A unique case of Central Neurocytoma and Concomitant Brain AVM in a 12- year-old girl with long term follow up and review of the literature.

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Case Report

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Abstract

Central neurocytoma (CNCy) is an exceedingly rare brain tumor occurring mainly within the ventricles in young adults. Anecdotal cases of CNCy occurring simultaneously with other brain lesions have been reported but to the best of our knowledge, no one was accompanied by brain AVM. A 12-year-old girl presented with signs of increased intracranial pressure. A multi-bleb CNCy originated from the septum in the midline, expanding to the lateral and third ventricles, back to the incisura and infratentorial- supra-cerebellar cistern concomitant with a left frontal parafalx AVM. The tumor was removed successfully, and hydrocephalus controlled by ventriculoperitoneal shunting. The AVM bled after 7 years and was extirpated surgically. She is tumor free after 15 years.

Presenting the first case of CNCy concomitant with brain AVM in a 12-year-old girl with more than 15 years surgical follow up. Even though we could not find any evidence regarding a genetic problem in our case but “Concomitance of CNCY and AVM” can suggest a congenital origin and a common genetic basis only as a hypothesis.

Introduction

Central neurocytoma (CNCy) is a rare brain tumor occurring mainly in young adults. To the best of our knowledge, about 100 cases of CNCy have been reported in the literature [1–3]. The main clinical presentations are those of increased intracranial pressure, visual problems, and mental changes. Lateral and third ventricles are the main location of CNCys. Safe total removal of the tumor is the therapy of choice followed by further long term follow up. Association of CNCy with other lesions have rarely been reported in the literature (Table 1) [4–7]. We intend to report the first case of CNCy concomitant with an AVM in a 12 year old girl with long term follow up.

Table 1
the cases of CNCy concomitant with another lesion reported in the literature. M = male, F = female, CNCy = central neurocytoma, mRS = modified Rankin Scale, N/A = not mentioned.

Author	Sex, age	CNCy + another lesion	Outcome
Cohen j et al, 1998,	M, 37	Right lateral ventricle partially calcified CNCy AND a *paraventricular cystic lesion* in the frontoparietal white matter.	persistent gait instability. No adjuvant therapies.
Horoupian DS et al, 1997	M, 44	Right lateral ventricle bubbly appearing CNCy AND a second fourth ventricle *Medulloblastoma* with intratumor hemorrhage.	Good three years follow up after 3,900 cGy radiation to the craniospinal axis.
Edward Vates G etal	M, 35	Intraventricular hemorrhage due to a 7-mm fusiform aneurysm originating from the lateral lenticulostriate branch of the right middle cerebral artery and a right lateral intraventricular neurocytoma.	Contralateral transcallosal exploration and resection of the tumor and excision of the adjacent lenticulostriate artery aneurysm. Improving hemiparesis after 3 months.
Woo PYM et al,2014	F, 58	CNCy arising from the atrium of the left lateral ventricle infiltrating through the choroidal fissure of the temporal horn into the extra-ventricular cisternal space. The extra ven- tricular *Epidermoid tumor* extended into the ambient, interpeduncular, prepontine and cerebellopontine cisterns.	N/A
Bohm J et al, 2006	M, 7	Lobulated CNCy of the fourth ventricle while analysis of CSF AND biopsy of the cortex showed neoplastic lymphatic cells compatible with *B-lymphoblastic leukemia*.	Whole axis radiotherapy and intensive chemotherapy. No tumor after six months.
Our case	F,12	Large CNCy probably arising from the septum pellucidum extending into the lateral ventricles and third ventricle. Left frontal parasagittal *AVM*, 3X3X2.5cm with 2 main arterial feeders and one/two main cortical draining veins.	mRS = 2 after 10 years.

Case report

A 12-year-old girl was admitted on June2007 complaining from headache, nausea and vomiting of 6 months duration. Severe deterioration of vision and bilateral papilledema with hemorrhage were the main findings in clinical examination. The MR images showed: A- a large midline, multi-bleb tumor with non-homogenous intensity in T1W (Fig. 1a) and T2W (Fig. 1b) images enhancing remarkably, and with a bubbly pattern after contrast material injection (Fig. 2c, d, e). Both lateral ventricles were dilated, and the lesion appeared to originate from the septum in the midline, expanding to the lateral and third ventricles, back to the incisura and infratentorial- supra-cerebellar cisterns. B- there was another 30x30x28mm mass, located in the left frontal parafalx region consisting of flow void curvilinear conglomerations of an

