

Central Neurocytoma on the Treatment and Outcome: Clinical Case Series Report

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Abstract: Central neurocytoma (CN) is a rare and elusive tumor. The relationship between clinical outcome, tumor nature, and treatment of CN remains controversial. There were eight CN patients in our hospital from 2014 to 2021, and the prevalence of CN accounted for 0.36% of brain tumors. All of them underwent surgical removal, and two of them were combined with adjuvant radiotherapy (RT). We found that four patients without surgical complications had small tumors ($33.0 \pm 19.5 \text{ cm}^3$), while the other four patients with surgical complications had larger tumors ($89.8 \pm 14.2 \text{ cm}^3$). This suggests that large tumors are prone to surgical complications. One particular patient with a large CN suffered from intraventricular hemorrhage (IVH) caused by damage to the internal cerebral vein (figure 3). Regarding the effect of total removal (TR) and subtotal removal (SR) on surgical complications, two patients with large CNs died of IVH after TR. However, two other patients with large CN had a good prognosis after SR. Regarding the effect of adjuvant RT on surgical complications, one patient with large CN who received RT after SR and one patient with atypical small CN (MIB-1 LI 5.3%) who received RT after TR had a good prognosis without recurrence. Therefore, we suggest SR combined with RT for large CNs in the deep-site ventricle, TR for small CNs, and TR combined with RT for atypical small CNs. Clinical features of patients due to hydrocephalus subsided after surgical treatment. We also review literature and discuss clinical outcomes and treatment associated with CNs. Further investigation with a larger sample size is warranted for the optimal treatment.

Keywords: Central Neurocytoma, MIB-1 Labeling Index, Internal Cerebral Vein, Transcallosal Surgery, Radiotherapy

1. Introduction

CN is derived from neuroepithelial tissue of the septum pellucidum in the lateral ventricles [1]. This tumor was first described by Hassoun in 1982. [2] CNs account for 0.1 - 0.5% of all brain tumors. [3] A higher incidence of CNs occurs in Asian countries, such as Korea, India and Japan. [4] CNs present in young adults with a median age of 34 year-old. [3] There is no correlation between gender and the incidence of CN. [5, 6] Patients may experience headache,

dizziness, seizures, weakness and memory or vision problems, which appear for 3-6 months. [3] Most CNs are located in the lateral ventricles, [1, 7] but a few CNs are located outside of the ventricles, such as the cerebrum, cerebellum, brainstem and spinal cord. [8-11] Typical CNs are benign in nature, [6, 8] but atypical CNs exhibit malignant behavior and recurrence. [12].

2. Methods

Eight cases of CN were collected in our hospital from 2014 to 2021. CNs were diagnosed based on MRI and histopathology. The living activity was assessed by Eastern Cooperative Oncology Group (ECOG) scale before and after surgery. [13].

Magnetic resonance imaging

The dimensions of the tumor were measured on MRI in the transverse, anteroposterior and vertical directions. [7] The volume of the tumor was calculated by multiplying the tumor surface area by the height of each MRI cut (the surface area was obtained by tracing the outline of the tumor).

Histopathology

The specimens were prepared with hematoxylin and eosin (H&E) staining, synaptophysin staining, as well as INSM-1 immunostaining. The immunohistochemical slides were assessed on MIB-1 immuno-stained sections (Ki-67 antigen). The number of labeled cells was expressed as MIB-1 labeling index (MIB-1 LI). [6, 14] The typical CNs are classified as a grade II tumor by the World Health Organization (WHO) with MIB-1 LI less than 3%, but the atypical CNs are classified as the WHO grade III tumor with MIB-1 LI greater than 3%. [15] Histopathology may differentiate CNs from other intraventricular tumors, such as oligodendroglioma and ependymoma. [11].

Surgical and radiotherapy Procedure

Surgical treatments were performed by transcallosal or transcortical approaches. Patients underwent surgical excision with total removal (TR) or subtotal removal (SR) of

CN tumors.

Conventional linear accelerators and fractionated radiotherapy (RT) were used to treat CN tumors. [1, 3].

3. Results (Tables 1-2, Figures 1-7)

Epidemiological and clinical findings (tables 1-2).

