Cavernous Angioma: The Year’s Literature in Review

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Compendium of Knowledge ?…

Monograph (813 pages) by William Ralston Balch
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“As cultivated people know, culture is above all a matter of orientation. Being cultivated is a matter of not having read any book in particular, but of being able to find your bearings within books as a system, which requires you to know that they form a system and be able to locate each element in relation to the others”

-- Pierre Bayard

How to Talk About Books You Haven’t Read
Translated by Mehlman J, Bloomsberry Press, 2007
METHODOLOGY

- PubMed search using the following terms:
  cavernous malformation OR cavernous angioma
  OR cavernous hemangioma OR cavernoma
- Limited to 11/1/07 - 10/30/08
- Omitted articles
  - First review of all 306 articles by title only
    - Omissions for articles not related to CCM, typically referring to other organ systems or dural arteriovenous fistula
  - Second review of all remaining articles by abstract
    - Articles omitted if not truly about CCM, no English abstract
The Year’s Literature in Review

Basic and Translational Science-- 20 papers

- Gene product complexes (n=4)
- Gene product expression and molecular phenotype (n=6)
- Gene function (n=4)
- Clinical Genetics and Genotyping (n=6)

Clinical Reports

-- 91 papers

- Seizures and epilepsy surgery (n=9)
- Natural history and clinical associations (n=25)
- Surgical technique (n=20)
- Spinal lesions (n=14)
- Pediatric cases (n=6)
- Radiation induced cases (n=6)
- Imaging features (n=11)
Using an iterative affinity-purification/mass spectrometry approach, a novel large multiprotein assembly, referred to as the STRIPAK (striatin-interacting phosphatase and kinase) complex was identified containing the PP2A catalytic (PP2Ac) and scaffolding (PP2A A) subunits, the striatins (PP2A regulatory B’’’ subunits), the striatin-associated protein Mob3, the novel proteins STRIP1 and STRIP2 (formerly FAM40A and FAM40B), the CCM3 protein, and members of the Germinal Center Kinase III family of Ste20 kinases.
CCM3 (PDCD10) is shown to coprecipitate and colocalize with CCM2, directly bind to serine/threonine kinase 25 (STK25, YSK1, SOK1) and the phosphatase domain of Fas-associated phosphatase-1 (FAP-1, PTPN13, PTP-Bas, PTP-BL) and is phosphorylated by STK25 but not by its other Yeast-Two hybrid interactor STK24, while the C-terminal catalytic domain of FAP-1 dephosphorylates CCM3.
From a discovery of a total of 15 novel and eight previously published mutations in the *CCM1*, *CCM2* and *CCM3* genes identified by direct sequencing and MLPA analysis, with mutation detection rate > 90% for familial cases and >60% for isolated cases with multiple lesions, formation of the CCM1/CCM2/CCM3 complex is shown to be inhibited by the expression of one of these mutations (an in-frame deletion in *CCM2*) within HEK293 cell cultures.
PDCD10 (the CCM3 product), as well as EF1A1, RIN2, and tubulin, is shown to bind to OSM (the CCM2 product), a scaffold for the assembly of the GTPase Rac and the MAPK kinase kinase MEKK3, for the hyperosmotic stress-dependent activation of p38 MAPK, and previously found to associate with the proteins KRIT1 (the CCM1 product), MEKK3, Rac, and the KRIT1-binding protein ICAP-1.
CCM3 mRNA is expressed in different areas of the brain between that in the embryonic and postnatal mouse, and CCM3 protein is expressed in the neurovascular unit within cortical, subcortical and brainstem tissue and in extracerebral arterial endothelium, but weakly or not at all in all venous structures.
Gene Product Expression and Molecular Phenotype
Kamida T, Takeda Y, Fujiki M, Abe T, Abe E, Kobayashi H.
Nitric oxide synthase and NMDA receptor expressions in cavernoma tissues with epileptogenesis.
Acta Neurol Scand. 2007 Dec;116(6):368-73. PMID: 17986094

Using immunohistochemistry on resected CCMs from eight patients, expression for all forms of nitric oxide synthases (NOS) and N-methyl-D-aspartate (NMDA) receptor subunits 1 and 2A/2B were upregulated in declining neuronal cells and in reactive astrocytes in tissue, with hemosiderin deposits, adjacent to the CCMs, with the degree of inducible NOS expression correlated with seizure frequency, suggesting a role for iron or nitric oxide in epileptogenesis.
Resected CCMs were shown to contain B, T and plasma cells by immunohistochemistry and IgG were oligoclonal by isoelectric focusing from CCM homogenates but not in peripheral blood from the same patients, suggesting an antibody-driven immune response within these lesions.
Gene Product Expression and Molecular Phenotype
Sakata H, Fujimura M, Watanabe M, Tominaga T.