AVM (Figs. 1 & 2). MR arteriography (Fig. 3f) and digital subtraction angiography (DSA) (Fig. 3g) showed the deep located lesion to be of low to moderate vascularity and the AVM 30x30x28mm in diameter, fed through at least two arterial feeders rising from early pericallosal branches and draining through one or two cortical draining veins (Spetzler -Martin grade II). Explaining the situation with family, we decided to remove the deep-seated tumor through a trans-sulcal trans-ventricular, right posterior temporo-parietal approach. The tumor was pinkish gray and meaty in texture with moderate bleeding which could be removed using microscopic dissection from within both ventricles. The surrounding ependymal layer could be preserved untraumatized as much as possible and the choroid plexus coagulated whenever necessary. Dissection of the tumor could be done deep to the quadrigeminal cistern and microscopic total tumor removal was achieved. The post operative brain CT scan (Fig. 4) showed no obvious tumor remnant and no intraventricular hematoma. The subarachnoid space around the AVM contained some blood clot in this CT scan. We assumed that could be either sedimented during the operation or due to brisk hemorrhage originating from the AVM during the operation. The postoperative period was uneventful, and we did not decide for any further intervention urgently. Headache improved remarkably but she was still suffering from impaired vison (VA = 2/10). Pathology report was compatible with low-grade (WHO Grade II) CNCy with uniform round nuclei and a fine chromatin pattern and fibrillary matrix. There was no nuclear atypia or any scattered vascular proliferation. Immunohistochemical findings included expression of synaptophysin (12/15), neuron specific enolase (10/15) and glial fibrillary acidic protein (GFAP) (2/15). MIB-1 proliferation index was less than 0.81% (Fig. 5). It was decided to follow the patient clinically and by imaging and the family did not agree for any intervention for the AVM while she was taking antiepileptic only. She underwent a right ventriculoperitoneal shunting procedure using a medium pressure valve system because of dilated ventricles and paraventricular edema. Headache improved but there was no change in her vision. There was no sign of tumor recurrence in MRI, 6 years after the first surgery and no change in the size of AVM. In September 2014 she was admitted in the emergency department because of sudden headache and epilepsy. She was hemiparetic and GCS = 10. There was a 50cm^3 intracerebral hematoma in the left frontoparietal region which had to be evacuated and the AVM could also be removed under microscopic dissection successfully. The postoperative period was uneventful and further follow up till January 2022 did not reveal any tumor recurrence (Fig. 6).

Discussion

Central Neurocytomas is a borderline benign/malignant lesion and surgery is suggested as the primary treatment for it [1, 2]. CNCy comprise only 0.1–0.5% of all primary brain tumors [1–4]. The overall survival (OS) of CNCy is mostly linked with, a) the amount of maximal safe resection and b) the outcome of surgery ($p < 0.05$) [1–3, 8]. They are more likely to be female, young, and of non-white race [2]. Inferior septum pellucidum and anterior lateral ventricles are the most common locations with lobulated / multibleb appearance due to intra-tumoral cyst formation as in our case [1, 7].

They are low-grade (WHO Grade II, 2000 classification) lesions arising from progenitor bipotential cells with capability of differentiating along the glial or neuronal lines arising from the subependymal layer of

the septum pellucidum or the ventricular walls. Neurocytomas can be extra-ventricular, however, the term CNCy is reserved exclusively for intraventricular lesions [6]. On MRI, the solid components of the tumors are hyperintense in T1- and T2-weighed images as in our case. Long TR sequences show cystic changes in two-thirds of the cases and broad attachment to the ventricular wall or septum is almost always detectable as shown in the fig. c in this case.

To the best of our knowledge, no common risk factors for these two diseases are discovered. Several mechanisms have been suggested for triggering development of multiple primary brain tumors of different histology in a patient [6, 7], but the etiology remains unknown. Different hypotheses suggested for development of concurrent/ adjacent double tumors may be summarised as: 1) they occur because of activation of the signaling pathways of receptor tyrosine kinases, 2) one tumor may secrete a growth factor that initiates growth of another lesion. [6, 7] The occurrence of upregulation of proinflammatory cytokines and the angiogenic factors necessary for growth of both lesions. [8] We did not have the facility to evaluate the signalling microarrays and factors. Our case occurring along with an AVM in a young girl can raise/suggest the hypothesis that both could have been of congenital origin.