There were 2239 cases of intracranial tumors (ICT), including glioma (406 cases), meningioma (508 cases), pituitary tumor (478 cases), acoustic neuroma (215 cases), metastatic and other brain tumors (632 cases). A total of eight cases confirmed by pathology were screened from ICT cases, and the prevalence of CN accounted for 0.36% of ICT. Among the eight CNs, six were males and two were females, with a mean age of 30.5 ± 9.6 years (18 to 43 years).

The main symptoms and signs were as follows: headache (six cases), dizziness (five cases), visual problems with blurred or double vision (five cases), memory impairment (two cases) and motor weakness with ECOG score 1 (two cases).

MRI findings (table 1, figures 1-3).

MRI showed CNs in the lateral ventricles with hydrocephalus for seven cases (figure 1), and in the extraventricular space (the temporal lobe) for one case (figure 2). The images of intraventricular hemorrhage (IVH) after operation showed edema of the left thalamus due to the internal cerebral vein damage (figure 3). The CN size of the eight patients ranged from $7.4 \times 6.0 \times 4.3$ cm to $3.8 \times 2.9 \times 2.2$ cm (Table 1).

Table 1. Age, sex, clinical features, MRI and pathology in 8 CN patients.

Case	Age	Sex	Clinical features	MRI		Pathology			
				Location	Size (cm ³)	Nature	WHO	MIB	
1	25	M	Headache visual problem	ventricle	$6.4 \times 5.3 \times 5.2$ (97.7)	typical	II	1.6	
2	34	M	Dizziness visual problem memory impairment	ventricle	$7.4 \times 6.0 \times 4.3$ (99.5)	atypical	III	4.5	
3	26	M	Headache weakness	ventricle	$5.0 \times 4.1 \times 3.5$ (50.2)	typical	II	1.5	
4	41	M	Headache dizziness visual problem weakness	ventricle	$5.9 \times 5.2 \times 4.6$ (71.4)	typical	II	0.7	
5	43	F	Headache dizziness	ventricle	$4.7 \times 4.0 \times 3.1$ (34.1)	typical	II	< 3	
6	27	F	Headache dizziness visual problem	temporal	$3.8 \times 2.9 \times 2.2$ (7.5)	atypical	III	5.3	
7	30	M	Visual problem memory impairment	ventricle	$7.5 \times 5.6 \times 4.8$ (92.8)	typical	II	< 3	
8	18	M	Headache dizziness	ventricle	$4.0 \times 3.8 \times 5.1$ (41.3)	typical	II	1.4	

Age (year-old), WHO = World Health Organization, MIB = MIB-1 labeling index (%).

Table 2. Treatment, complication, ECOG and follow-up in 8 CN patients.

Case	Surgical approach	Treatment	Complications	ECOG		Follow up (Months)
				Bt	At	
1	transcallosal	total removal	IVH (mortality)	0	5	-
2	transcallosal	total removal	IVH (mortality)	0	5	-
3	transcortical	total removal		1	0	66
4	transcortical	subtotal removal radiotherapy	seizures	1	0	52
5	transcallosal	total removal		0	0	47
6	transcortical	total removal radiotherapy		0	0	20
7	transcallosal	subtotal removal	cerebral infarct	0	0	18
8	transcortical	total removal		0	0	15

Bt/At = before treatment/after treatment, IVH = intraventricular hemorrhage.

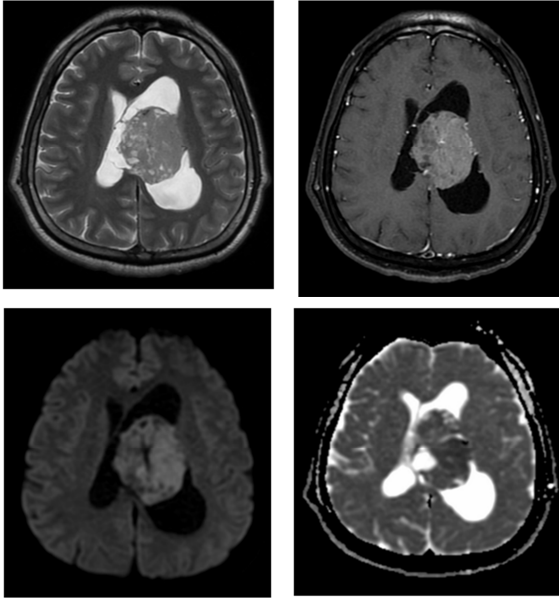


Figure 1. Typical CN in a 26-year-old man. (upper left) Axial T2-weighted image shows a mass located within the left lateral ventricle around the septum pellucidum. Foci of hyperintensity consistent with cystic areas. Hydrocephalus is present. (upper right) Axial contrast-enhanced T1-weighted image shows heterogeneous enhancement. (lower left and right) Diffusion-weighted images show hyperintensity with decreased ADC in the solid portion of the mass which may reflect the increased cellularity of CN.

