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RESEARCH

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Clinicopathological features and treatment outcome of central neurocytoma: a single institute experience

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Abstract

Background: Despite the increased interest in publishing data on central neurocytoma, its management remains controversial. The overall incidence is approximately 0.5% of brain tumors. The reporting of institutional experience is of major need for such category of tumors to increase our knowledge and experience. In this study, we describe the clinical presentation, pathological data, and treatment outcomes of central neurocytoma.

Results: Medical records of patients with neurocytoma treated in our center from July 2008 to December 2018 were retrospectively reviewed. Extra ventricular neurocytomas were excluded from analysis due to the known aggressive behavior compared to central neurocytoma. Seventeen patients treated at our center as central neurocytoma were included in the study. The frequent clinical presentation was headaches (58.8%) and paresis (35.3%). Ten patients (58.8%) developed symptoms before the age of 30 years. All patients were treated with surgical resection. Gross total resection was performed in 11 cases (64.7%) and subtotal resection was performed in 3 cases (17.7%). Four patients developed disease progression following the first excision (23.5%), for which additional resection was performed. Two patients received fractionated radiotherapy; one after the first resection due to residual disease postoperatively and the other patient following the third excision due to multiple recurrences with radiotherapy doses of 50.4 Gy and 54 Gy, respectively. The median follow-up time was 51 months (range of 14–106). The 5-year progression-free survival was 70 ± 13%. The overall survival for our cohort of patients was 100%.

Conclusions: Central neurocytoma is a rare tumor of neuronal origin and surgery is the mainstay of treatment with a favorable prognosis. Adjuvant radiotherapy can be offered in patients with residual disease or multiple recurrences, especially in patients with tumors of high MIC-1 LI.

Keywords: Neurocytoma, Saudi population, Clinicopathological study, Treatment

Background

Brain and central nervous system tumors are uncommon and account for 2.9% of cancers in Saudi Arabia [1]. Neurocytoma is a rare neuronal tumor that was recognized by the World Health Organization (WHO) as a separate entity in 2007. Central neurocytomas predominantly arise from the ventricles, with an estimated incidence of 0.1–0.5% of all primary brain tumors [2, 3]. Neurocytomas have also been reported to arise rarely from the brain parenchyma as well as from the spinal cord and are termed as extra ventricular neurocytomas (EVNs) [4]. Central neurocytoma has a more favorable prognosis compared to EVNs and is composed of uniform small round cells with neuronal differentiation belonging to WHO Grade II category. The key features of central neurocytoma include a ventricular location (mostly Lateral

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ventricle), an occurrence at a young age, and an excellent prognosis with benign biological behavior [5–9]. However, the management of this tumor remains controversial [10–17].

Aim of the study

Being rare among brain tumors, studying neurocytoma is warranted and adds to our experience. Herein, a retrospective review of central neurocytoma patients treated at our center which is considered one of the largest tertiary care centers with a neuronavigational facility in Saudi Arabia. The clinical, radiological, and pathological criteria of those patients in addition to treatment outcome presented.

Methods

After formal approval from the institutional review board. The computer database of the pathology department was used to collect cases of neurocytoma. Pathologically questionable cases and EVNs were excluded from the study. The pathologically confirmed central neurocytoma patients, who were treated in our hospital during the period of July 2008 and December 2018, were included in the study. Medical records of included patients were reviewed.

The following data were retrieved; demographic data, pathological data, radiological data, treatment modalities used, and outcome. The demographic data include; age at diagnosis, gender, and symptomatology. The pathological data include; histopathology and immunohistochemical (IHC) staining for neuron-specific enolase (NSE), synaptophysin, neuronal nuclear antigen (Neu-N), and MIB-1 labeling index (LI) of recombinant parts of ki-67 representing the percentage of immunoreactive tumor cells in the evaluated area. The radiological data were collected to confirm the central neurocytoma versus EVNs.

All patients were treated by surgical resection. Our center is equipped with MRI neuronavigational surgical suite that allows safe resection for such well-known hyper-vascular tumors. The surgical approaches differ according to the patient and were either trans-cortical trans-ventricular or trans-callosal. The degree of resection; including gross, near-total, and subtotal resections was determined by reviewing the operative notes and post-operative imaging. The total surgical excision is called gross total resection. Tumor excision of 90% and more is called near-total resection. The resection of less than 90% and or evidence of gross residual by post-surgical imaging are called subtotal resection. The adjuvant postoperative radiotherapy is not offered at our hospital routinely and is considered as per the referring neurosurgeon.

