Journal Homepage: -www.journalijar.com
INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)
Article DOI:10.21474/IJAR01/3227
DOI URL: http://dx.doi.org/10.21474/IJAR01/3227
ISSN NO. 2320-5407

RESEARCH ARTICLE

INTRAVENTRCULAR CENTRAL NEUROCYTOMA- A NEUROSURGICAL ENIGMA.

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Manuscript Info

Manuscript History

Received: 19 December 2016
Final Accepted: 05 January 2017
Published: February 2017

Abstract

Introduction: Almost 30 years after recognition as histologically distinct tumors, neurocytomas remain enigmatic. Central neurocytomas are rare intraventricular tumors that arise from neuronal cells of septum pellucidum and represent 0.1-0.5% of primary brain tumors. Although they are relatively benign tumors, they have been classified as who grade 2 tumors.

Materials and methods: Here we are reporting 2 cases of this rare enigmatic entity. Case 1: 25 year old female presented with headache, vomiting, giddiness and transient blurring of vision since 1 month.OnMRI ,lesion was in frontal horn of left lateral ventricle.Patient was operated by trans-cortical transventricular approach and tumor was excised.Histopathology sections revealed features of central neurocytoma. Patient had no recurrence at the end of 12 month follow-up. Case 2: 38 year old male presented with headache, frequent falls, decreased vision and vomiting since 2 months. MRI studies revealed solid cystic lesion in the body of right lateral ventricle .Shunt surgery was performed and followed by trans-cortical transventricular excision of tumor.Histopathology showed features of central neurocytoma with some degree of anaplasia.This patients underwent radio-therapy and there was no recurrence of the tumor at the end of 1.5 year follow-up.

Conclusion: Central neurocytomas are rare entities and are classified as WHO grade 2 tumors. Early diagnosis and treatment are imperative as patients with these neoplasms are potentially salvageable.

Cases:-

Case 1:-

35 year old married right handed female patient presented to us with chief complaints of headache,giddiness,transient blurring of vision of both the eyes and vomiting since 1 month.Headache was dull aching intermittent type and more during morning hours and relieved partially by bout of projectile vomiting. Patient had occasional episodes of blurring of vision in both eyes which was sudden in onset and relieved