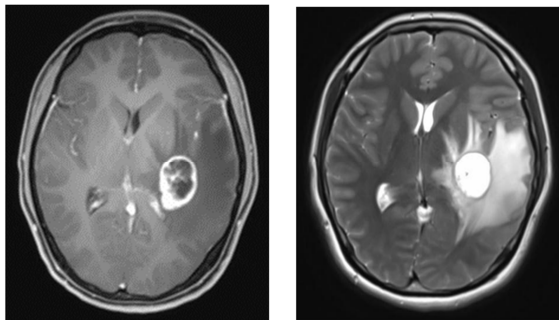


Figure 2. Atypical extraventricular CN in a 27-year-old woman. (left) Axial T2-weighted image shows a cystic lesion located in the left deep temporal lobe with conspicuous peritumoral brain edema. (right) Axial contrast-enhanced T1-weighted image shows thick, nodular, rim enhancement.

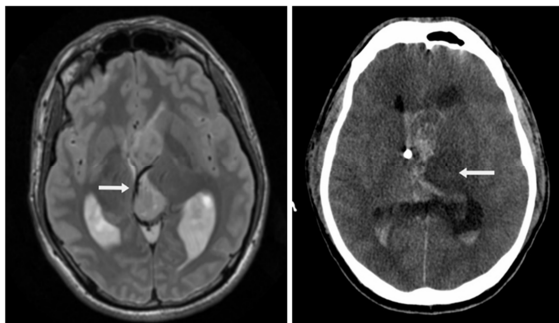


Figure 3. Postoperative IVH and left thalamus edema in a 25-year-old man. (left) Before operation. Axial T2-weighted image shows a typical CN abutting the internal cerebral veins (arrow). (right) After operation. Nonenhanced axial CT image shows left thalamus edema (arrow). Venous drainage insufficiency/damage may explain this imaging finding. IVH is also present.

Pathological findings (table 1, figures 4-7).

The diagnosis of CN was confirmed in eight patients, six showed typical CN (WHO grade II and MIB-1 LI range 0.7 - <3.0%), and two showed atypical CN (WHO grade III and MIB-1 LI range 5.3% and 4.5%).

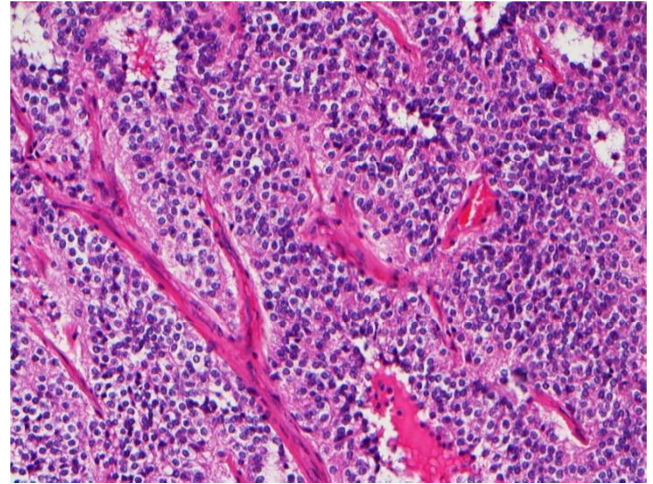


Figure 4. H&E staining showing histological features of central neurocytoma (CN).