Regarding the best surgical approach in this case, the transcortical approach to the tumor was selected according to its size and location and the surgeon's preference. This approach had several advantages in our case, including easy access to the lateral ventricle by using a short route, a reduced risk of damage to the fornix, and avoiding the parasagittal veins and pericallosal arteries. Surgery was uneventful in this case and hydrocephalus was managed with VP shunt revised only once during the follow up period and no adjuvant therapy.

Modern management of CNCy has been planned by several institutional case series. Outcomes of interest have been the progression free survival (PFS) and OS from the date of first surgery as in our case which has been long enough possibly to be considered cure. Given the rarity of CNCYs, the optimal management strategies are still evolving. Both fractionated conventional radiotherapy and stereotactic radiosurgery are suggested for cases with residue or recurrences. There also exists marked heterogeneity in chemotherapy used to treat CNCYs and Temozolomide is incorporated into treatment regimens in the setting of tumor recurrences. [1–3, 6].

It is reported that there is a higher incidence of CNCy in Korea, India, and Japan, possibly attributed to genetic differences among racial groups but we are not aware of this in Iran [3, 7]. The higher incidence in these Asian countries, make CNCy an important consideration when dealing with intraventricular tumors in these contexts.

Combination of CNCy with another tumor and aneurysm in CNS have been anecdotally reported in the literature (Table 1) [8]. Our case occurring along with an AVM could raise the hypothesis that both could have been of congenital origin and without any flow associated mechanism. These unusual associations suggest a common genetic basis for pathologies of seemingly different and obscure origin. To the best of our knowledge, no common risk factors for these two diseases are discovered. Several mechanisms have been suggested for triggering development of multiple primary brain tumors of different histology in

a patient, and the etiology remains unknown [6, 7]. Some believed that concurrent adjacent double tumors occur because of activation of the signaling pathways of receptor tyrosine kinases or, one tumor may secrete a growth factor that initiates growth of another lesion [6, 7]. To our idea, *this presentation can still be a co-incidence*.

Conclusion

We reported the first case of CNCy concomitant with brain AVM in a 12 year old girl with successful total resection of both lesions and no tumor recurrence after more than 15 years follow up.

Abbreviations

Central neurocytoma = CNCy

Arteriovenous malformation = AVM

Glial fibrillary acidic protein = GFAP

Overall survival = OS

Progression free survival = PFS

Declarations

Ethics approval:

The authors confirm that they have read and agreed to the following terms and conditions of this Submission Statement, including that the submission is original and has not been published previously.

Consent for publication:

The dataset generated and/or analysed for this study is not publicly available but is available from the corresponding author on reasonable request. Declarations Ethics approval and consent to participate in this study received ethics approval by the Arad Hospital Medical Science Ethics Committee (AHMSEC-0132-22). All methods were carried out in accordance with relevant guidelines and regulations. All permissions and written consent have been obtained and the patient and her parents agreed in writing, to the publication of this case report and the accompanying images.

Conflict of Interest Statement:

Authors of this manuscript ‘A unique case of Central Neurocytoma and Concomitant Brain AVM in a 12-year-old girl with long term follow up and review of the literature.’ declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Availability of data and material:

The authors confirm that all data and material for this communication are being kept in its original folder and available upon request.

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Authors contribution:

- AA contributed to study design, the definition of intellectual content, conceptualization of the of the idea, data gathering and preparing the manuscript.
- AA, KA, SBG contributed equally to reviewing the draft.

