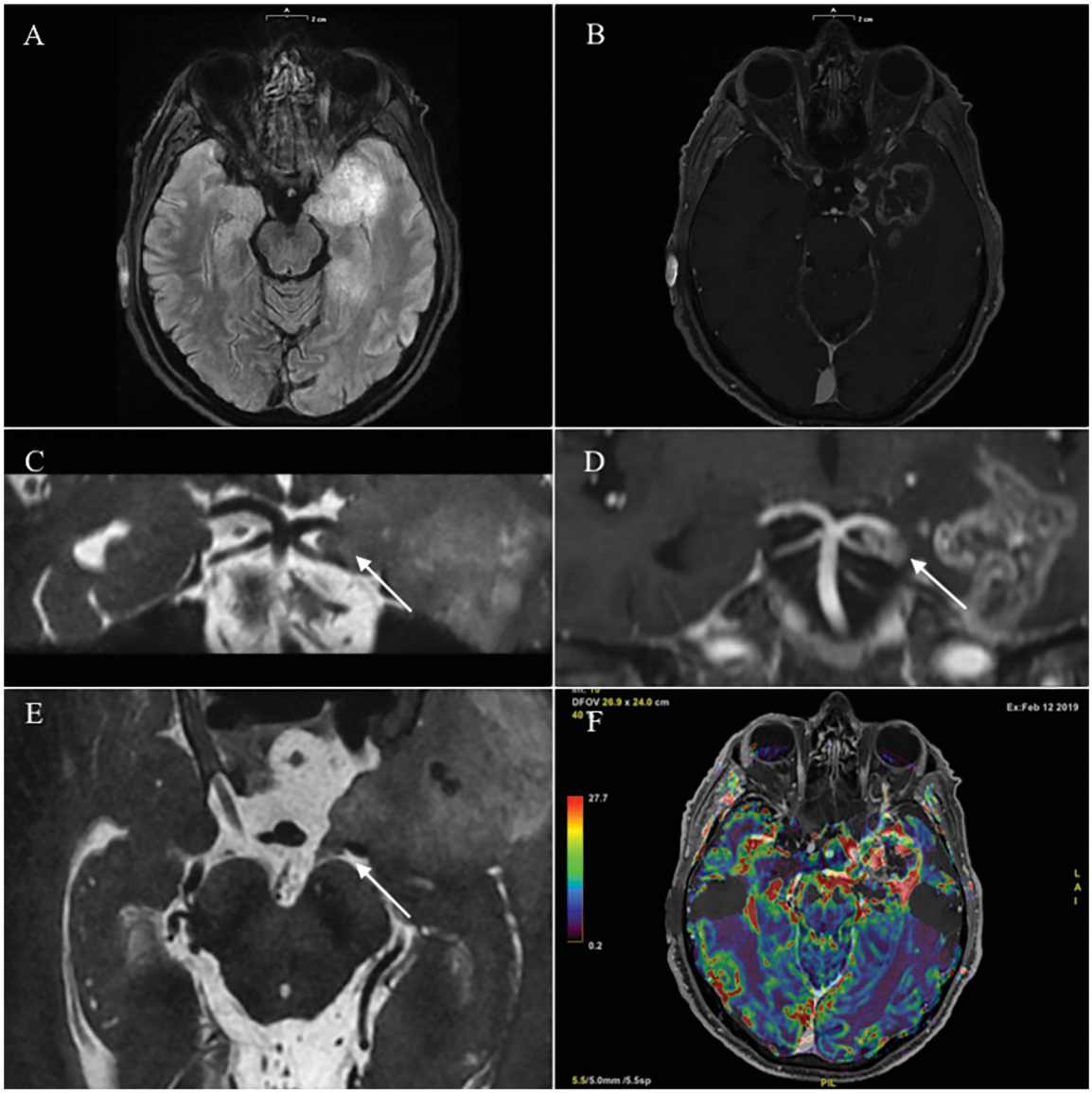

Figure 1. Axial T2-FLAIR and T1-weighted MR images with gadolinium (A and B) showing an enhancing cystic-necrotic lesion in the left temporal lobe extended to the oculomotor cistern. The midbrain appeared not involved. On coronal and axial CISS sequences the oculomotor nerve (white arrow) appeared markedly enlarged (C, E) and characterized by a visible contrast enhancement (D). DSC MRI perfusion study showed high rCBV values within the tumor and within the left oculomotor nerve, without midbrain involvement (F).