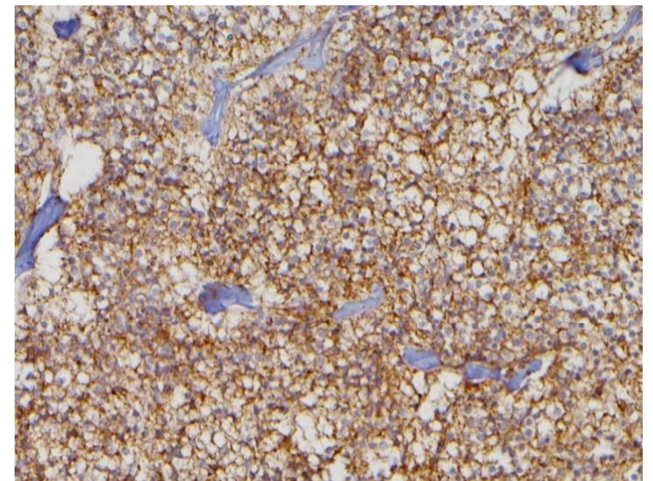


Figure 5. Tumor cells showing positivity for synaptophysin by immunostaining.

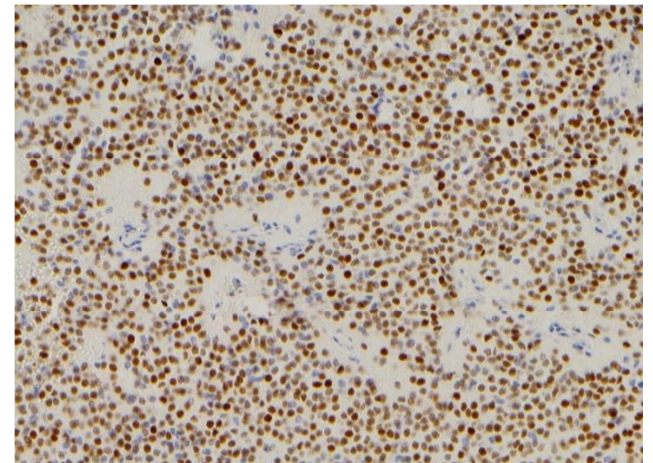


Figure 6. Tumor cells showing positivity for INSM-1 by immunostaining.

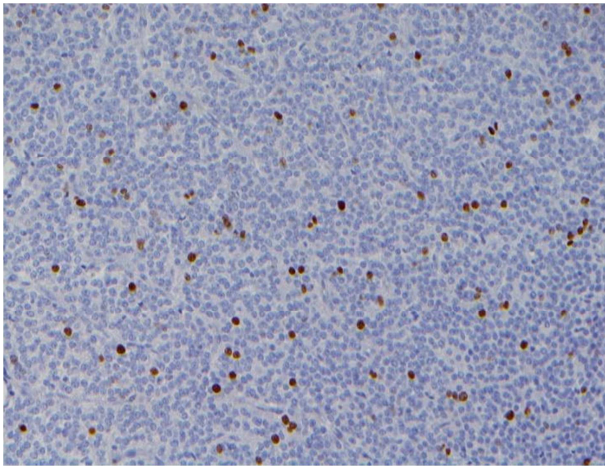


Figure 7. Ki-67 immunostaining: proliferative index 5.3%, indicating atypical CN.

Surgical and radiotherapy findings (Table 2).

Six cases underwent TR and two cases underwent SR. Among them, the tumor sizes of four CN patients without surgical complications ranged from 5.0x4.1x3.5 cm³ to 3.8x2.9x2.2 cm³ (mean volume 33.0±19.5 cm³). The other four CN patients with surgical complications had tumors ranging from 7.4x6.0x4.3 cm³ to 5.9x5.2x4.6 cm³ (mean volume 89.8±14.2 cm³).

CN with surgical complications were all larger than 60 cm³ (mean tumor volume in both groups with and without complications). Among these CN patients with complications, two patients with large tumors (99.5 cm³ and 95.7 cm³, respectively) died of IVH after TR. One patient with 92.8 cm³ large tumor developed cerebral infarction after SR, who subsequently recovered. Another patient with 71.4 cm³ large tumor developed seizure after SR combined with RT, which was later controlled by anticonvulsants.

Two cases required postoperative adjuvant RT. One patient with a 71.4 cm³ large CN tumor received SR combined with 54 GY/30 FR RT, and another patient with atypical CN (MIB-1 LI 5.3%) small tumor received TR combined with 60 GY/30 FR RT. None of them were found to have tumor recurrence or radiotoxicity.

Clinical outcomes (table 2).

Clinical outcomes of the follow-up patients after treatment showed that six patients recovered (ECOG score 0) and two patients died (ECOG score 5). The average follow-up time was 36.3±21.6 months (range 15-66 months).