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Figures

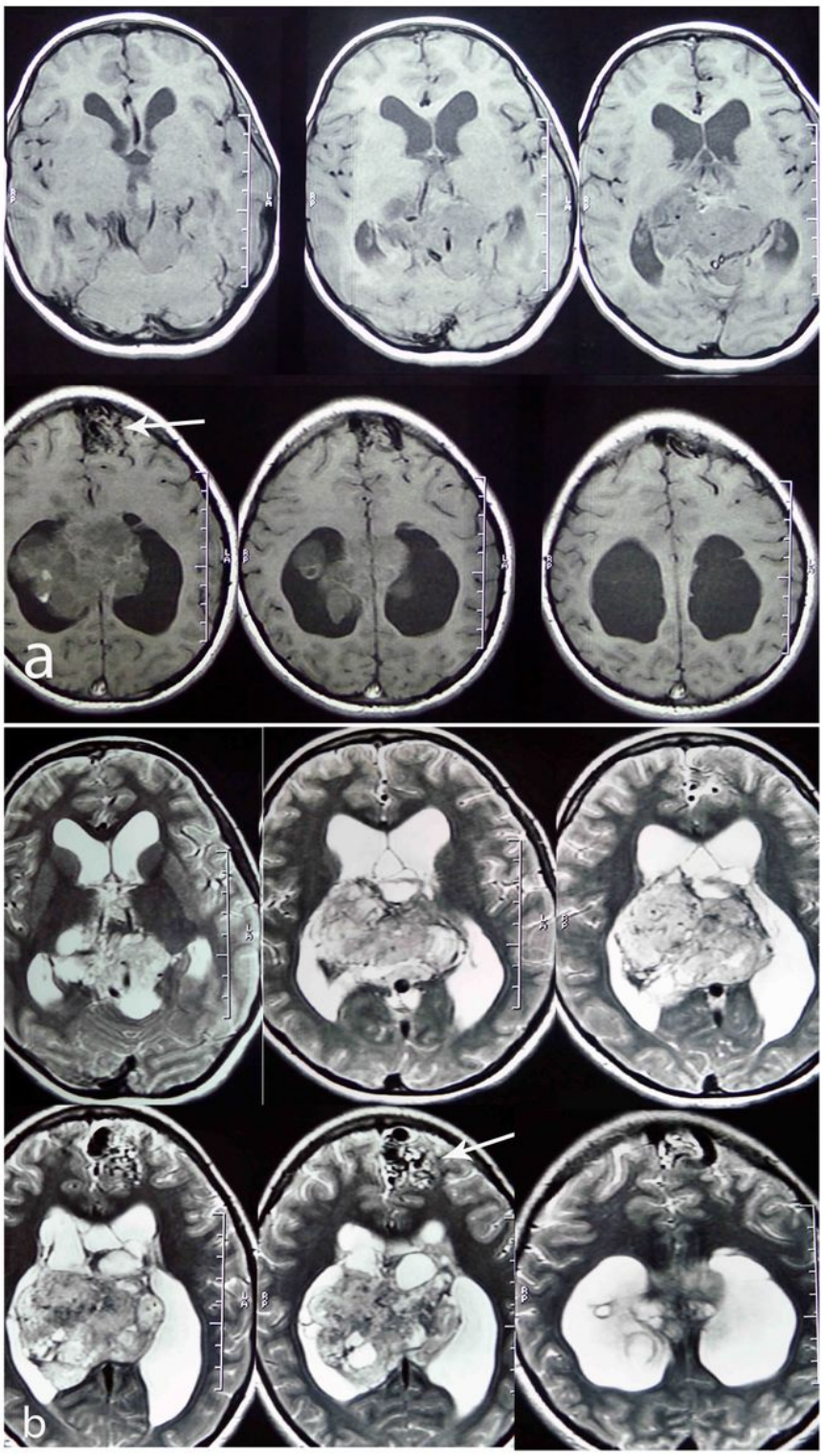

Figure 1

a) Axial T1W MRI showing a large non-homogenous, iso-intense lesion located in the midline, growing into the lateral ventricles, posterior third ventricle, ambient cistern and supra-cerebellar region. Lateral ventricles are dilated. The left frontal parasagittal AVM is pointed by *a white arrow*. b) Axial T2W MRI showing the same mass with non-homogenous intensity and dilated ventricles. The concomitant AVM is also identified.

