Unusual Cerebral Cavernous Malformation Mimicking Intracranial Malignancy: Role of Computed Tomography, Conventional MR Sequences and Susceptibility Weight Images with Outcome of the Disease

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Abstract: Cerebral cavernomas are vascular malformations of great neurological interest due to their potential to bleed. Most of the micro hemorrhages occur intralesionally, but rarely do they bleed into surrounding brain parenchyma, forming an intracerebral hematoma. Such lesions are not usually life-threatening but may require hospitalization. Epilepsy is another typical manifestation of cerebral cavernomas. Here we are presenting a case of 42 years old hypertensive female with Sporadic Multiple Cerebral Cavernous Malformations (MCCMs), diagnosed with various imaging modalities especially higher MRI sequences. Almost all the lesions were Type IV CCMs with one lesion complicated by intra and extra lesional hemorrhage producing neurological manifestations as seizures, headache and delirium. Fortunately, the patient is alive without any symptom, but was advised antihypertensive treatment to prevent further bleeding.

Keywords: Unusual Cerebral Cavernoma, Imaging Modalities, Disease Outcome.

1. BACKGROUND & INTRODUCTION

Multiple cerebral cavernous malformations are a rare clinical entity with prevalence rate of about 0.5% in general population. They comprise of 5-13% of all the vascular malformations of central venous system [1,2]. A solitary lesion of CCM is usually sporadic in nature. However, multiple lesions are thought to be familial in nature with autosomal dominant transmission, requiring baseline imaging of the family members.

Histologically, CCMs are blood filled sinusoidal cavities having a single layer of endothelium, without any muscle tissue or intervening parenchyma [1,2]. The etiology of CCMs remains obscure, though certain specific mutations may play a role in the development of these lesions. Three genes are known to be associated with the formation of CCMs: Type I CCM is found on chromosome 7q (KRIT1), Type II CCM found on 7p (malcaverin) and Type III CCM on 3p (Programmed Cell Death 10) [6,8,9].

The patients with familial type of CCMs are prone to develop new lesions throughout their lifetime. Hence periodic MRI studies should be advised with screening of family members, genetically and radiologically.

Cerebral Cavernous Malformations can be incidental and may not cause any symptoms. They may present with a variety of neurological signs and symptoms depending upon the anatomic site involved. They most commonly present with headache, hemorrhage, seizure, or focal neurological deficit [6]. Intracranial CCMs can cause hemorrhages that exert a mass effect on the surrounding brain tissues. The extravasation of blood into brain parenchyma creates a hemosiderin ring that may predispose susceptible tissue to seizure [7].

Of the various imaging modalities, MRI is the best imaging technique in the evaluation of Cerebral Cavernous Malformations. On T2 Weighted sequences, the lesion shows areas of mixed signal intensity, with a central reticulated core and a peripheral rim of decreased signal intensity [3]. T2 Weighted Gradient Echo (GRE) is taken as the gold standard for both familial and sporadic cases of CCMs [4].

Susceptibility Weight Images are a newer MRI technique that exploits the magnetic properties of the tissues, like blood or iron contents. It has a great sensitivity to various venous structures, blood products and vascular malformations, giving it an edge over T2 Weighted images for evaluation of CCMs [5].

Zabramski et al. [4] Classification of 4 types of CCMs (based on T1 and T2 Weighted FSE and GRE MR Sequences) is represented in a tabulated form below:
### Unusual Cerebral Cavernous Malformation Mimicking Intracranial Malignancy

<table>
<thead>
<tr>
<th>CCM Type</th>
<th>MRI features</th>
<th>Pathological features</th>
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| Type I   | T1: Hyperintense core  
T2: Hyper/Hypo intense Core | Subacute Hemorrhage |
| Type II  | T1: Reticulated mixed signal  
T2: Reticulated mixed signal intensity core with hypo intense rim | Lesions with thrombosis of variable age |
| Type III | T1: Iso to Hypo intense  
T2: Hypointense lesion with hypo intense rim magnifying the size of lesion | Chronic Hemorrhage with Hemosiderin staining within and around the lesion |
| Type IV  | T1: Lesion not seen  
T2: Lesion not seen  
GRE: Punctate hypo intense lesions | Tiny cavernous malformations or telangiectasia |

#### 2. CASE SUMMARY

A 42 years old hypertensive female presented with a severe headache over a period of three days, that gradually got worsened during the time. She had mild episodes of headache previously also, which were thought to be due to chronic hypertension. The last episode of severe intractable headache was not relieved with analgesics and medical treatment, which was followed by episodes of vomiting, occasional seizures and delirious state.