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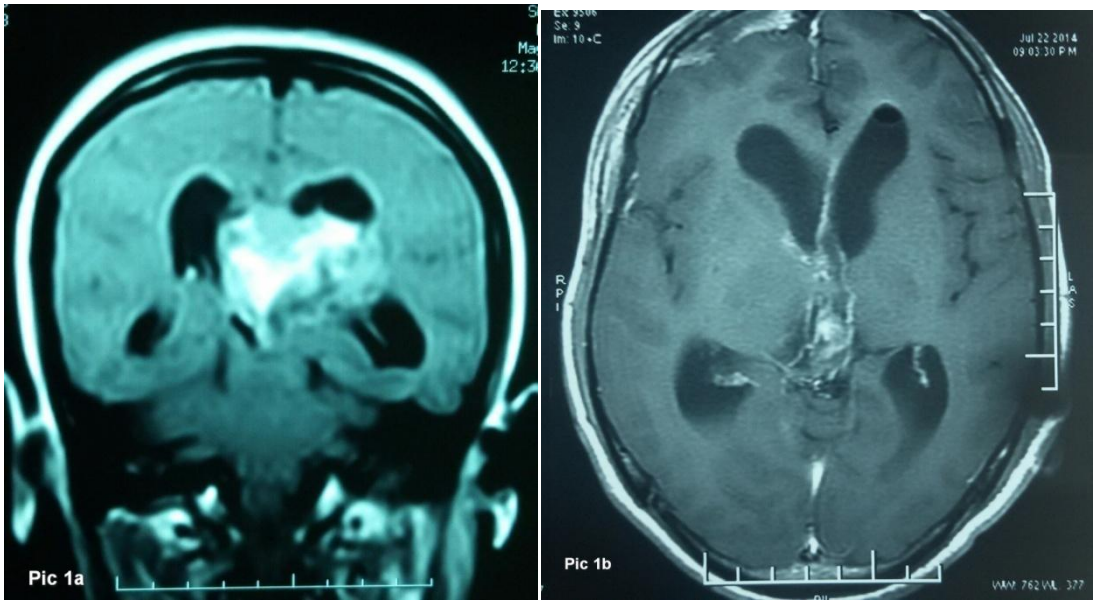
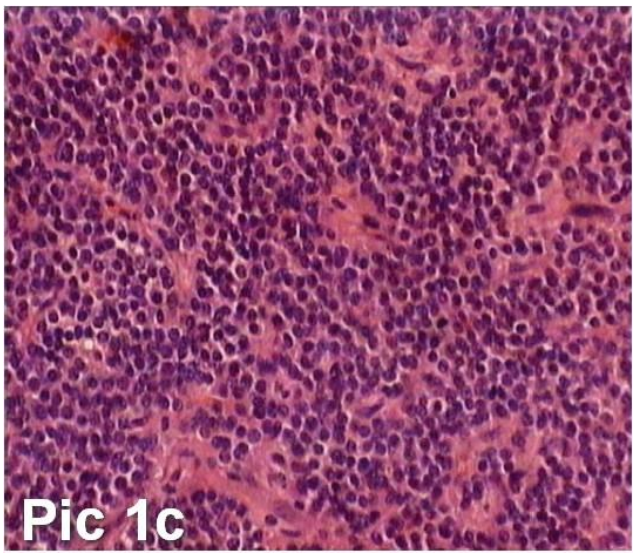
spontaneously. There was no history of convulsions, ear discharge, loss of consciousness and trauma.no significant past and personal history. On examination, patient was drowsy and not fully oriented to time placee and person.Patient was able to follow verbal commands and speech was normal.Ophthalmological evaluation revealed bilateral vision 6/36 and features of early papilloedema were present. There were no cranial nerve deficits. Her motor and sensory examination was essentially normal .Bowel and bladder were continent. Contrast computed tomography study showed well defined inhomogenously enhancing lesion in left lateral ventricular region measuring 5.9*4.5*4.0 cms with areas of calcifications and cystic changes with hydrocephalus. Ventriculo-peritoneal shunt was immediately performed followed by contrast magnetic resonance imaging (Pic 1A) was done which showed 5.7*5.1*4.0cms lesion at septum pellucidum extending both in lateral and third ventricle, more in left lateral ventricle which showed patchy dense enhancements with no definite wall or sub-ependymal infiltration of the mass. In this patient left posterior parietal craniotomy was done and under ultra-sound and brain lab guided microscopic assisted trans-cortical trans-ventricular near total excision of tumor was performed. Hisopathology (PIC: 1c) showed ovoid to fusiform cells with cytological atypia.Cells were uniformormly monotonous and with single nuclei with perinuclear halo. Delicate fibrillary matrix with plexiform arcade with occasional mitosis and no evidence of necrosis s/o central neurocytoma.This was confirmed by immunohistochemical staining which showed positive for neuron specific enolase, synaptophysin and GFAP antibodies.Postoperativeperiod was uneventful and patient was discharged on 12th post-op day with no residual weakness.Patient was followed up regularly and there was no recurrence of tumor at the end of 1 year follow-up.