Its distal tract appeared enlarged, swollen and clearly infiltrated by the tumor which was in continuity with the uncus (Figure 2). The involved uncus was separated from the oculomotor nerve and resected. We attempted to remove tumour from the oculomotor nerve. Small fragments were obtained and sent for histopathological examination but the nerve was clearly extensively

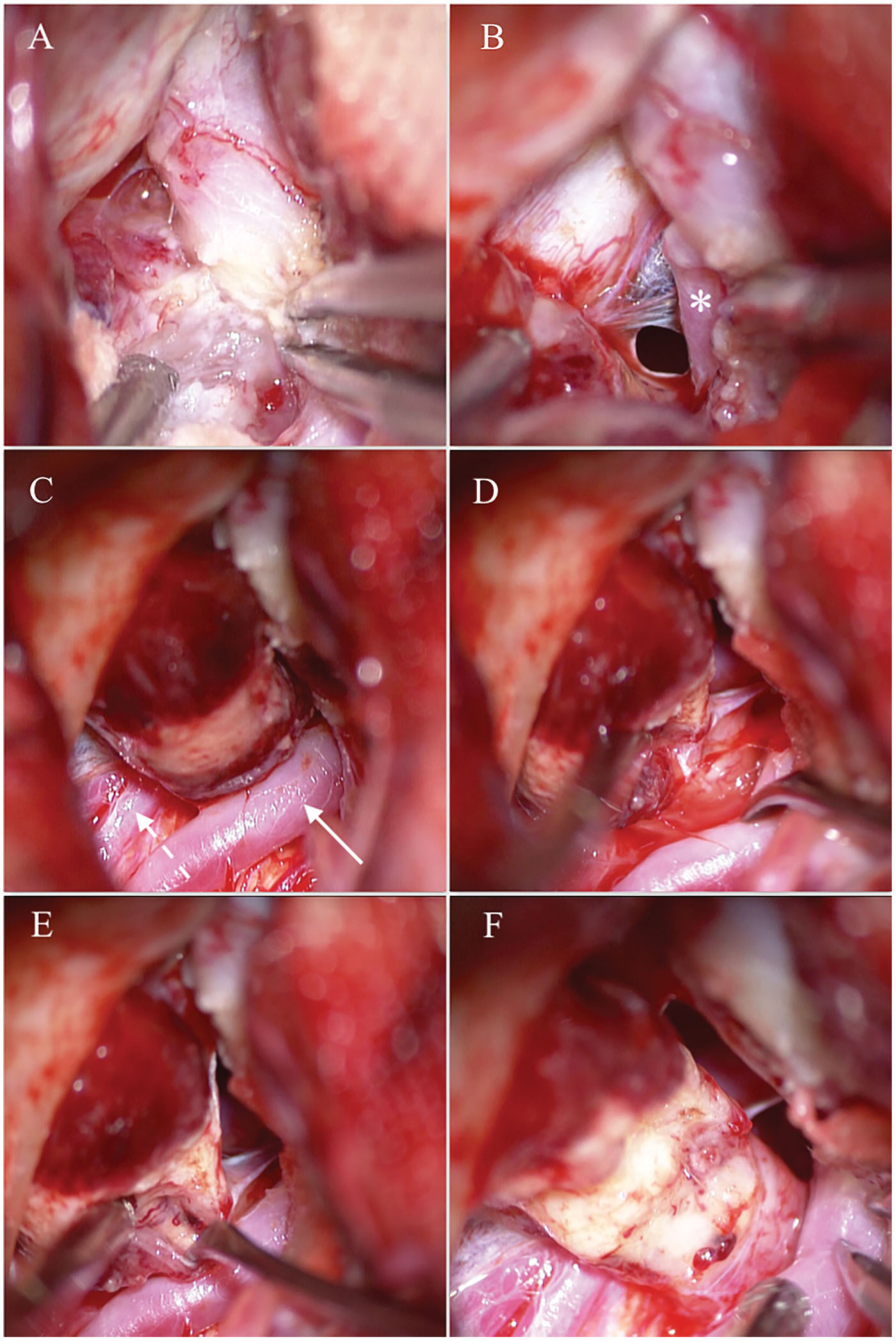

Figure 2. Intraoperative views from a left pterional craniotomy. The proximal portion of the Sylvian fissure appeared invaded by a soft pink-greyish tissue that invaded the arachnoid planes and partly encased the supraclinoid tract of the carotid artery. The tumor was gently dissected from the internal carotid artery and the posterior communicating artery (*) (A, B), isolating a markedly enlarged and infiltrated oculomotor nerve. Between the left superior cerebellar artery (white dashed arrow) and the left posterior cerebral artery (white arrow) a markedly enlarged oculomotor nerve is visible (C). The tumor was gently dissected from the nerve, but it clearly violated the outer sheet of the nerve. A clear cleavage plan between the tumor and the nerve couldn't be found. The resection was incomplete (D, E, F).

infiltrated and was left in place. Resection was judged as near-total.