Progression rate is defined as the ratio of progressed cases to the total number of patients. The time to progression is the time between the end of treatment and documented disease progression. Statistical Package for the Social Sciences (BM SPSS Statistics for Windows, Version 27.0. Armonk, NY: IBM Corp, 2020) was used for statistical analysis. Descriptive statistics were employed to characterize the patient cohort. The Kaplan–Meier method was used to estimate progression-free survival (PFS).

Results

Symptoms and baseline characteristics of the patients are shown in Table 1. The cohort was female predominant (11 patients; 64.7%) with male to female ratio was 1:2 and their ages ranged from 17 to 46 years (mean: 29 years).

Ten patients (58.8%) developed symptoms before the age of 30 years. Presenting symptoms at the time of initial diagnosis included headaches (58.8%), blurred vision (29.4%), paresis (35.3%), and generalized seizures (17.7%). The duration of symptoms varied from 3 to 13 months (mean: 5.5 months).

All our reviewed patients were central type neurocytoma. The main radiological appearance was reviewed in computed tomography and magnetic resonance (CT/MRI) scans. Most of the lesions were relatively

Table 1 Patients' characteristics

Variable	*n*	%
Total number	17	100
Age in years (mean range)	29 (17–46)	
Gender		
Male	6	35.5
Female	11	64.7
Baseline symptoms		
Paresis	6	35.3
Seizers	3	17.7
Diminished vision	5	29.4
Headache	10	58.8
Tumor location		
Central intraventricular	8	47
Intraventricular lateralized	9	53
Surgical resection		
Gross total resection	11	65
Near total resection	3	17.5
Subtotal resection	3	17.5
Local radiation		
Yes	2	12
No	15	88
Median follow-up in months (median range)	51 (4–106)	

well-circumscribed and isointense to mild hyperdense. The lesions located intraventricular either in the midline in 47% (as shown in Fig. 1) or intraventricular lateralized to the left side (29.5%) or right side (23.5%). Cystic changes were present in 11 cases (64.7%) and calcifications were found in eight cases (47.1%), usually punctate in nature.

Histopathological features noticed in all the studied cases are similar. The infiltrate is composed of monotonous medium-sized cells with rounded nuclei with salt and pepper chromatin. The cytoplasm is eosinophilic with perinuclear halos resembling oligodendroglia cells. The cells are embedded in a fibrillary stroma with rare Homer Wright rosettes. Infiltrative margin, necrosis, endothelial proliferation and mitotic figures were not identified. All cases were studied for synaptophysin and neuron-specific enolase (NSE). Eighty-eight percent of the cases showed strong IHC reaction with NSE and synaptophysin antibodies. The synaptophysin staining is noted in the neuropil, especially in fibrillary zones and perivascular cell-free areas, and not in the cell bodies of normal neurons.

Neu-N was performed for 11 cases of the studied patients and all of them proved positive. MIB-1 labeling index was calculated as a percent of Ki-67-positive cells for evaluating tumor proliferation and studied in 10 out of 17 patients. It ranged from 0.7 to 5% in the ten studied cases with 4 scoring more than 2%. Figure 2 shows pathologic features and IHC staining for one of the studied patients.

All patients were discussed in neuro-oncology multidisciplinary meetings and treatment decisions were taken as per the standard institute's policy. All patients underwent radical surgery. Gross total resection (GTR) was performed in 11 cases (64.7%), near-total resection (NTR) was performed in 3 cases (17.7%) and subtotal resection (STR) was performed in 3 cases (17.7%).

There is no reported postoperative mortality. The main complication was hydrocephalus which resolved spontaneously in most of the patients and only 5 patients (29%) with persistent hydrocephalus required placement of a temporary ventriculoperitoneal shunt.