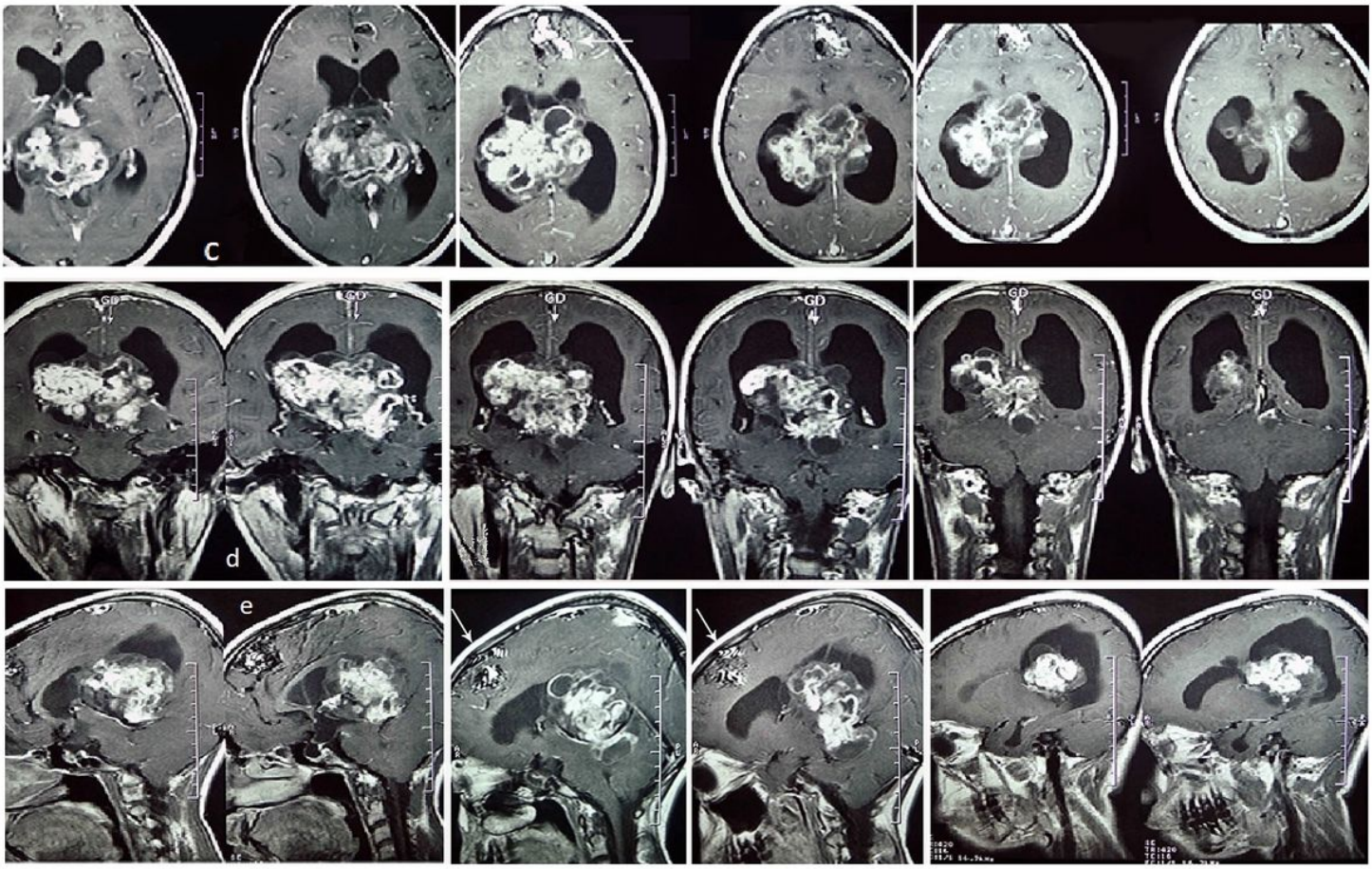

Figure 2

c) Axial contrast enhanced T1W MRI showing non-homogenous bubbly enhancement of the lesion and the enhancing draining vein of the frontal AVM pointed by the white arrow. d) Coronal contrast enhancing T1W MRI showing extension of the lesion on the roof and posterior part of the third ventricle, above the thalamic communication (small white arrow within the 3rd. ventricle) and tectal plate to the incisura and supra-cerebellar region. e) Sagittal contrast enhanced T1W MRI showing extension of the tumor to the sub-tentorial posterior fossa compartment and supra-cerebellar cistern. The AVM is demarcated by white arrow.