**2.1. Imaging Features**

She was advised Computed tomography of brain for any suspected intracerebral hemorrhage or aneurysmal rupture. CT showed a well-defined oval to round hyperdense lesion with 69-84HU in the right frontal cortex with a few specks of calcification were noted. The periphery of this lesion showed another faintly hyperdense halo with 38-50HU around it. Moderate degree of peripheral white matter hypodensities was noted suggestive of edema causing mass effect. Slight contralateral shift of anterior the interhemispheric fissure was noted with effacement of adjacent sulcogyrinal spaces. Intravenous contrast was given which showed no significant changes in the contour and density of the lesion. The rest of the cerebral tissue was unremarkable. Keeping in view, the above CT findings the diagnosis of intracranial bleed was made with possibly some underlying vascular pathology (Figure 1).

**Figure 1:** CT scan in axial, coronal and sagittal planes (120KV, ST: 1.0mm) show a well-defined oval hyperdense lesion is seen in right frontal lobe with suggestion of small specks of calcification in it. Faint hyperdense halo is also seen around this lesion. Marked degree of surrounding edema noted around it with moderate mass effect (B,C,D).

MRI with routine T1 & T2 weighted sequences was done. The T1-weighted images showed a well-defined oval hyperintense lesion with a small hypointense central area. Mild central edema was also noted (Figure 2). The T2-weighted images showed irregular shaped hyperintense lesion measuring about 3.3x3.2x2.0cm in size with a thin irregular shaped

**Figure 2:** Axial T1 weighted MR Images (Early stage) shows a well-defined oval hyperintense lesion is seen in right frontal lobe (subacute haemorrhage) with a small hypointense area in it (B) Mild III-defined white matter hypointensity is noted suggestive of surrounding edema.
hypointense rim around it, thought to be due to hemosiderin deposition (Figure 3). Hence, the final diagnosis of subacute hemorrhage was made on routine MRI sequences.

MR venography of the cerebral venous system was done using 2D TOF technique to rule out any venous malformation. It showed diminished flow in transverse sinus, sigmoid sinus and internal jugular vein on the left side, with increased signal intensity in the superior sagittal sinus, inferior sagittal sinus and straight sinus. The transverse sinus, sigmoid sinus, petrosal sinuses and internal jugular vein on the right side were unremarkable. No thrombosis was detected on MRV (Figure 4).

The patient was put on antihypertensive, antiepileptic, antiemetics with decompression therapy to reduce intracerebral edema. Unfortunately, not much improvement in symptomatology was noted by the clinicians.

Subsequent MRI was advised in later stages of disease. Axial T1 3D BRAVO MR images done were done which showed an irregular shaped mixed signal intensity lesion, which had enlarged in size as compared to previous scans measuring about 5.3x4.5cm in size. It showed a central reticulated pattern with a peripheral hyperintense rim and increased surrounding edema (Figure 5).

Axial & Sagittal T2W FSE & GRE images showed a large mixed signal intensity lesion in right frontal lobe with central reticulated areas and a thin hypointense rim around it. Marked surrounding edema was noted (Figures 6, 7, 8). Axial DWI MR Images (late stage) showed a large well-defined irregular shaped mixed intensity lesion in right frontal lobe with irregular hypointense rim (Figure 9).

Keeping in view gradual increase in size of the lesion and deterioration of the condition of the patient, the possibility of intracranial malignant pathology was suspected.

The case was referred to the neurosurgeon for any surgical intervention of this intracranial space.
occupying lesion. For further evaluation, neurosurgeon advised T1W, T2W MRI with newer MR sequences like DWI, VEN_BOLD and 3D FLAIR images. A large late subacute hematoma was seen in right frontal lobe. The core of lesion was hyperintense on T1 and T2 with hypointense rim. The lesion showed “Bloom effect” attributable to slow sinusoidal peripheral blood products. About 2-3 small focal areas of susceptibility were seen adjacent to frontal lesion. On VEN_BOLD sequences, multiple focal areas of susceptibility were noted in both the cerebral hemispheres, pons and cerebellar hemispheres. Susceptibility was also noted in occipital horns probably old intraventricular hemorrhage. The peripheral edema was mildly reduced (Figure 10).