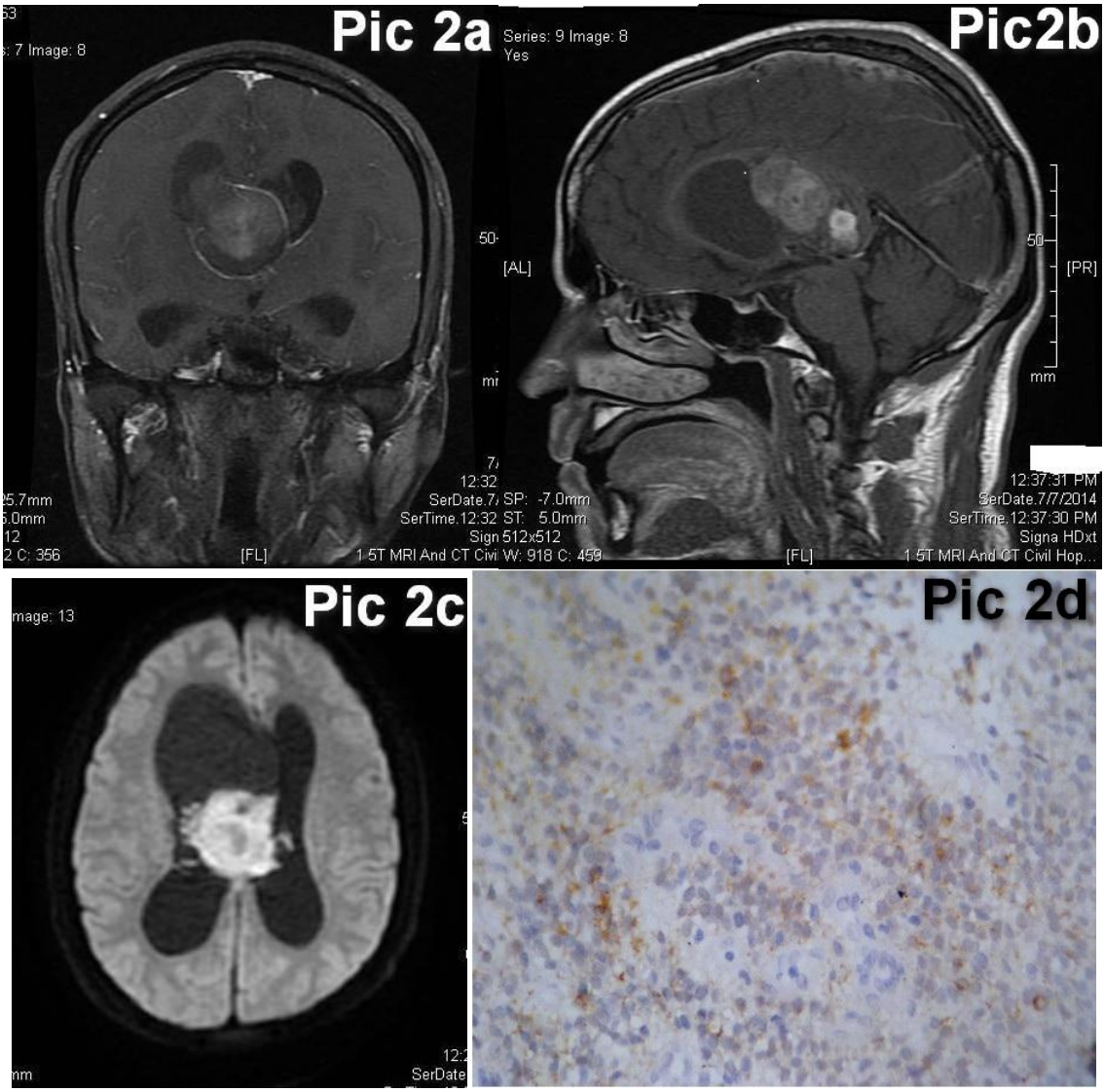
PIC 1A:





Case 2:-

38 year old male patient presented with chief complaints of headache, vomiting, convulsions and frequent falls with giddiness since 1 month. Headache was intermittent dull aching type. Patient had 3 episodes of generalized tonic clonic seizures since 1 month. Patient had recurrent attacks of giddiness and blurring of vision and frequent falls since 1 month which increased in past 15 days. On examination patient was drowsy and following verbal commands on repeated asking with slurred speech. Ophthalmological evaluation showed signs of established papilloedema. Cranial nerve examination was normal and there was no sensory and motor deficits. Contrast CT scans showed right lateral ventricle body solid cystic mass lesion abutting septum pellucidum with hydrocephalus. Ventriculo-peritoneal shunt surgery was performed. MRI contrast studies showed 3.3*3.4*3.5 cms solid cystic intraventricular lesion in the body of right lateral ventricle abutting septum pellucidum and obstructing foramen of munroe causing ballooning and out-trapped frontal horn of right lateral ventricle(Pic 2a,2b). The lesion showed solid with few internal cystic areas with few foci of internal calcifications with heterogenous contrast enhancements. In This patient right temporo-parietal craniotomy was done and ultra-sound guided microscope assisted near total excision of tumor was performed. Patient had moderate intraventricular hemorrhage in the immediate post operative period for which external ventricular drainage was done for 5 days. Patient had no residual weakness and sensorium improved at the end of 15th post operative day. Histopathology(Pic 2d) showed uniformly round cells with hyperchromatic nuclei and peri-nuclear hallo with fibrillary matrix. Few cells showed anaplasia. Immunohistochemical assay showed positivity for synaptophysin and neuron-specific enolase s/o central neurocytoma. Patient was discharged on 5th post operative day and was followed up regularly.In the view of anaplasia , patient was given radiotherapy.Patient had no recurrence at the end of 1.5 year follow-up.



Discussion:-

Central neurocytomas are a rare intraventricular tumors representing 0.1-0.5% of all primary brain tumours.[1] Almost 30 years after recognition as histologically distinct tumors, neurocytomas remain enigmatic[2].Because of advanced imaging techniques and developments in immune-histochemical techniques more and more of these tumors are being diagnosed recently.The majority of central neurocytomas grow inwards into ventricles forming intraventricularneurocytomas. This leads to primary symptoms of blurred vision and features of increased intracranial pressure as in our cases. Treatment for a central neurocytoma typically involves surgical removal, with 1 in 5 chance or recurrence[3]. Central neurocytomas are classified as a grade II tumor under world health organization tumour grading[4].

Historical perspective:-

Central neurocytoma is an uncommon neuro ectodermal tumor of young adults, usually situated in the lateral ventricles at the foramen of Monroe , and was first individualized by Hassoun et al[5].In 1985, Wilson had also described a rare case of "differentiated neuroblastoma " in the lateral ventricle that resembles oligodendroglioma on light microscopy. However, the name central neurocytoma was given by Hassoun[6]. Neurocytomas were probably historically misdiagnosed as intraventricularoligondedro-glioma or clear cell ependymoma prior to this. With its non-aggressive behavior the tumor has often been called "benign central neurocytoma". It is believed to occur in young adults from the neuronal cells of the septum pellucidum and the subependymal cells of the lateral ventricles.

Initially these were reported to be benign. However, as more information was gathered the name benign central neurocytoma was started to be seen as a double misnomer because these tumors are not always benign nor centrally located. Many recent studies suggest that their location, biological potential and clinical behavior are observed be more variable than previously thought. Recent studies indicate their uncommon location, aggressive biological behavior and frequent recurrences following after surgical resection have generated significant interest in various treatment modalities and also in their terminology, lineage potential and molecular regulation[6] .

Epidemiology:-
CNC represent 0.1-0.5% of primary brain tumours[7]. There is a genetic predisposition of this tumors in people of Asian origin[8]. Central neurocytomas predominantly occur in young adults, most commonly during the second or third decade of life. In our study both the patients presented during 3rd decade of life.There is no sex predeliction[9].

Pathology:-
Grossly these tumors are grayish in color, resembling the gray matter that comes with areas of hemorrhage. The tumors are soft, lobulated to nodular masses that are generally well circumscribed. Some variants exhibit calcifications[10].

Tumor samples examined under the microscope revealed that these are well-differentiated tumors with benign histological features. The tumor is composed of uniform, small-to-medium-sized cells with rounded nuclei, finely stippled chromatin and inconspicuous nucleoli, along with scant cytoplasm. These are characterized by perivascular pseudo-rosettes, circular/flower-like arrangements of cells with a small blood vessel at the center, and polygonal small cells with a clear perinuclear halo, sometimes called the 'fried egg' appearance and is clear or slightly eosinophilic. The main differential diagnosis is oligodendroglioma[11]. While the tumor cells are dense in some areas, areas with anuclear, less dense tumor parts were dispersed throughout. The anuclear areas may have a fine fibrillary matrix, like that of neuropil regions. Long, thin-walled, capillary-sized vessels represent the vascularity of these tumors. These vessels are arranged in a linear branching pattern, with an endocrine appearance. Thin-walled dilated vascular channels, as well as foci of calcification, were readily identified in many cases.[10] In our casesboth the patients had common feature of uniformly round cells with perinuclear halo with fibrillary matrix.(Figure 1)