Postoperative radiotherapy (PORT) of 50.4 Gy in 28 fractions was given to one patient (5.8%) by 3-dimensional conformal radiotherapy (3D-CRT). The radiotherapy is given because of documented residual disease post-operatively of more than 2 cm. This patient is still alive with residual stable disease for more than 5 years. All patients were followed up with imaging. The treatment outcome is shown in Table 2. At the time of analysis, all patients were alive with overall survival of 100%. Four patients (23.5%) developed disease progression; two

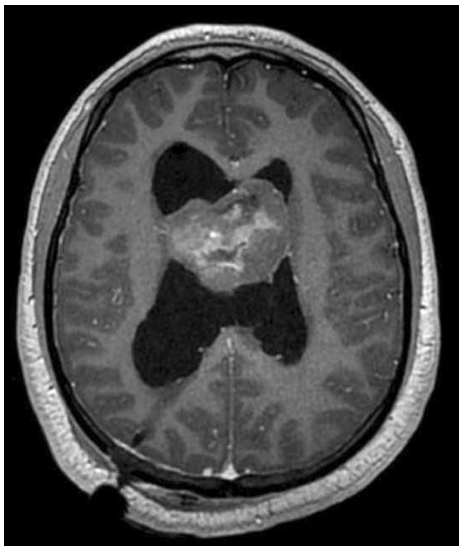

Fig. 1 MRI axial cut for a case of neurocytoma. MRI axial cut showing central intraventricular neurocytoma with some cystic changes

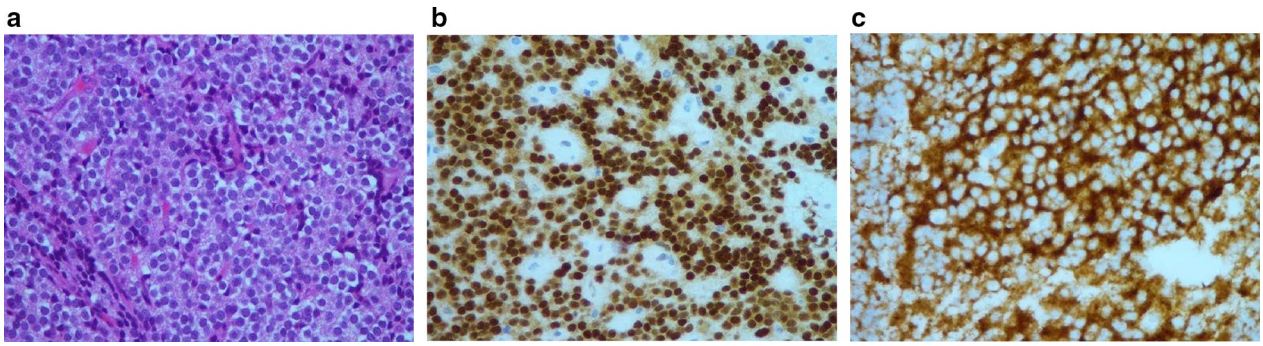

Fig. 2 Pathological features of a case of neurocytoma. **a** Shows monomorphic cells with vesicular nuclei, clear cytoplasm (oligo-like), and delicate arborizing blood vessels (40×). **b** Neu-N positive nuclear staining (40×). **c** Synaptophysin granular cytoplasmic positivity (40×)

Table 2 Treatment outcome

Outcome	*N* (total *n* = 17)	%
Alive		
Yes	17	100
No	0	0
Recurrence rate		
No recurrence	13	76.5
Recurrence[a]	4	23.5
5-year progression free survival	70 ± 13%	
Median time to progression (months)	39 (11–48)	

[a] Two patients had 1 recurrence, 1 patient had 2 recurrences and 1 patient had 3 recurrences

of them had initially GTR and the other 2 patients had STR. The 5-year PFS was 70 ± 13%, as shown in Fig. 3.

The four documented recurrences were treated by surgical re-excision; two of them remained free till the time of analysis without any adjuvant treatment. The other two patients developed further recurrences and were treated by surgical excisions; one out of them had radiation therapy (RT) following the excision of 3rd recurrence, while the other one did not receive RT. A dose of 54 Gy over 30 fractions was given to the recurrent patient by rapid arc intensity-modulated radiotherapy (IMRT). This patient has been recurrence free now for 24 months after RT. Figure 4 shows the RT plans for the 2 patients who received RT; one received adjuvant PORT and the other one received RT following recurrence excision.

The MIB-1 LI of KI 67 was more than 2% in 2 patients out of the 4 recurrent cases. MIB-1 LI for the other 2 recurrent patients was not available. None of the studied patients received adjuvant chemotherapy. The neurological status for the progressed patients who underwent multiple resections showed deterioration in the form of residual neurological deficit and paresis.