Association of cavernous malformation within vestibular schwannoma: immunohistochemical analysis of matrix metalloproteinase-2 and -9.

Immunohistochemistry of a resected CCM within vestibular schwannoma showed strong expression of matrix metalloproteinase-2 and -9 and tissue inhibitors of metalloproteinase-2 in endothelial cells, but not in the interstitial structures, suggesting an upregulation in CCMs for these molecules which have been implicated in angiogenesis and hemorrhage.

Fig. 3 Photomicrographs showing strong immunohistochemical expression of CD34 (A), matrix metalloproteinase-2 (B) and -9 (C), and tissue inhibitors of metalloproteinase-2 (D) in the endothelial cells of the cavernous malformation, but not in the interstitial structures. A–D: ×400.
No differences were found in the expression of thrombomodulin and von Willlebrand factor between fresh-frozen surgical specimens from 18 arteriovenous malformations (AVM), seven CCMs and 3 control epilepsy specimens, or whether or not AVMs have undergone irradiation or embolization.
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*Thrombin activated endothelial cell proliferation-- vWF vs thrombomodulin (Shenkar et al. 2005; Abe et al. 2005)*
Preliminary work showing more RNA expression of inflammatory molecules in CCMs than control AVM and STA, an enrichment of gamma globulin in CCM lesion and oligoclonality of IgG in CCMs, suggest the hypotheses that immune response may have a role in CCM maturation or maintenance, and that an antigen trigger may be involved in CCM disease.
Modulation of icap by krit1 is suggested by results showing that depletion of either krit1 or icap by RNAi decreases cell number and proliferation in HeLa cells and human umbilical vein endothelial cells and depletion of krit1 alone decreases icap1, allowing no detection of icap in the nucleus of Hela cells.
Gene Function
Glading A, Han J, Stockton RA, Ginsberg MH.
KRIT-1/CCM1 is a Rap1 effector that regulates endothelial cell cell junctions.

By using small interfering RNA-mediated depletion of KRIT-1, Rap-1 was shown to increase KRIT-1 targeting [independent of its band 4.1/erzin/radixin/moesin (FERM) domain] to bovine arterial endothelial cell-cell junctions, where it suppressed stress fibers and stabilized junction integrity.
Gene Function
Hogan BM, Bussmann J, Wolburg H, Schulte-Merker S.
ccm1 cell autonomously regulates endothelial cellular morphogenesis and vascular tubulogenesis in zebrafish.

Endothelial cellular morphogenesis is suggested to be regulated by CCM proteins during development and pathogenesis in zebrafish since both ccm1 and ccm2 mutants cause severe and progressive dilation of major vessels, progressive spreading of endothelial cells and thinning of vessels in embryos, despite normal endothelial cell fate and number, and ultrastructurally normal cell-cell contacts.
Krit1 adopts two conformational states [a closed conformation in which its N-terminal NPAY motif interacts with its C-terminus and an opened conformation bound to integrin cytoplasmic domain associated protein (ICAP)-1, a negative regulator of focal adhesion assembly], forms an *in vitro* ternary complex with Rap1 and ICAP-1, localizes on microtubules in baby hamster kidney cells with delocalization from microtubules upon coexpression with activated Rap1V12, and binds to phosphatidylinositol 4,5-P(2)-containing liposomes with Rap1 enhancing this binding.
Clinical Genetics and Genotyping

ZPLD1 gene is disrupted in a patient with balanced translocation that exhibits cerebral cavernous malformations.