Strong immune-staining for synaptophysin has been recognized as the most suitable and reliable diagnostic marker (Figure2). Typically, synaptophysinimmunoreactivity is noted in the neuropil, especially in fibrillary zones and perivascular cell-free areas, and not in the cell bodies of normal neurons[10].Tumor cells have been reported to express neuron-specific enolase. Immunostaining for synaptophysin and neuron- specific enolase confirm the neuronal nature of the neoplasm. Neuronal nuclear antigen expression is generally associated with tumor cells displaying terminal neuronal differentiation and is often helpful in resolving ambiguous synaptophysinstaining . The significance of GFAP reactivity in tumor cells is difficult to explain, but *in vitro* experiments with neurocytomas have shown a shift from synaptophysin to GFAP expression with cell passages[11]. It has been suggested that CN originates from bipotential (neuronal and astrocytic) progenitor cells in the periventricular region that persist into adulthood [11] .In our cases cells stained positive for synaptophysin and neuron-specific enolase thus confirming diagnosis of central neurocytomas.

Yasargil *et al.* reported that 2 of the 8 patients had evidence of anaplasia and were treated with post-operative radiation after total excision. In our cases, one patient had some degree of anaplasia and hence was given radiotherapy. This patient had no recurrence at 1 year and 1.5 year follow-up.

The MRI images of central neurocytoma are usually characteristic. Most of them occur as an exophytic, well circumscribed, globular mass that protrudes into the ventricles. Large tumors are not uncommon. Calcifications are common and easily identified by CT scans. Central neurocytomas that arise in the lateral ventricles typically adhere to the septum pellucidum. Hydrocephalus is common. On T2-weighted image, they are isointense to gray matter. Contrast enhancement is common but variable and it can be intense. From the imaging point of view, the differential diagnoses include heterotopia, oligodendroglioma, ependymoma, subependymoma, subependymal giant cell astrocytoma, choroids plexus papilloma, and intraventricular meningioma .[12](figure 3,4,5,6,7,8,9)

Clinical features:-
There is a wide range of symptoms that patients show. Symptoms can lie dormant, but come about due to obstructive hydrocephalus. These include: Headache, blurring of vision, Vomiting,Lightheadedness,Impaired mental

activity, gait instability. In rare and extreme cases, more severe symptoms can be observed: Memory disturbance, dementia, hemiparesis, seizures and hemorrhage[13].In our cases both the patients had features of obstructive hydrocephalus.

Treatment:-
The mainstay of treatment is surgical excision[14].Two adjuvant therapeutic strategies are stereotactic radiosurgery and fractionated convention radiotherapy (FCRT). Both are highly effective means of treatment[7].

Surgery:-
Surgical excision of the central neurocytoma is the primary consensus among practicing physicians. Craniotomy is performed.The ability to remove the tumor and to what extent it is removed is dependent upon the location of the tumor and surgeon experience and preference. The extent of the disease plays a large part in determining the effectiveness of surgery. The main goal of a complete surgical resection, of the tumor, can also be hindered by the adherence of the tumor to adjoining structures or hemorrhages[13] .If there is a recurrence of the central neurocytoma, surgery is again the most notable treatment[14] .In our report, both the patients underwent microscope assisted trans-cortical trans ventricular near total excision of tumor. In one patient ,where tumor was in left lateral ventricle, underwent brain lab and ultra-sound guided excision to prevent motor strip injury.