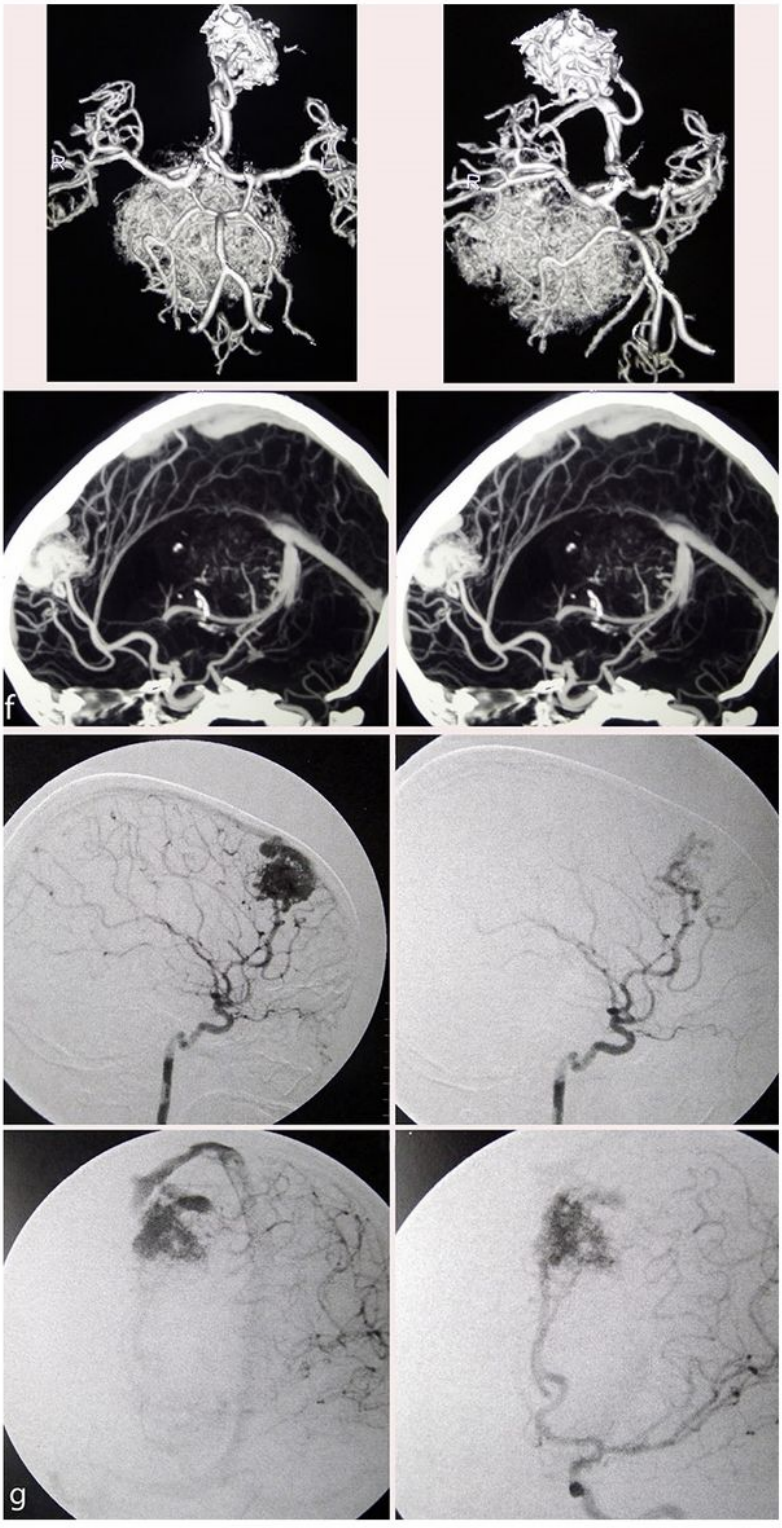

Figure 3

f) MR angiogram showing the AVM with the feeding arteries and main draining vein. The midline large tumor with moderate vascularity can be identified pushing the deep venous structures downwards. g) DSA showing the bowed/stretched middle and anterior cerebral arteries compatible with the pattern of hydrocephalus. The main arterial feeders and draining vein of the AVM are also visible.