Discussion

The present study aimed to examine the clinicopathological characteristics and treatment outcomes for central neurocytoma in a Saudi population. Inconsistent with the majority of the reported cases, our cohort was predominantly young adults below 30 years with female preponderance. Our patients' mean age was 29 years compared to Zubair cohort which was 26 years [11] and Hallock cohort of patients which was 31 years [9].

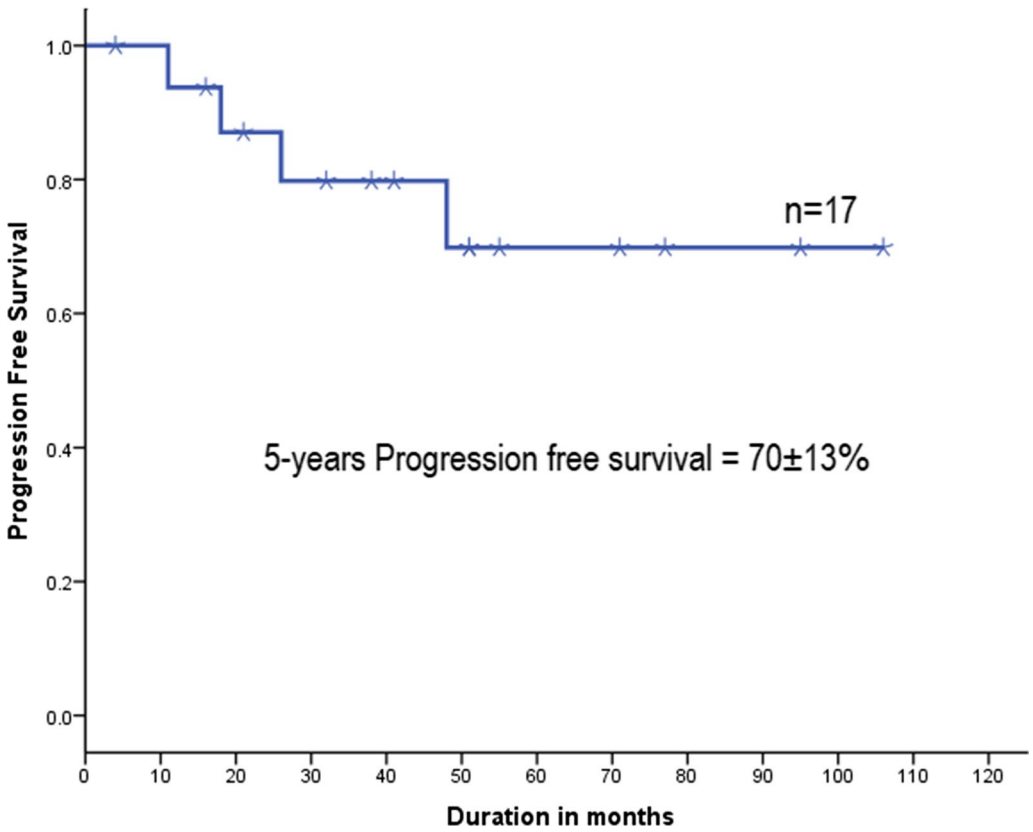

Fig. 3 Progression free survival. The curve showed the progression-free survival

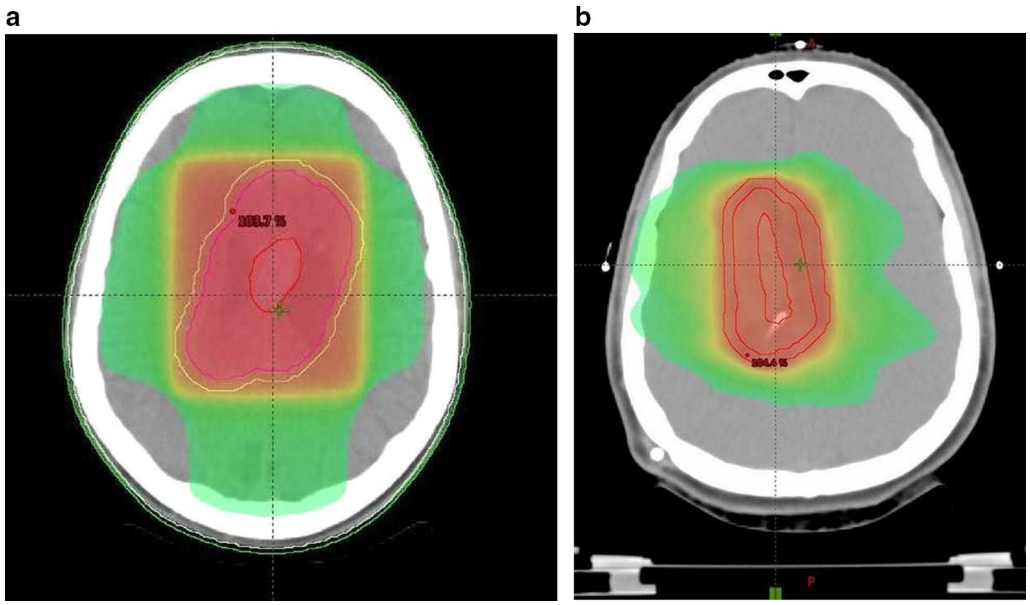

Fig. 4 Radiotherapy plan for cases of central neurocytoma. **a** Radiotherapy plan of three-dimensional radiotherapy treatment for a post-operative case. **b** Shows the radiotherapy plan of rapid arc radiotherapy treatment in a case of recurrent neurocytoma post 3rd resection

We reported a wide range of symptoms, with headache and paresis being the most commonly found symptoms in over two-thirds of the cases, in agreement with many studies [7–9]. Chen et al. reported seizures and weakness in all studied patients [6]. The presence of seizures in 17.7% of our cases is comparable to the data presented by Garcia et al. [8].

We found that all of our patients had intraventricular located tumors which were comparable to the series of Zubair and Leenstra [11, 13]. Radiologically, 64.7% of cases presented with a cystic mass with heterogeneous contrast enhancement which is somewhat highly reported in our patients compared to Chen data who reported 5 out of 9 patients (55%) to have cystic changes only [6]. Calcification within the tumor was noted in 47.1% of cases which is less reported compared to Zubair data which reported 60% of cases to have calcification [11]. These radiological findings also highlight the importance of keeping neurocytoma as a differential diagnosis, along with oligodendroglioma, and anaplastic ganglioglioma, among young adults [12].