A patient with a CCM had an X/3 balanced translocation with a 2.5 fold decreased mRNA expression for the ZPLD1 gene, but no effect on the expression for the CCM1, CCM2 and CCM3 genes.
A patient with multiple CCM lesions located in the cerebral hemisphere, brain stem and cervical and thoracic spinal cord had an Arg35X mutation in the *CCM3* gene.
While large genomic deletions in the \textit{CCM2} gene represent 22\% of mutations in a large cohort from the USA, including a 77.6 kb deletion spanning \textit{CCM2} exons 2-10 in eight CCM probands/families, an Italian CCM cohort consisting of 24 proband families did not contain the common CCM2 deletion spanning exons 2-10, suggesting that this particular deletion specific to the US population might be due to a founder effect.
The descriptions and accession numbers for recently discovered human pathological mutations are listed, including those for eleven mutations in the *CCM1* gene (three substitutions, five insertions and three deletions).

Example:

**Missense/nonsense mutations (single base-pair substitutions)**

<table>
<thead>
<tr>
<th>Accession number</th>
<th>Codon number</th>
<th>Nucleotide substitution</th>
<th>Amino acid substitution</th>
</tr>
</thead>
<tbody>
<tr>
<td>HM070065</td>
<td>714</td>
<td>aCAG-TAG</td>
<td>Gln-Term</td>
</tr>
</tbody>
</table>
Three patients with myoclonus-dystonia harbored heterozygous large deletions in the 7q21.13-21.3 region, in two of these patients (9 and 59 years of age), the deletions removed the paternal allele of the *CCM1* gene, with only the adult patient exhibiting CCM lesions.
Genetic causes for twenty-two vascular malformations are reviewed and focused on venous malformation, capillary malformation, capillary malformation-arteriovenous malformation, hereditary hemorrhagic telangiectasia, cerebral cavernous malformation and lymphatic malformation and lymphedemas, with relationships discussed between gene products responsible for these malformations.

Case report of a woman with no history of seizures who presented with refractory status epilepticus at 10 weeks gestation. Cranial MRI revealed a right frontal cavernous hemangioma. The seizures remained refractory to conventional anticonvulsant medications and 48 h of general anesthetic. Termination of the pregnancy resulted in almost immediate resolution of the seizures.


The histopathological study showed the coexistence of cavernoma and cortical dysplasia. This is an interesting combination of epilepsy-related pathologies that have so far not been documented.


Retrospective analysis of 14 patients who presented with seizure found to be due to cavernoma, who subsequently underwent surgical resection with complete resolution (12) or significant reduction (2) in seizures.


Case series of 32 patients with seizure thought to be due to a cavernoma demonstrating good outcomes up to 3 years following surgical resection in 10 of these patients who failed medical therapy and underwent surgical resection.
Seizures, Epilepsy Surgery


  At last follow-up, 74% (43/58) of all patients were seizure-free; seizure-free rates for specific conditions were 88% (14/16) for MTS, 33% (1/3) for dual pathology, 81% (13/16) for tumor, 62% (8/13) for CD, and **80% (4/5)** for CM. Seizure-free rates were 85% (28/33) for temporal locations and 60% (15/25) for extratemporal locations. There were no permanent neurological complications or deaths. CONCLUSION: Surgery for localized epilepsy in carefully selected children has good seizure control rates with minimal complications. Outcomes for patients with resections in temporal locations were better than those for patients with extratemporal resections.


  Retrospective analysis of 42 children who underwent temporal lobe surgery for medically intractable epilepsy demonstrating better long term outcomes in patients with tumors or cavernomas in comparison to other etiologies for seizure (Engel class I achieved in 79% of those with tumor or cavernoma vs 50% in other pathologies)


  Case report demonstrating that medically intractable seizures associated with multiple cavernous malformations can be diagnosed by non-invasive preoperative monitoring and controlled by single surgical resection.
Seizures, Epilepsy Surgery


  Prospective study of 17 patients with a cavernoma monitored with electroencephalography and magnnetoencephalography demonstrating that the detectability of mirror and remote spikes was higher by MEG than by EEG, whereas the detectability of perilesional spikes was similar by MEG and EEG. Therefore, the use of both EEG and MEG will provide the maximum information about spike distribution and propagation.