Postoperative course

Postoperatively, the patient experienced a transient mixed aphasia. Over the following days he showed a marked improvement and was discharged with a slight non-fluent dysphasia. The oculomotor palsy was unchanged. Post-operative MRI showed no residual areas of contrast enhancement. After the diagnosis of GBM had been confirmed (IDH1 wild-type, R132H mutated; Figure 3), the patient was referred to the oncologic-radiotherapy service but the post-operative course was rapidly progressive. Adjuvant treatment was not given due rapid neurological decline. The patients died 8 weeks after the operation.

Discussion

Gliomas directly involving the cranial nerves are rare, with only a few cases previously reported.[7] Ten of these have been GBMs (Table 1). Tumors of cranial nerves I and II were excluded as these are considered part of the central nervous system and are

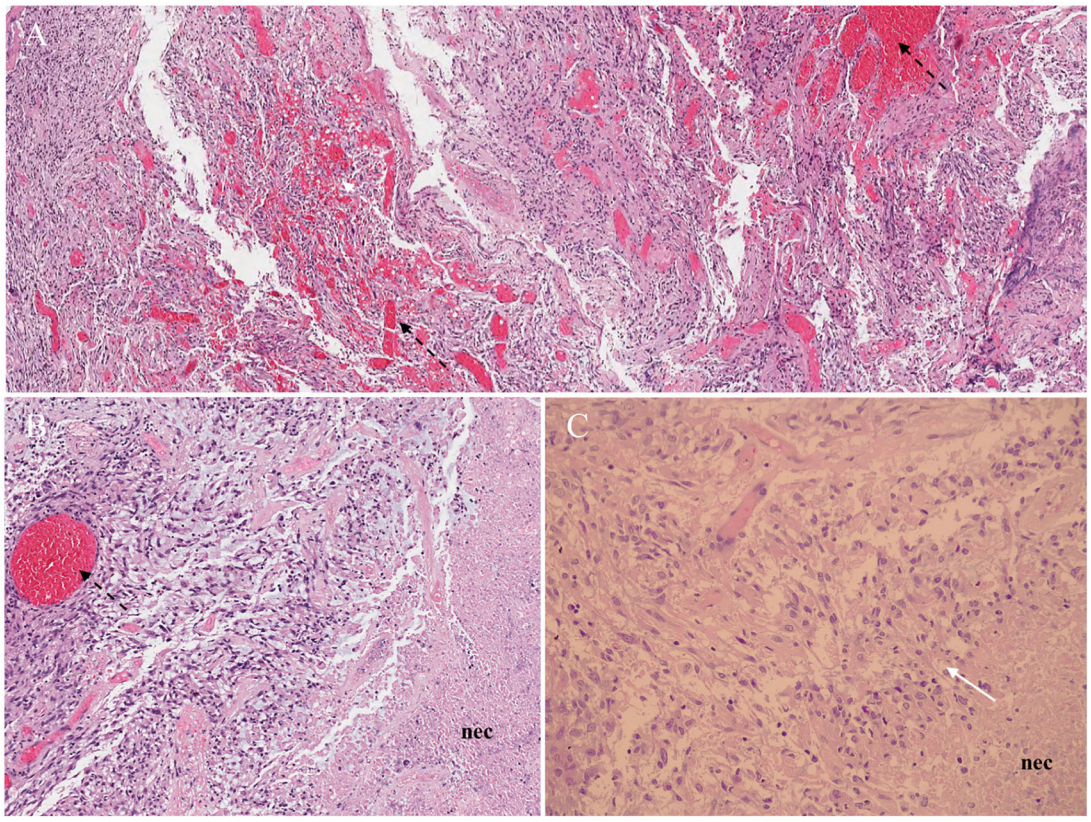

Figure 3. H & E (original magnification ×5: A; ×10: B; ×40: C) photomicrographs demonstrating a highly cellular tumor consisting of poorly differentiated, sometimes pleomorphic tumor cells with nuclear atypia. Marked microvascular proliferation is seen (black dashed arrows, A, B). Areas of marked necrosis are present (nec, B, C), with typical palisading tumor cells (white arrow, C).