4. Discussion

The prevalence of CN in our brain tumors is extremely low, about 0.36%. A higher incidence of CNs have been reported in Asian countries, which is possibly due to genetic differences among racial groups. [4] Our patients are Chinese from East Asia.

The main features of our patients were headache, dizziness and blurred vision, which are due to the increased intracranial pressure caused by CNs obstructing the foramen of Monro. [6, 16] These symptoms subsided after treatment.

Surgical excision is currently the most preferable treatment for CNs. [4, 16] A survey of 301 CN patients between 1982 and 2001 at institutions around the world using four different treatments (TR alone, TR+RT, SR alone, SR+RT) showed that TR alone was better than SR alone in improving tumor recurrence and survival ($P < 0.0001$ and $P=0.0085$, respectively), but adjuvant RT was better after SR than after TR in improving local control ($P < 0.0001$ and $P=0.0474$, respectively). [1] Among our six cases undergoing TR, two large tumors (99.5 cm³ and 95.7 cm³, respectively) had surgical complications leading to death from IVH, and the other four small tumors (mean volume 33.0±19.5 cm³) had good prognosis without surgical complications. In the two cases undergoing SR, two large tumors (92.8 cm³ and 71.4, respectively) had surgical complications: seizure and cerebral infarct. In our case series, tumors with surgical complications were all larger than 60 cm³ (Table 1), indicating that the tumor size of CN may be closely related to surgical complications.

In addition, the two SR patients recovered from surgical complications during follow up. One of them with large CN received adjuvant RT after SR and the tumor subsided without recurrence. Therefore, mandatory TR is not required for larger tumors in the ventricle, and SR combined with adjuvant RT may be better for these cases. Currently, stereotactic radiosurgery may be an alternative treatment. [16, 19].

CN has been reported to easily cause IVH or intratumoral hemorrhage, suggesting that CNs are highly vascular in nature. [17, 18] Particularly, our deceased patient developed IVH after operation. MR imaging before and after operation in the young patient showed damage to the internal cerebral vein, resulting in brain congestion and subsequently IVH (figure 3). Normally, the internal cerebral vein located at the roof of the third ventricle drains into the vein of Galen. Therefore, blood vessels near the third ventricle, such as the internal cerebral vein or the thalamic vein, are prone to injury.

Furthermore, atypical CNs have a higher MIB-1 index ($LI > 3\%$), indicating more malignant behaviors and a higher relapse rate. [3, 20, 21] The effect of adjuvant RT on CNs has been reported to improve local tumor control. [1, 3, 16] However, there are no consensus guidelines for systemic chemotherapy for CN, and its merit remains obscure. [22] This report did not use chemotherapy as the primary treatment for atypical CNs. Our atypical CN in the temporal lobe underwent postoperative adjuvant RT with good results and no tumor recurrence.

5. Limitation

Any clinical trial has limitations. Although our medical center is one of the largest in the country, the total number of diagnosed cases remains low due to the rarity of CN (only eight patients since the hospital started using the electronic database). Therefore, it is not easy to conduct large prospective studies to confirm the findings of retrospective

analyses. While surgical complications are associated with large tumors in the deep ventricle, it may also be inevitably related to the skill and experience of the surgeon.

6. Conclusion

Careful SR combined with RT may yield favorable outcomes for large CNs in the deep ventricle. Reviewing the treatment and prognosis of published CN cases, the data demonstrate that TR is superior to SR for local control and survival, but adjuvant RT improved local control after SR better than after TR. The use of MRI and MIB-1 LI to determine tumor size, location, and malignant potential helps surgeons assess surgical risk and optimize treatment.

Statement of Ethics

This study was approved by Kaohsiung Chang Gung Memorial Hospital Research Ethics Board (IRB: 202002093BO).

Conflict of Interest Statement

The authors have no conflict of interest.