Fourteen patients (82.5%) were able to undergo GTR and NTR, whereas 17.5% of patients had STR due to technical challenges of removing intraventricular lesions. Sharma et al. [18] stated that a quarter of neurocytoma patients had STR in their comprehensive review, while Aftahy et al. showed 10% STR in their studied patients [19]. The superiority of GTR compared to STR regarding the local control rate is reported in the literature [16–19]. Considering the theoretical and data supporting the correlation between STR and local recurrence, still we cannot study that in our patients to a small number of patients.

As regards pathological data, we reported 88% positivity of NSE and synaptophysin. These data are comparable to Chen's data which showed 7 out of 9 cases (78%) to have synaptophysin positivity and 100% NSE positivity [14]. In addition, Zubair et al. showed 100% synaptophysin positivity for his studied 35 patients [11]. We reported 100% positive Neu-N test performed for 11 cases of our patients which is comparable to the review of Lee et al. [12]. On the other hand, we reported MIB-1 labeling index as 0.7–5% in the 10 studied cases which was more than 2% in 4 out of 10 cases, while Chen reported levels of 0.1–6.8% [14].

In a multicenter retrospective multicenter study conducted by Vasiljevic et al., neuronal markers synaptophysin and Neu-N proved to be positive in all patients, similar to our data.

Overall survival reported in our cohort of patients was 100% compared to 83% in Mayo clinic data reviewed by Leenstra et al. that included 45 patients treated between 1971 and 2003 [13]. The 5-year progression-free survival (5-year PFS) was 70% in our study compared to 60% after 10 years in Leenstra data [13]. Mayo Clinic patients whose tumor had a low mitotic index experienced a 10-year local control rate of 74% compared with 46% for patients with a tumor of a high mitotic index. A

comparison of GTR with STR showed no significant difference. They also showed that PORT improved local control at 10 years (75% with RT vs. 51% without RT).