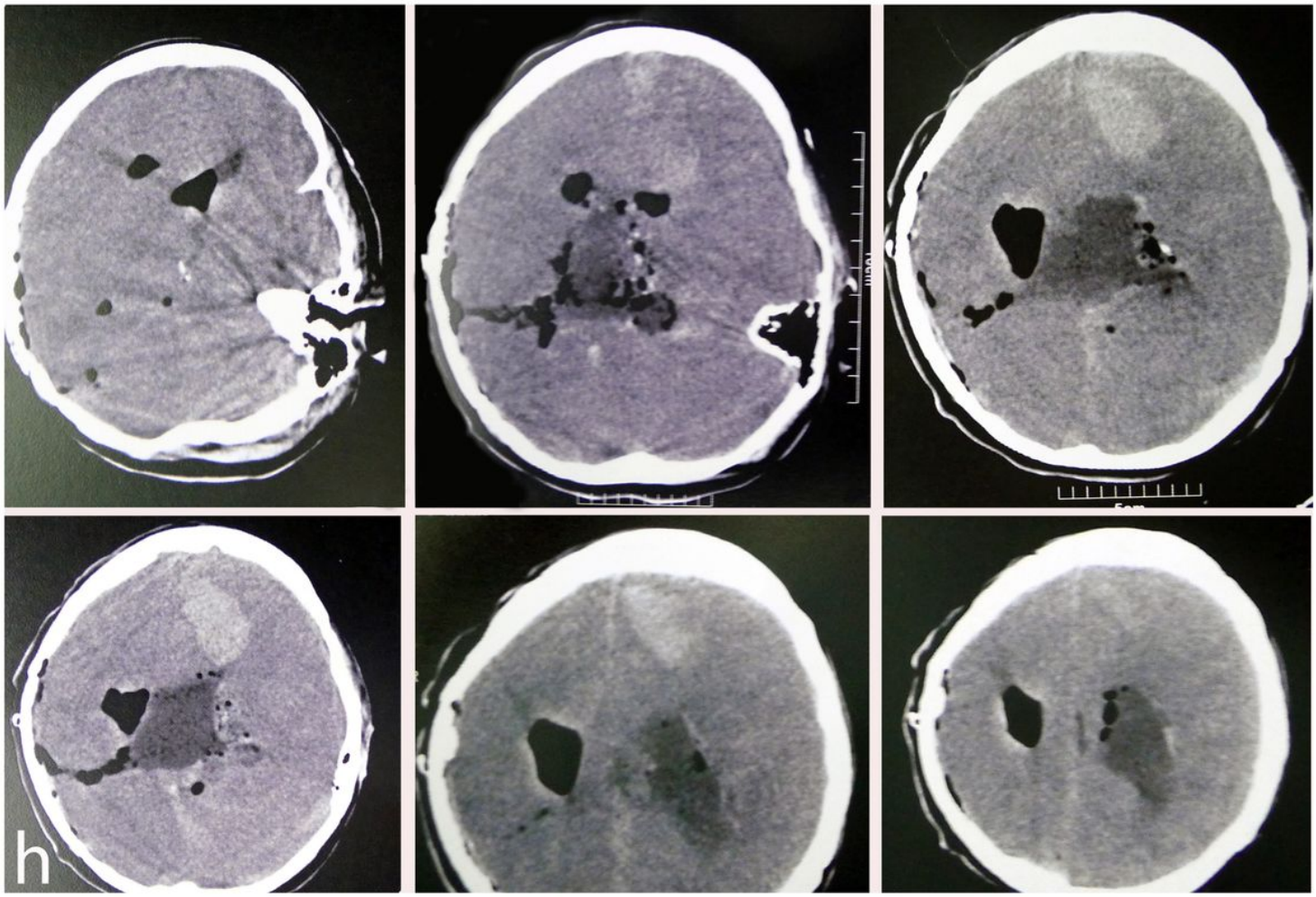

Figure 4

h) CT scan taken just after operation showing tumor bed containing fluid and the area around the AVM containing some blood sediment.

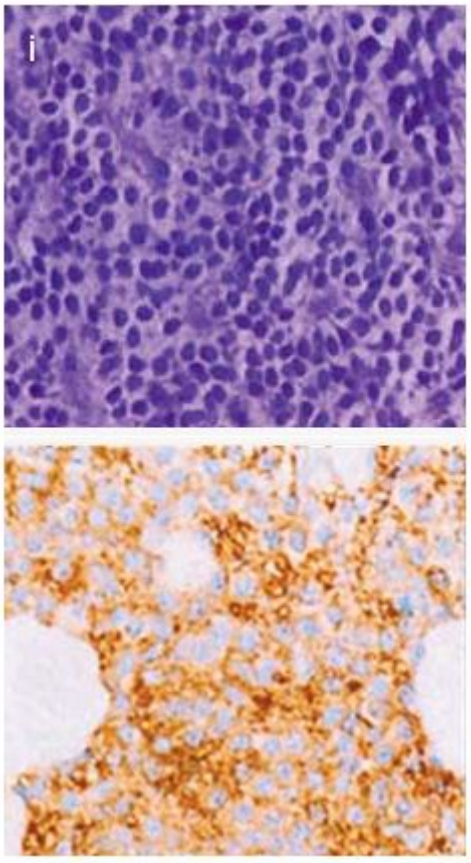

Figure 5

H&E staining showing uniform round nuclei with fine chromatin pattern, a fibrillary matrix, and no nuclear atypia. Immunohistochemical findings included expression of synaptophysin in synaptic terminals of tumor cells.