anatomically and functionally different.[8] Reifenberger was the first to describe a pure cranial nerve GBM, reporting an extra-axial oculomotor nerve tumor. Post-mortem examination confirmed that it had arisen within the nerve and not spread there from the brainstem or elsewhere. Microscopically, spots of infiltration of the temporal cerebral cortex and peduncle were documented.[2] Wu, Yang and Takami reported cases of GBMs at the pontocerebellar angle involving the nerve VIII complex.[3,5,6] In the first two, no areas of infiltration within the brainstem or cerebellum were seen at surgery. In the third, multiple areas of infiltration were observed of the brainstem adjacent to the nerve's exit. Breshears's report described a patient with a purely extra-axial GBM of the trigeminal nerve.[4] All the cases reported by Mabray (including a case of oculomotor nerve) had radiologically proved brainstem involvement.[7]

Several theories regarding the origin and spread of cranial nerves' GBMs have been proposed. According to a first theory, they arise primarily within the nerve. A 'transition zone' from the central to the peripheral nervous system is well described at the brainstem exit point of each cranial nerve where glial cells could undergo malignant transformation.[9] Nerves with a longer 'transition zone' would be more exposed (VIII > V > III), as suggested by the progressively higher proportion of cases of malignant glial tumors for these nerves.[4] A second theory suggests that they could originate from heterotopic neuroglial cell nests, usually considered secondary to primary leptomeningeal gliomas and gliomatosis.[10] Some nests could be located in the pia in proximity of the nerve's exit point and undergo malignant progression. These hypothesis could fit for the cases with purely extra-axial involvement.[3–6] According to a third theory, more appropriate for the cases with brainstem involvement, they could be brainstem GBMs extending and growing within the cranial nerves. In Mabray's series some patients had separate supratentorial localization, suggesting the further hypothesis of advanced multifocal GBMs.[7]

We believe that our case could offer some new insights to speculate about the origin or progression of these tumors. Subarachnoid seeding through the CSF is a well-known behavior of GBMs, occurring in up to 15–20% of patients.[11] Tumors can reach the cortical surface, invade the sub-pial space and finally reach the perivascular surface, thus disseminating within the subarachnoid space. Nerve roots and their sleeves are relatively common sites of malignant cells spread.[12] Due to the proximity of the uncus to the left nerve III, we aver that GBM cells could have invaded the nerve through arachnoid and pial planes. Another possibility is a direct invasion by an exophytic extension to the basal cisterns of the uncal portion of the tumor. Exophytic growth is a well-known behavior for brainstem and cerebellum gliomas but not for supratentorial GBMs.[13–17] Possible but we think less probable is that it may have originated within the nerve and subsequently expanded within the basal cistern and the temporal lobe by CSF spreading or direct invasion. In the case of Reifenberger it was proved that the tumor had, at least partially, invaded the temporal lobe [2] and our case could represent a larger progression of similar origin. Another rare feature of our patient is the clinical onset. In the literature, only 4 cases of isolated oculomotor palsy caused by high-grade temporal glioma are reported, a direct compression being the suggested most plausible mechanism.[18–21] The theory of a direct infiltration was

also considered due to some intraoperative findings in one case, but it was not proved radiologically nor histopathologically.[20]

In conclusion, we recognize it is not possible to establish with certainty the origin of the oculomotor nerve involvement in our case. It looks anyway clear that the radiological and intraoperative findings of our patient differentiate it from most of the previously reported cases, allowing us to exclude an origin within the midbrain. We could finally suppose this is the first case of a temporal tumor with direct invasion of the oculomotor nerve or, less probably, the first case of an oculomotor nerve GBM with a supratentorial extension.

Conclusions

In summary, we report the third case of a GBM directly involving the oculomotor nerve. Despite the fact that the precise origin of this tumor could not be ascertain, we believe it may be considered the first description of a cranial nerve III invasion by a temporal exophytic GBM or otherwise by subarachnoid spread of a supratentorial GBM.

Disclosure statement

No potential conflict of interest was reported by the author(s).