Radiotherapy:-

There is not much evidence supporting whether radiotherapy is a beneficial and effective means of treatment. Typically, radiotherapy is used postoperatively in respect to whether or not a partial or complete excision of the tumor has been accomplished[15,16]. It is not clear if tumors with anaplasia have a higher relapse rate or if they need additional treatment. Yet it appears that some cases of CN may be more aggressive despite benign histological feature[2].The histopathological features of CNC, neuronal differentiation, low mitotic activity, absence of vascular endothelial proliferation, and tumor necrosis, suggest that the tumor may be resistant to ionizing radiation. However, when radiotherapy is used, whole brain or involved-field treatment is given. This method utilizes a standard fractionation schedule and a total tumor dose of 50-55 Gy[13].One of our cases who had some degrees of anaplasia on hisopathology received post operative radiotherapy and patient had no recurrence at the end of 1.5 year follow up.Gamma knife surgery is a form of radiotherapy, more specifically radiosurgery that uses beams of gamma rays to deliver a certain dosage of radiation to the tumor. Gamma knife surgery is incredibly effective at treating neurocytoma and maintaining tumor control after the procedure when a complete excision has been performed.[17]Some studies have found that the success rate of tumor control is around 90% after the first five years and 80% after the first ten years. Gamma knife surgery is the most recorded form of radiotherapy performed to treat remnants of the CNC tumor after surgery.[17]

Chemotherapy:-
Chemotherapy is typically limited to patients with recurrent central neurocytoma. The course of chemotherapy used for CNC is one of two platinum-based regimes. The two regimes are:

- Carboplatin + VP-16 + Ifosfamide
- Cisplatin + VP-16 + Cyclophosphamide

Because chemotherapy is used in rare cases there is still information to be gathered as to the efficacy of chemotherapy to treat benign CNC. Therefore recommendations must be viewed as limited and preliminary.[18]

Outcome and Recurrence:-

The majority of patients can be expected to be cured of their disease and become long-term survivors of central neurocytoma. As with any other type of tumor, there is a chance for recurrence. The chance of recurrence is approximately 20%[3].Some factors that predict tumor recurrence and death due to progressive states of disease are :high proliferative indices,degree of anaplasia, and disseminated disease with or without the spread of disease through CSF[13] .

Long-term follow up examinations are essential for the evaluation of the outcomes that each treatment brings about. It is also essential to identify possible recurrence of CN. It is recommended that a brain MRI is performed between every 6–12 months[2] .in our study, both the cases had no recurrences and no residual neurological deficits at 6 month and 12 month follow-up.

Conclusion:-

Central neurocytomas are rare entities and its early diagnosis and treatment is necessary as patients with these neoplasms are potentially salvageable.Effective surgical treatment and accurate histopathological diagnosis are crucial in proper management of these cases. The role of radiotherapy is yet to be fully established. As some of these tumors show anaplasia and in the event of incomplete excision, radiotherapy can be effective in preventing recurrence.