Figure 6: Axial & Sagittal T2 weighted MR Images (late stage) shows a large mixed signal intensity lesion in right frontal lobe with reticulated areas in it with a thin hypointense rim around it. Marked surrounding edema is around it.

Figure 7: Axial T2 FSE MR Images (late stage) shows a large well-defined irregular shaped mixed intensity lesion in right frontal lobe with a thin hypointense rim around it. Minimal edema is noted around it.

Figure 8: Axial & Sagittal T2 GRE MR Images (late stage) shows a large well-defined irregular mixed intensity lesion in right frontal lobe. Minimal edema is noted around it.

Figure 9: Axial DWI MR Images (late stage) shows a large well-defined irregular shaped mixed intensity lesion in right frontal lobe with irregular hypointense rim. Minimal edema is noted around it.

2.2. Final Diagnosis

Zabramski Type II Cerebral Cavernous Malformations Right frontal cortex with peripheral bleed
along with multiple scattered Zabramski Type IV lesions.

Figure 10: Axial Susceptibility Weighted MR images showing an irregular shaped mixed signal intensity lesion in right frontal lobe with a reticulated pattern with "blooming effect". A thin hyperintense rim is also seen around it suggestive of hemosiderin deposits. Ill-defined hypointense areas are seen around it suggestive of surrounding edema with mass effect.

2.3. Clinical Outcome

Surgery of frontal lesion was advised, but the patient refused to undergo brain surgery. She was prescribed medication and over the course of time her symptoms gradually resolved and luckily she is hale and hearty after about one and half year of diagnosis of the disease. She is now on medication for hypertension in view the danger of rebleed from CCMs. None of Kindred or children are known to have any of above symptoms related to CCM, but caution is advised to them. Though it appears to be sporadic in nature, the possibility of multiple CCMs favors familial trait.

3. DISCUSSION

CCMs are slow flowing vascular malformations consisting of clustered, dilated sinusoidal like vascular channels, with absence of smooth muscle that are filled with blood in different stages of degradation [10].

As per MRI imaging and pathologic findings, the prevalence of CCMs is 0.5% in the general population. However, about 70-80% patients are asymptomatic at the time of diagnosis. Sporadic and familial forms have been described, the latter being associated with mutations of three genes: KRIT1 (CCM1), CCM2 (MGC4607) and PDCD10 (CCM3). The familial form is autosomal dominant with a prevalence of 20% [8,9].

Since the CCM contains blood products in different degradation stages, such as methemoglobin and hemosiderin, they give a specific peripheral ring of hypointensity on MRI. Zebramski et al. [4] Classified CCMs into four types which helps in their differential diagnosis and management. On MRI, Type II lesions have mixed-signal intensity core on both T1 & T2 weighted images, with a hypointense rim on T2 weighted images giving classical cerebral cavernous malformations with ‘popcorn’ appearance. Type IV lesions appear as minute hypointense punctate foci on T2 images representing an early stage of cavernomas commonly seen in familial forms. Due to the high sensitivity of MRI T2 sequences, it is believed to be the method of choice in familial forms of diagnosis [11].

The Susceptibility Weighted MR images are believed to be the best imaging method, capable of detecting various types of CCMs [11,12]. An interesting feature of inherited lesions is that they have variable presentations on diagnosis and the lesions disappear over the course of time.

Patients with seizures are treated with antiepileptic drugs. Uncontrolled seizures and recurrent hemorrhages need surgical intervention. Poorly accessible deep lesions may be treated using stereotactic radiosurgery [13,14].

In our case study, fortunately after so much of suffering and symptomatology, the patient was treated with medication treatment. Even with such a large frontal cortex lesion, surgery was refused; the patient recovered completely and is living happily without any significant neurological deficit.

4. CONCLUSION

CCMs are classified into four types. Type IV cavernous malformations remain stable over time, however a few lesions may progress into Types I and II cavernous malformations. T2 weight GRE can detect most of the CCMs. Susceptibility Weight Images are a newer MRI technique that exploits the magnetic properties of the tissues, which has a great sensitivity to various venous structures, blood products and vascular malformations, giving its edge over T2-weighted images for evaluation of CCMs. Surgical extirpation of the most active cavernoma usually the largest lesion with signs of recent hemorrhage was safe and prevented further bleedings.
CONFLICT OF INTEREST

The authors declare no conflict of interest whatsoever arising out of the publication of this Manuscript.

ABBREVIATIONS

CCM = cerebral cavernous malformations

REFERENCES


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