  Case report detailing the recording of intrinsic optical signals (IOS) from human cortex intraoperatively during spontaneous seizures arising from brain surrounding a small cavernous malformation in an awake patient using only local anesthesia with simultaneous electrocorticography. These findings demonstrate that the hemoglobin becomes deoxygenated in spite of large increase in CBV during spontaneous human focal seizures and that optically recorded hemodynamic events can be used both to predict and localize human focal epilepsy.
Natural History, Clinical Associations


  A novel syndrome, combining features of CCM and GCPS, can be added to the group of entities that result from deleterious genetic variants involving GLI3, including GCPS, acrocallosal syndrome, Pallister-Hall syndrome, and contiguous gene syndrome. The deletion responsible for this new entity can be easily detected using either array-based chromosomal analysis or quantitative RT-PCR.


  This is a quite rare case with cavernous malformation which appeared in a moyamoya disease patient. The association may suggest the existence of some interaction in the pathogenesis of these diseases. Since cavernous malformations with a de novo appearance may grow and become clinically significant, careful observation is necessary.


  The association of moyamoya syndrome with CCM and venous malformation is extremely rare. The coincidence of the progressive moyamoya syndrome with these newly formed vascular malformations may give a clue to the underlying mechanism of the progression of this rare entity.

Case report that demonstrates the truly dynamic nature of CCMs and the increased incidence of new lesions in the setting of CCM1 mutation. This case is remarkable not only for the unprecedented rate of lesion formation (approximately 22 per yr), but also because of the nearly unilateral distribution of the lesions.


Retrospective analysis of 30 patients with brainstem cavernoma who presented with progressive neurological symptoms who ultimately underwent surgical resection advocating for the use of post-operative brain MRI scans and if a residual is detected early re-intervention is less risky than the natural history.


The pathogenesis of this malformation may be referred to a developmental deviance of the brainstem capillary-venous network associated with transitional vessels and loculated endothelial vascular spaces related to genetic and acquired origins, probably in a restrictive venous outflow milieu.


The natural history of disease is described in a female with developmental venous anomaly, cavernous malformation, and capillary telangiectasias appearing in sequence.

Intracranial haemorrhages found to be due to IVMs differ in adults' age of presentation and clinical severity, as well as the volume and distribution of the haematoma within the brain compartments.


Educational conference discussing the diagnosis, monitoring, and treatment of cavernomas relative to sports medicine.


The association of cavernous and venous angioma is frequent (30%). This association has prognostic implications, due to bleeding risk, and surgical as it is not recommended the resection of the venous anomaly due to the possible venous infarction. To detect venous angiomas is necessary the administration of contrast material.


Brain parenchymal abnormalities were associated with DVAs in close to two thirds of the cases evaluated. These abnormalities are thought to occur secondarily, likely during post-natal life, as a result of chronic venous hypertension. Outflow obstruction, progressive thickening of the walls of the DVA and their morphological organization into a venous convergence zone are thought to contribute to the development of venous hypertension in DVA.
Natural History, Clinical Associations


Because a high frequency of family CM occurs in MCMs, a detailed family investigation is mandatory for each patient with MCM. Selection of higher sensitive MRI sequence would contribute to detection of more CM lesions. Microsurgery assisted with the neuroimaging techniques is the treatment of choice for symptomatic MCMs.


When multiple cerebral cavernomatosis are identified in a patient, a detailed neurologic family history should be sought despite the possibility of its being a sporadic case. Our main intention is to present a patient who is surgically controversial and to point out the importance of genetic predisposition.


Case report of three cases of cavernous sinus hemangiomas treated with 10-13 Gy Gamma Knife radiotherapy revealing that low-dose Gamma Knife radiosurgery seems to be very effective for management of cavernous sinus hemangiomas, and can be considered as a treatment modality of choice for these lesions.


On the basis of our review of 50 cases of cavernous angioma of the CPA, we propose that these tumors can be classified according to whether they develop from the venous plexus of the dura matter or of a cranial nerve. We also suggest that the site of origin affects the postoperative symptoms.

An illustrative case is presented in which CCM occurred together with different dysplasias (multiple CCM, liver cavernoma, and cardiac atrial myxoma), which are all thought to arise from abnormal mesenchymal cell differentiation processes.


Case report of a 48 year old male who developed sudden onset right ear tinnitus from acute hemorrhage from a left inferior colliculus cavernoma.


Case report of a patient with vocal cord palsy in a 30-year-old male resulting from the brain-stem lesion. The patient became symptomatic each time the lesion bled and improved gradually when the bleeding resolved.