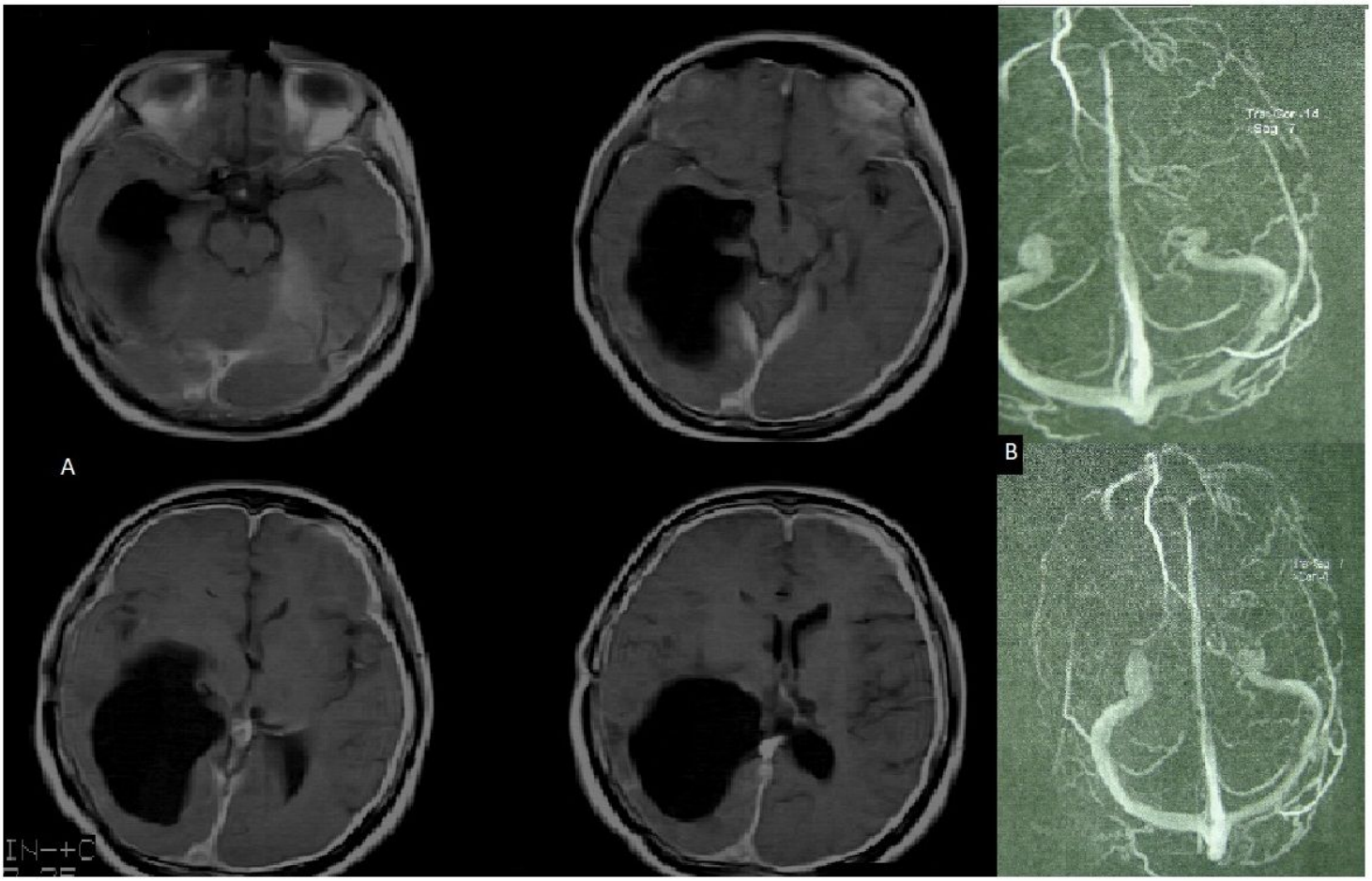

Figure 6

A- Contrast enhanced MRI after 12 years showing no tumor recurrence, no AVM (white arow) and well controlled hydrocephalus. B- postop. MR venogram showing no AVM remnant.