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References

- [1] Rades D, Fabian F, Katrin L, Steven ES, Christian H, Manfred W, Winfried Ai, et al: Well-differentiated neurocytoma: What is the best available treatment? *Neuro-Oncology* 2005; 7: 77–83.
- [2] Hassoun J, Gambarelli D, Grisoli F, Pellet W, Salamon G, Pellissier JF, Toga M: Central neurocytoma. An electron-microscopic study of two cases. *Acta Neuropathol* 1982; 56: 151–156.
- [3] Seung JL, Timothy TB, Cheng H, Jacky C, Isaac Y, et al.: Central Neurocytoma: A review of clinical management and histopathologic features. *Brain Tumor Res Treat* 2016; 4 (2): 49-57.
- [4] Vajrала G, Jain PK, Surana S, Madigubba S, Immaneni SR, Panigrahi MK: Atypical neurocytoma: Dilemma in diagnosis and management. *Surg Neurol Int* 2014; 5: 183.
- [5] Sharma MC, Deb P, Sharma S, Sarkar C: Neurocytoma: a comprehensive review. *Neurosurg Rev* 2006; 29: 270-285.
- [6] Yu Li, Xiu FY, Guo Q, Yu Y, Qian GP: Pathologic features and clinical outcome of central neurocytoma: analysis of 15 cases. *Chin J Cancer Res* 2012; 24: 284–290.
- [7] Kreshnike D, Serbeze K, Mehmet SU, Naser R, Sefedin M, Kamber Z: Magnetic resonance imaging of a case of central neurocytoma. *Acta Inform Med* 2016; 24: 419-421.
- [8] Giangaspero F, Cenacchi G, Losi L, Cerasoli S, Bisceglia M, Burger PC: Extraventricular neoplasms with neurocytoma features - A clinicopathological study of 11 cases. *Am J Surg Pathol* 1997; 21: 206-212.
- [9] Liang W, Xiaofeng D, Chenlong Y, Lei Z, Tao Y, Yulun X, et al: Primary spinal neurocytoma involving the medulla oblongata: Two case reports and a literature review. *Neurol Med Chir (Tokyo)* 2014; 54, 417–422.
- [10] Soontornniyomkij V, Schelper RL: Pontine neurocytoma. *J Clin Pathol* 1996; 49: 764–765.
- [11] Yu CJ, Jing XH, Yan L, Peng XY, Huan CZ et al: Extraventricular neurocytoma in the left temporal lobe: A case report and review of the literature. *Oncol Lett* 2016; 11 (6): 3579–3582.
- [12] Mozes P, Szanto E, Tiszlavicz L, Barzo P, Cserhati A, Fodor E, et al: Clinical course of central neurocytoma with malignant transformation: an indication for craniospinal irradiation. *Pathol Oncol Res* 2013; 20: 319-325.
- [13] Oken MM, Creech RH, Tormey DC, Horton J, Davis TE, et al.: Toxicity and response criteria of the eastern cooperative oncology group. *Am J Clin Oncol* 1982; 5: 649-655.
- [14] Rades D, Schild SE, Fehlaue F: The prognostic value of the MIB-1 labeling index for central neurocytomas. *Neurology* 2004; 62: 987-989.
- [15] Louis DN, Ohgaki H, Wiestler OD, et al: The 2007 WHO classification of tumors of the central nervous system. *Acta Neuropathol* 2007; 114: 97-109.
- [16] Sue JP, Tae YJ, Seul KK, Kyung HL, et al: Tumor control of third ventricular central neurocytoma after gamma knife radiosurgery in an elderly patient. *Medicine* 2018; 97: 50.
- [17] Jamshidi J, Izumoto S, Yoshimine T, Maruno M: Central neurocytoma presenting with intratumoral hemorrhage. *Neurosurg Rev* 2001; 24, 48–52.
- [18] Seo E, Yang N. Extraventricular neurocytoma with spontaneous tumor hemorrhage. *Neuro-oncology* 2017: 94.
- [19] Bui TT, Lagman C, Chung LK, Tenn S, Yang I, et al: Systematic analysis of clinical outcomes following stereotactic radiosurgery for central neurocytoma. *Brain Tumor Res Treat* 2017; 5 (1): 10-15.
- [20] Söylemezoglu F, Scheithauer BW, Esteve J, Kleihues P: Atypical central neurocytoma. *J Neuropathol Exp Neurol* 1997; 56: 551-556.
- [21] Imber BS, Braunstein SE, Wu FY, Nabavizadeh N, Boehling N, Weinberg VK, et al: Clinical outcome and prognostic factors for central neurocytoma: twenty year institutional experience. *J Neurooncol* 2016; 126 (1): 193-200.
- [22] Johnson MO, Kirkpatrick JP, Patel MP, Desjardins A, Peters KB, et al: The role of chemotherapy in the treatment of central neurocytoma. *CNS Oncol* 2019; 8 (3).