Contrary to the current clinical definition, the absence of intervening brain parenchyma does not represent an essential histopathological criterion of CCMs in our series. Furthermore, the diameter of the vessel lumina and the thickness of vessel walls varied considerably. Based on these findings, adaptation of the current definition on the basis of interdisciplinary interaction needs to be considered.
Natural History, Clinical Associations


  A case report of a patient with a parietal cavernous hemangioma, traditionally a contraindication to electroconvulsive therapy, safely received electroconvulsive therapy.


  Skull cavernous hemangiomas are rare benign tumors. The preferred treatment is complete tumor removal with normal bony margins. Sometimes, the classic radiographic appearances are not evident. Consequently, the diagnosis is most often made during surgical resection.


  Case report of R forehead mass where en bloc resection was performed. The histological diagnosis was primary intraosseous cavernous hemangioma. Total resection is recommended for definitive diagnosis of intraosseous tumor.


  Case report of a patient who presented with a Holmes tremor found to be secondary to a brainstem cavernoma.


Literature based expert consensus definition of acute CCM hemorrhage as a clinical event involving acute or subacute onset headache, epileptic seizure, impaired consciousness, and/or new/worsened focal neurological deficit referable to the anatomic location of the CCM, associated with radiological, pathological, surgical, or rarely only cerebrospinal fluid evidence of acute extra- and/or intra-lesional hemorrhage
Surgical Technique


Case report of 2 cases of intracranial giant vasogenic tumors (1 cavernous hemangioma, 1 hemangiopericytoma) with radiofrequency thermocoagulation demonstrating that radiofrequency thermocoagulation is extremely effective in controlling bleeding during surgical excision of intracranial giant vasogenic tumors. This improves the ease and safety of such procedures and allows for complete removal of tumors.


Surgical treatment of the lesion resulted in complete remission of the eating disorder at two years follow-up. CONCLUSION: Evidence for organic brain contribution to anorexia nervosa is strong and can be illustrated by this case report of anorexia nervosa associated with cerebral tumor


Anatomy of approaches for various brainstem lesions demonstrating that white fiber dissection technique is a valuable tool for understanding the three-dimensional disposition of the anatomic structures. The lateral mesencephalic sulcus, the peritrigeminal area, and the inferior olivary nucleus provide surgical spaces and delineate the relatively safe alleys where the brainstem can be approached without injuring important neural structures.


With an optimal surgical approach, fairly safe entry zones on the anterior face of the rostral brainstem may be accessible, which makes it possible for successful resection of a ventral mesencephalic cavernoma without postoperative complications.


A safe surgical routes for the radical removal of thalamic cavernous angioma.
Surgical Technique


Case report of a 33 year old male with symptomatic thalamomesencephalic junction cavernoma introducing a new approach via orbitozygomatic craniotomy utilizing a trajectory dorsal to M1 leading through the perforating branches of M1 and avoiding violating any arterial perforators. Finally, a small opening into the brain was created near the optic tract to reach the lesion resulting in complete resection of the lesion, symptomatic improvement and temporary post-operative hemiparesis.

- Zsoldos T, Molnar A, Janossy A, Kuncz A, Nagy E, Deak G, Barzo P. Successful surgical removal of a mesencephalic cavernous angioma, which was responsible for progressive neurological deficits Ideggyogy Sz. 2008 Jul 30;61(7-8):244-9. Hungarian

Case report of a 51 year old female demonstrating successful removal of a mesencephalic cavernous angioma causing progressive neurological deficits and symptoms.


Retrospective case series of 10 patients suggesting that surgical intervention for symptomatic brainstem cavernomas is safe and effective even in the setting of lesions without superficial representation. However asymptomatic incidentally found cavernomas should not undergo surgery and should be followed with serial imaging and in patients who experienced complete recovery following a hemorrhage, the decision for surgical intervention must be carefully individualized.


Retrospective analysis of 38 patients with spontaneous intracerebral or spinal hemorrhage due to cavernoma advocating that surgery for such lesions is safe and effective regardless of clinical presentation.
Surgical Technique


  Description of novel minimaly invasive technique for accessing lesions of the spinal canal including cavernous hemangiomas.