Acknowledging the limitation of low patient numbers in our data, we suggest that there may be improved local control for patients who underwent RT after STR or recurrent diseases. Chen et al. studied 63 patients and concluded that the group who had RT after incomplete resection enjoyed the same overall and progression-free survival compared to those who had GTR [14].

Hallock et al. studied 19 patients treated surgically and reported 8 recurrences; 4 out of them received radiation and chemotherapy with a 10-year PFS of 62% and concluded that surgery provides durable local control rates in two-thirds of patients. Our results are marginally higher (5-year PFS 70%) compared to Hallock data, probably because the number of patients who had GTR and NTR are higher in our patients and our salvage treatment was mainly surgery.

The appropriate treatment of residual/recurrent disease remains ambiguous, with options including re-resection, salvage fractionated radiotherapy, stereotactic radiosurgery (SRS), and/or chemotherapy [15–17]. In our study, one patient out of the 3 cases had STR received local radiation adjuvant to surgery. In addition, among the four recurrent cases, re-resection has opted for all except one patient in whom salvage fractionated radiotherapy was offered after the third recurrence.

Genc et al. have reported one of the largest series of SRS for residual or recurrent neurocytomas. Twenty-two residual or recurrent neurocytomas patients were treated by Gamma-knife SRS. They showed a durable reduction in tumor size for 68% of patients [17].

Furthermore, a systematic review concluded that both fractionated RT and SRS were reasonable options for recurrent or residual tumors, with a trend toward better local tumor control and fewer complications among residual neurocytomas treated with SRS [8].

A multicenter retrospective study by Hung et al. stated that SRS achieves good tumor control rates with a reasonable complication profile for 60 patients with central neurocytomas. They showed a 13% recurrence rate following SRS with 93% 5-year local control and 89% 5-year progression-free survival [20].

Conclusions

In conclusion, maximum safe resection should remain the first-line therapy for central neurocytoma. The MIC-1 LI is an important prognostic tool for the determination of high-risk patients for local recurrence. Although re-excision is a standard treatment option for recurrent central neurocytoma, the neurological deficit that could happen with multiple excisions justifies offering adjuvant RT for selected cases. STR and multiple recurrences could be considered the main indications for adjuvant RT following resection especially if MIC-1 LI is high.

Abbreviations

WHO: World Health Organization; EVNs: Extra ventricular neurocytomas; IHC: Immunohistochemical; NSE: Neuron-specific enolase; Neu-N: Neuronal nuclear antigen; LI: Labeling index; SPSS: Statistical Package for the Social Sciences; PFS: Progression free survival; CT/MRI: Computed tomography and magnetic resonance; GTR: Gross total resection; NTR: Near total resection; STR: Subtotal resection; PORT: Post operative radiotherapy; 3D-CRT: 3-Dimensional conformal radiotherapy; IMRT: Intensity-modulated radiotherapy; RT: Radiotherapy; SRS: Stereotactic radiosurgery.

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Author contributions

RM designed the study, reviewed the data, evaluated the results, edited the manuscript, and prepared the manuscript for publishing. VG designed the study, reviewed the data, edited the manuscript, and prepared the manuscript for publishing. YO, MA, MB, AA reviewed statistical analysis and contributed to the drafting of the final manuscript. WA collected the data, reviewed the pathology data and contributed to the drafting of the final manuscript. AB contributed to the drafting of the final manuscript. All authors read and approved the final manuscript

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Availability of data and materials

The data sets used during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This study was approved by Institutional Review Board (IRB) and ethics committee of King Fahad Medical City, MOH, Saudi Arabia with Reference Number IRB/18-666 at 23/12/2018. I confirm that all steps of scientific research were performed in accordance with relevant guidelines and regulations.

Consent for publication

All authors give the consent for publication.

Competing interests

The authors declare that they have no competing interests.

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References

1. SCR. Cancer incidence report. In: Saudi Arabia, vol 2016. Report: Saudi Health Council/National Health Information Center/Saudi Cancer Registry; 2019. https://nhic.gov.sa/en/eServices/Documents/2016.
2. Kim DG, Park CK. Central neurocytoma: establishment of the disease entity. Neurosurg Clin N Am. 2015;26:1–4.