References

1. Louis DN, Perry A, Reifenberger G, *et al.* The 2016 World Health Organization Classification of Tumors of the Central Nervous System: a summary. *Acta Neuropathol* 2016;131:803–20.
2. Reifenberger G, Boström J, Bettag M, Bock WJ, Wechsler W, Kepes JJ. Primary glioblastoma multiforme of the oculomotor nerve: case report. *J Neurosurg* 1996;84:1062–6.
3. Wu B, Liu W, Zhu H, Feng H, Liu J. Primary glioblastoma of the cerebellopontine angle in adults: case report. *J Neurosurg* 2011;114: 1288–93.
4. Breshears JD, Ivan ME, Cotter JA, Bollen AW, Theodosopoulos PV, Berger MS. Primary glioblastoma of the trigeminal nerve root entry zone: case report. *J Neurosurg* 2015;122:78–81.
5. Yang D, xu Jing Y, Xu Z, ming, *et al.* Primary glioblastoma of cerebellopontine angle in adult mimicking acoustic neuroma. *World Neurosurg* 2019;122:48–52.
6. Takami H, Prummer CM, Graffeo CS, *et al.* Glioblastoma of the cerebellopontine angle and internal auditory canal mimicking a peripheral nerve sheath tumor: case report. *J Neurosurg* 2018; 21:1835–39
7. Mabray MC, Glastonbury CM, Mamlouk MD, Punch GE, Solomon DA, Cha S. Direct cranial nerve involvement by gliomas: case series and review of the literature. *Am J Neuroradiol* 2015;36:1349–54.
8. Wolters Kluver, Wilkins LW (ed.). *Board review series – neuroanatomy*. 4th edn. Maryland; 2008.
9. Arnautovic KI, Husain MM, Linskey ME. Cranial nerve root entry zone primary cerebellopontine angle gliomas: a rare and poorly recognized subset of extraparenchymal tumors. *J Neurooncol* 2000;49: 205–12.
10. Ahmad E, Mohamed M, Vrettos A. Primary diffuse leptomeningeal gliomatosis: radiological/pathological features. *Case Rep Neurol Med* 2016; 2016:1–4.
11. Kong X, Wang Y, Liu S, *et al.* Brain stem and entire spinal leptomeningeal dissemination of supratentorial glioblastoma multiforme in a patient during postoperative radiochemotherapy: case report and review of the literatures. *Medicine* 2015;94:e962
12. Lawton CD, Nagasawa DT, Yang I, Fessler RG, Smith ZA. Leptomeningeal spinal metastases from glioblastoma multiforme: treatment and management of an uncommon manifestation of disease. *J Neurosurg Spine* 2012; 17:438–48.
13. Matsuda M, Onuma K, Satomi K, Nakai K, Yamamoto T, Matsumura A. Exophytic cerebellar glioblastoma in the cerebellopontine angle: case report and review of the literature. *J Neurol Surg Rep* 2014;75:e67–e72.
14. Jhawar S, Sarvpreet G, Shadangi T. Exophytic pontine glioblastoma multiforme presenting as cerebellopontine angle mass. *Asian J Neurosurg* 2017;12:302–4.
15. Luetjens G, Mirzayan MJ, Brandis A, Krauss JK. Exophytic giant cell glioblastoma of the medulla oblongata: Case report. *J Neurosurg* 2009; 110:589–93.
16. Burger PC, Heinz ER, Shibata T, Kleihues P. Topographic anatomy and CT correlations in the untreated glioblastoma multiforme. *J Neurosurg* 1988;68:698–704.
17. Velasquez C, Caballero H, Vazquez-Barquero A, *et al.* Insular gliomas with exophytic extension to the sylvian cistern: a glioma growth pattern that has gone previously unnoticed. *World Neurosurg* 2016;87: 200–6.
18. Sharma K, Kanaujia V, Lal H, Jaiswal S, Jaiswal AK. Isolated oculomotor nerve palsy: an unusual presentation of temporal lobe tumor. *Asian J Neurosurg* 2010;5:70–2.
19. Singh D, Singh N, Singh R. Isolated third nerve palsy: a rare presentation of high grade glioma. *Asian J Neurosurg* 2016;11:171–2.
20. Al-Yamany M, Al-Shayji A, Bernstein M. Isolated oculomotor nerve palsy: an unusual presentation of glioblastoma multiforme. Case report and review of the literature. *J Neurooncol* 1999;41:77–80.
21. Tanaka K, Sasayama T, Kawamura A, Kondoh T, Kanomata N, Kohmura E. Isolated oculomotor nerve paresis in anaplastic astrocytoma with exophytic invasion. *Neurol Med Chir* 2006;46:198–201.