  Novel endoscopic approach for 3rd ventricular lesion


  Case report of a patient who had almost complete bilateral loss of the rostral columns of the fornix and much of the surrounding septum in the left hemisphere following the surgical resection of a cavernoma. Stable anterograde memory impairment that was still present 4 years postsurgery, but performed within normal levels on most tests of recognition memory.


  49M with pontine symptomatic hemorrhagic cavernoma associated with hemophilia safely resected with the use of pre-operative factor IX administration.


  Should be recognized as a possible complication of surgery within the brainstem and must be diagnosed promptly so that patients can be appropriately counseled and symptoms can be treated.


  Another report of danger of commonly used surgical adjunct in CCM resections
Surgical Technique


Prospective study following 20 patients with intracranial cavernomas who underwent resection with stereotactic navigation with useful feedback in the preoperative anatomical orientation, the planning and simulation of surgical approach, avoiding vital neurovascular structures, in the assessment of the degree of resection and the identification of possible residual parts.


After the operation, seizures disappeared in 19 patients and symptoms improved in 5. CMs can be determined in patients even if patients are asymptomatic. An operation with the guidance of neuronavigation is safe and can decrease the occurrence of disability following the procedure.


Discussion of use of virtual reality 3D planning system for neurosurgical operations for various pathologies including cavernomas.


Prospective study demonstrating that MRI based corticography is a practical, time-saving neuronavigational aid ideal for localizing superficial lesions underlying the cerebral cortex because it unmistakably characterizes the adjacent sulcal anatomy.


The first report on a symptomatic cavernous malformation arising from the trochlear nerve and on its successful surgical management.
**Spinal Cavernous Angiomas**


This study has defined clinical and MR patterns of spinal cavernomas. Surgery lastingly improved more than half of the patients, mostly those with posterior lesion location.


Neurological status of the patients can worsen in the early postoperative period; but it usually improves relative to preoperative status. Surgical removal seems to be a safe and a promising way of treatment of symptomatic SCMs.


Case report describing the clinical course of a 25M with paraplegia secondary to a conus cavernoma who improved following surgical resecion.


We report this case to underline the importance and difficulties concerning the preoperative diagnosis of a hemorrhagic intramedullary lesion.


Case report of a patient with a dorsal medullary cavernous angioma concluding that a restricted lesion of medullary lesion interrupting the catecholaminergic transtegmental tract arising from the sympathoexcitatory C1 neurons of the rostral ventrolateral medulla could result in severe orthostatic hypotension.
Spinal Cavernous Angiomas


  Case report of a 57 year-old woman carrying a dumbbell-shaped epidural cavernoma located at C7 – T1 that was surgically removed.


  Although soft-tissue tumors such as Kaposi’s sarcoma and lymphomas have been well documented in association with HIV infection, this is the first reported case of spinal epidural cavernous hemangioma. This may be an incidental finding or perhaps a causal relationship exists.


  The first case of a histologically confirmed epidural capillary-cavernous haemangioma of the thoracic spine in pregnancy, with MRI features.


  In this report, a unique case of an intradural extramedullary spinal cavernoma was surgically treated in a patient who presented only with an intramedullary hemorrhage.


  We concluded that the presence of spinal AVM should be suspected if the patient with familial CCM develops the signs of space-occupying lesion of the spinal cord, facilitating early diagnosis of the spinal AVM.
Spinal Cavernous Angiomas


  The microscopic appearance was suggestive of cavernous angioma with intraneural growth. Clinical, radiological, and surgical features of this unusual lesion (to date, only 12 cases are reported) are discussed.


  Despite the small number of cases reported in children, this one contributes to the literature identifying special features of presentation and management of ImCA for pediatric patients. Because a higher risk of recurrent bleeding has been demonstrated for ImCA, with dramatic clinical consequences, microsurgical removal remains the only definitive treatment.


  The rarity of the pediatric intramedullary cavernoma, the familial occurrence, and the spontaneous regression of the pontine cavernoma make this case very peculiar.


  Comprehensive care of patients with familial CCM includes screening of all the tissues that can be affected and appropriate management by specialists. We emphasize the importance of spinal MRI in the diagnosis of spinal and vertebral cavernous angiomas in all patients with familial CCM.
Pediatric Cases


  Case report detailing the clinical course of a 10-month-old baby with a giant multilobular cavernous haemangioma in the left parietal lobe who presented with seizures.