3. Abbad F, Sellami S, Hazmiri F, IdrissGanouni NE, Benali SA, Khouchani M, Rais H. Central neurocytomas: clinical and radiopathological correlations. Pan Afr Med J. 2017;25(27):222.
4. Sweiss FB, Lee M, Sherman JH. Extraventricular neurocytomas. Neurosurg Clin N Am. 2015;26:99–104.
5. 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 Neuro-Oncol. 2016;126(1):193–200.
6. Chen CL, Shen CC, Wang J, Lu CH, Lee HT. Central neurocytoma: a clinical, radiological and pathological study of nine cases. Clin Neurol Neurosurg. 2008;110(2):129–36.
7. Smith AB, Smirniotopoulos JG, Horkanyne-Szakaly I. From the radiologic pathology archives: intraventricular neoplasms: radiologic-pathologic correlation. Radiographics. 2013;33:21–43.
8. Garcia RM, Ivan ME, Oh T, Barani I, Parsa AT. Intraventricular neurocytomas: a systematic review of stereotactic radiosurgery and fractionated conventional radiotherapy for residual or recurrent tumors. Clin Neurol Neurosurg. 2014;117:55–64.
9. Hallock A, Hamilton B, Ang LC, Tay KY, Meygesi JF, Fisher BJ, Watling CJ, Macdonald DR, Bauman GS. Neurocytomas: long-term experience of a single institution. Neuro Oncol. 2011;13:943–9.
10. Mallick S, Roy S, Das S, Joshi NP, Roshan V, Gandhi AK, et al. Role of adjuvant radiation in the management of central neurocytoma: experience from a tertiary cancer care center of India. Indian J Cancer. 2015;52:590–7.
11. Ahmad Z, Din NU, Memon A, Tariq MU, Idrees R, Hasan S. Central, extraventricular and atypical neurocytomas: a clinicopathologic study of 35 cases from Pakistan plus a detailed review of the published literature. Asian Pac J Cancer Prev. 2016;17:1565–70.
12. Lee SJ, Bui TT, Chen CHJ, Lagman C, Chung LK, Sidhu S. Central neurocytoma: a review of clinical management and histopathologic features. Brain Tumor Res Treat. 2016;4(2):49–57. https://doi.org/10.14791/btrt.2016.4.2.49.
13. Leenstra JL, Rodriguez FJ, Frechette CM, Giannini C, Stafford SL, Pollock BE, Schild SE, Scheithauer BW, Jenkins RB, Buckner JC, Brown PD. Central neurocytoma: management recommendations based on a 35-year experience. Int J Radiat Oncol Biol Phys. 2007;67:1145–54. https://doi.org/10.1016/j.ijrobp.2006.10.018.
14. Chen YD, Li WB, Feng J, Qiu XG. Long-term outcomes of adjuvant radiotherapy after surgical resection of central neurocytoma. Radiat Oncol Lond Engl. 2014;9:242.
15. Choudhari KA, Kaliaperumal C, Jain A, Sarkar C, Soo MYS, Rades D, Singh J. Central neurocytoma: a multi-disciplinary review. Br J Neurosurg. 2009;23:585–95.
16. Vasiljevic A, François P, Loundou A, Févre-Montange M, Jouvet A, Roche PH, Figarella-Branger D. Prognostic factors in central neurocytomas: a multicenter study of 71 cases. Am J Surg Pathol. 2012;36:220–7.
17. Genc A, Bozkurt SU, Karabagli P, Seker A, Bayri Y, Konya D, Kilic T. Gamma knife radiosurgery for cranial neurocytomas. J Neuro-Oncol. 2011;105:647–57.
18. Sharma MC, Deb P, Sharma S, et al. Neurocytoma: a comprehensive review. Neurosurg Rev. 2006;29:270–85.
19. Aftahy AK, Barz M, Krauss P, Liesche F, Wiestler B, Combs SE, Straube C, Meyer B, Gemp J. Intraventricular neuroepithelial tumors: surgical outcome, technical considerations and review of literature. BMC Cancer. 2020;20:1060–74. https://doi.org/10.1186/s12885-020-07570-1.
20. Hung Y-C, Lee C-C, Yang HC, Sheehan JP, et al. Stereotactic radiosurgery for central neurocytomas: an international multicenter retrospective cohort study. J Neurosurg. 2020;134(4):1–10. https://doi.org/10.3171/2020.1.JNS191515.

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