Referrences:-

1. Chuang, MT.; Lin, WC.; Tsai, HY.; Liu, GC.; Hu, SW.; Chiang, IC. "3-T proton magnetic resonance spectroscopy of central neurocytoma: 3 case reports and review of the literature.". *J Comput Assist Tomogr* 29 (5): 683–8. PMID 16163043.
2. Yasargil MG, von Ammon K, von Deimling A, etalCentralneurocytoma: Histopathological variants and therapeutic approaches. JNeurosurg 1992;76:32-37.
3. Kim JW, Kim DG, Chung HT, Choi SH, Han JH, Park CK, Kim CY, Paek SH, Jung HW. Radiosurgery for central neurocytoma: long-term outcome and failure pattern. J Neurooncol (2013) 115:505-511. DOI: 10.1007/s11060-013-1253-9
4. David N. Louis, Hiroko Ohgaki, Otmar D. Wiestler, Webster K. Cavenee, Peter C. Burger, Anne Jouvet, Bernd W. Scheithauer, Paul Kleihues, The 2007 WHO Classification of Tumours of the Central Nervous System ActaNeuropathol. 2007 August; 114(2): 97–109. Published online 2007 July 6. doi: 10.1007/s00401-007-0243-4 PMCID: PMC1929165
5. Hassoun, J.; Gambarelli, D.; Grisoli, F.; Pellet, W.; Salamon, G.; Toga, M. (1982). "Central neurocytoma. An electron-microscopic study of two cases.". *ActaNeuropathol,* 56 (2):151–6.
6. doi:10.1007/bf00690587. PMID 7064664.
7. Choudhari, K. A., Kaliaperumal, C., Jain, A., Sarkar, C., Soo, M., Rades, D., & Singh, J. (2009). Central neurocytoma: A multi-disciplinary review. British Journal Of Neurosurgery, 23(6), 585-595. doi:10.3109/02688690903254350
8. Garcia, RM.; Ivan, ME.; Oh, T.; Barani, I.; Parsa, AT. "Intraventricularneurocytomas: A systematic review of stereotactic radiosurgery and fractionated conventional radiotherapy for residual or recurrent tumors". Clinical Neurology and Neurosurgery. Feb. 2014;117:55-64
9. Sharma, Mehar Chand; Deb, Prabal; Sharma, Suash; Sarkar, Chitra (August 2006). "Neurocytoma: a comprehensive review".*Neurosurgical Review* 29: 270–285. doi:10.1007/s10143-006-0030-z. PMID 16941163.
10. Hassoun J, Soylemezoglu F, Gambarelli D, Figarella-Branger D, von Ammon K, Kleihues P (1993) Central neurocytoma: a synopsis of clinical and histological features. Brain Pathology 3:297–306
11. Li Y, Ye XF, Qian G, Yin Y, Pan QG. Pathologic features and clinical outcome of central neurocytoma: analysis of 15 cases. Chin J Cancer Res 2012;24(4):284-290. DOI: 10.3978/j.issn.1000-9604.2012.08.025.
12. Robbins P , Segal A, Narula S, et al. Central neurocytoma: a clinicopatho-logical, immunohistochemical and ultrastructural study of 7 cases.Pathol Res Pract 1995;191:100-111.
13. Atlas SW, Lavi E, Fisher PG. Intraaxial brain tumors. In *Magnetic Resonance Imaging of the Brain and Spine*. Ed. Atlas SW. 3rd edt. pp 627-632. Lippincott Williams and Wilkins.Philadelphia, 2002.
14. Chamberlain, Marc C. Treatment of Central Neurocytoma. USC/Norris Cancer Center.Seattle Cancer Care Alliance. https://www.seattlecca.org/client/Chamberlain_Treatment%20of%20Central%20Neurocytomas.pdf> Feb. 20 2014.
15. Schmidt, MH.; Gottfried, ON.; von Koch, CS.; Chang, SM.; McDermott, MW. (Feb 2004). "Central neurocytoma: a review.". *J Neurooncol* 66 (3): 377–84. doi:10.1023/b:neon.0000014541.87329.3b. PMID 15015671.
16. Kim Dg, Paek SA, Kim IH, Chi JG, Jung H-W, Han DH, Choi KS, Cho BK. Central Neurocytoma: The Role of Radiation therapy and Long Term Outcome. Cancer 1997; 79: 1995-2002.
17. Haihui Chen, Rongrong Zhou, Jiayi Liu, Jintian Tang, Central neurocytoma, Journal of Clinical Neuroscience, Volume 19, Issue 6, June 2012, Pages 849-853, ISSN 0967-5868,http://dx.doi.org/10.1016/j.jocn.2011.06.038. (http://www.sciencedirect.com/science/article/pii/S0967586811006564
18. Karlsson, Bengt; Guo, Wan-Yuo; Kejia, Teo; Dinesh, Nivedh; Pan, David Hung-Chi; Jokura, Hidefumi; Kawagishi, Jun; T.C.J. van Eck, Albertus; Horstmann, Gerhard A.; Yeo, Tseng Tsai; Yamamoto, Masaaki. Gamma Knife surgery for central neurocytomas. J Neurosurg (Suppl) 117:96-101, 2012.
19. Brandes AA, Amista P, Gardiman M, Volpin L, Danieli D, Guglielmi B, Carollo C, Pinna G, Turazzi S, Monfardini S. Chemotherapy in Patients with Recurrent and Progressive Central Neurocytoma. Cancer 88(1): 169-174, 2000.