  Case report of a 16-year-old child who was admitted with a swelling lesion in the right parietal bone and diagnosed as cavernous hemangioma after total extirpation.


  12-year-old girl with multiple cavernomas accompanied by supravermian arachnoid cyst detected by neuroimaging techniques. This is the first report that demonstrates a case of pediatric multiple cavernous malformation coexisting with arachnoid cyst of the supravermian cistern


  Suggest that pediatric patients with symptomatic CMs should be considered for surgical treatment because of the risk of recurrent hemorrhaging and the general benefits of CM removal.


  Review discussing intracerebral hemorrhage in children one etiology of which is cavernoma. The etiology of such hemorrhage in order of incidence is AVM, cavernoma, and finally aneurysm.


  Case report of a 16 year old boy who presented with acute onset visual loss and headache and was found to have chiasmal apoplexy due to a cavernoma. Prompt craniotomy and cavernoma resection resulted in significant improvement in vision.
Radiation Induced Lesions


47M underwent LINAC SRS (25 Gy) for right caudate AVM, resulting in complete radiographic obliteration, later developed expanding lesion in targeted area found after resection to be a cavernoma.


Case report details the treatment of nasopharyngeal carcinoma with radical chemo-radiotherapy with development of histopathology proven temporal cavernoma within the radiation field.


Epidemiological and pathogenic features of radiation-induced cavernoma discussed in the context of two cases of radiation induced cavernomas.


Spectrum of radiation induced pathologies


Cavernomas may be found incidentally during the neuroimaging surveillance studies that are performed to children with brain tumors previously treated with radiotherapy. In these cases, a conservative attitude seems to be advisable, reserving surgery only for those lesions that grow or bleed.


CCMs may occur after irradiation of the brain several years after the end of therapy irrespective of the radiation dose and type of malignancy. Particularly children < 10 years of age at the time of irradiation are at higher risk. Imaging of the central nervous system should be performed routinely for longer follow- ups, particularly in patients who were treated as young children.
Imaging Features


The sensitivity of SWI in assigning the number of CCM lesions in patients with the familial form of the disease is significantly higher than that of T2-weighted FSE and GRE sequences.


We report a case of a giant cavernous malformation with multilobular involvement and a focal infiltrative pattern.


Most giant CCMs in this series presented as multicystic lesions with complete hemosiderin rings on MRI, giving a "bubbles of blood" appearance. The correct diagnosis in the remaining cases may not be apparent until histopathological evaluation of the specimen is made.
Imaging Features


  Progressive contrast "filling in" in the tumors on conventional contrast-enhanced MR images can aid in differentiating between cavernous sinus lesions and suggest the diagnosis of cavernous hemangiomas.


  Radiology case report of a skull mass found to be a calvarial cavernous hemangioma.


  Radiology case report of cerebral hemorrhage characteristics that suggest cavernoma as the etiology
Imaging Features


Compared with the information provided by conventional MR imaging, DTI and WMT provided superior quantification and visualization of lesion involvement in eloquent fibre tracts of the brainstem. Moreover, DTI and WMT were found to be beneficial for white matter recognition in the neurosurgical planning and postoperative assessment of brainstem lesions.


Diffusion tensor imaging (DTI) MRI to validate the hypothesis of central tegmental tract interruption in pathophysiology of oculopalatal tremor in a patient with a mesencephalic cavernoma treated with gamma knife radiosurgery.
High-field MRI techniques demonstrate novel features of CCM angioarchitecture, visible at near histological resolution, including regions with apparently different biological activity (bland versus honeycombed domains), will likely motivate future research, correlating lesion biological and clinical activity with features of MRI at higher field strength.
Imaging Features

T2*-weighted MRI scans of brains in vivo and ex vivo revealed lesions similar to human CCMs in mutant mice, but not in control animals and stereotactic localization and hematoxylin and eosin staining of correlative tissue sections confirmed lesion histology and revealed other areas of dilated capillaries in the same brains, offering new opportunities for further investigation of disease pathogenesis in vivo, and the localization, staging, and histobiological dissection of lesions, including the presumed earliest stages of CCM lesion development.