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Original Research Article

Assessment of Neuropathological Spectrum of all the Surgically Resected Vascular Malformations of Central Nervous System: An Observational Study

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Abstract

Aim: The aim of the present study was to assess the neuropathological spectrum of all the surgically resected vascular malformations of central nervous system.

Material & Methods: The present study was conducted at department of General Surgery for one year and patients with neurological, neurosurgical, and psychiatric disorders were included. All VMs diagnosed in the department of neuropathology over a period of 1 year were retrieved from the archives. The study included a total of 100 cases of surgically resected VMs.

Results: Among 100 cases, CCMs were most common (44%), followed by AVMs (39%), capillary telangiectasia (11%), venous angioma (2%), and AVFs (4%). Clinical presentation varied from focal deficit to features of raised intracranial tension.

Conclusion: Imaging and histopathology plays an important role in the diagnosis and management of VMs. Histopathological examination is essential for characterization of the VMs, which influences the prognosis.

Keywords: Vascular Malformation, Histopathology, CNS

Introduction

Vascular malformations (VMs) are inborn errors of vascular development that result in abnormally formed vessels. They are classified into slow- and fast-flow malformations based on the absence or presence of an arterial component, respectively. They include venous, lymphatic, arterial, capillary and mixed malformations, alongside those associated with other anomalies. [1] While majority of VMs are present at birth, they can sometimes form de novo in post-natal development. Of those present at birth, 5% are caused by inherited loss-of-function (LOF) germline mutations with a somatic second hit, while the remaining 95% are sporadic in nature, meaning that they occur due to gain-of-function (GOF) mutations occurring after conception in clusters of non-gametal cells. [2]

Slow-flow malformations include venous malformations (VeMs), lymphatic malformations (LMs), and mixed vascular malformations, alongside overgrowth syndromes. These malformations are characterized by overactivation of phosphoinositide 3-kinase (PI3K) through mutations in the PI3K/AKT/mTOR signaling pathway. [3,4]

Vascular lesions of the brain and spinal cord are commonly encountered in clinical practice and can lead to diagnostic, prognostic and therapeutic challenges. [5] Central nervous system (CNS) vascular malformations encompass a wide range of arterial and venous anomalies with various presentations, clinical course, and complication rates. [6] Patients with CNS vascular lesions can present with a variety of presentations from headache and seizure to isolated cranial nerve deficits and progressive motor and sensory alterations.

This highlights the importance of high clinical suspicion and early detection to reduce future risk of complications. Due to increased utilization of imaging techniques of the cranio-spinal axis over the past decades, more vascular malformations are being detected. This necessitates an increased level of expertise with the diagnosis, characterization, and timely management of these lesions. [7] There are

several reports in literature that describe individual VMs with regard to its clinical features, treatment modalities, and radiological details. However, a comprehensive report of the pathological spectrum of the VMs of CNS is lacking.

Henc this study was conducted to present the neuropathological spectrum of all the surgically resected VMs of CNS

Material & Methods

The present study was conducted at department of General Surgery Netaji Subhas Medical College and Hospital, Bihta, Patna, Bihar, India and patients with neurological, neurosurgical, and psychiatric disorders were included. All VMs diagnosed in the department of neuropathology over a period of 1 year were retrieved from the archives. The study included a total of 100 cases of surgically resected VMs. Demographic details, clinical features, and follow-up, wherever available, were obtained from the medical records. Resected tissues were subjected to routine processing for paraffin embedding after fixation in 10% buffered formalin. Serial sections stained with hematoxylin and eosin (H&E), Masson trichrome for evaluating collagen, and Verhoeff's modification of elastic Van Gieson were reviewed in order to categorize the cases as AVMs, CCMs, venous angiomas, arteriovenous fistulas (AVFs), and capillary telangiectasia, in accordance with the McCormick classification.

Results

Table 1: Histological spectrum of VMs with frequency, age, and gender distribution

Histological type	Frequency (%)	Mean age (age range [in years])
CCM	44 (44%)	32.8 (2–65)
AVM	39 (39%)	28.2 (6–74)
Capillary telangiectasia	11 (11%)	42.4 (13–73)
AVF	4 (4%)	52.8 (35–66)
Venous angioma	2 (2%)	43.27 (25–60)
Total	100	34 (2–74)

Among 100 cases, CCMs were most common (44%), followed by AVMs (39%), capillary telangiectasia (11%), venous angioma (2%), and AVFs (4%).

Table 2: Clinical features of VMs

Type	Location	Presenting symptoms	Type of presentation
CCM	Lobar =22 Brainstem =5 Cerebellar =3 Ventricular=3 Cavernous sinus =4 Spinal =7	Focal deficits=18 Raised ICP=10 Combined symptoms =8 Chronic seizure=8 Unknown=1	Acute=2 Subacute=22 Chronic =17 Unknown =1
AVM	Lobar =30 Cerebellar =6 Ventricular =3 Spinal=5	Raised ICP =22 Combined symptoms =8 Chronic seizure5 Focal deficits =5	Acute =4 Subacute=10 Chronic=6
Capillary telangiectasia	Intracranial=1 Spinal =9	Focal deficits=9 Combined symptoms=1	Acute=1 Subacute7 Chronic=2
AVF	Lobar dural= 1 Spinal=4	Raised ICP=1 (10%) Focal deficit=4	Subacute=2 Chronic=3
Venous angioma	Dural=1 Cavernous sinus=1	Focal deficits=2	Acute=1 Subacute=2 Chronic=1

Clinical presentation varied from focal deficit to features of raised intracranial tension.

Discussion

The key pathology underlying vascular malformations is impairment in integrity of capillary, venous, and arterial beds. This loss of integrity can be due to external causes such as mechanical injuries and/or defects in vascular development during angiogenesis, vessel growth, and maturation. [8] Various factors such as vascular endothelial growth factors, fibroblast growth factors, platelet-derived growth factors, and angiopoietins act in concert to regulate angiogenesis. Alterations in the complex interactions between these factors can lead to the

development, progression, and regression of vascular malformations. [9] In the last decades, the genetic basis of several CNS vascular malformations has been further explained. Certain vascular malformations classically present in an autosomal dominant fashion such as familial cases of cavernous malformation, hereditary hemorrhagic telangiectasia, and capillary malformation–arteriovenous malformation as detailed later in this article. However, the vast majority of vascular malformation occurs sporadically. Several genetic variants have been identified that can render individuals susceptible to vascular malformation formation and complications. [10]

Among 100 cases, CCMs were most common (44%), followed by AVMs (39%), capillary telangiectasia (11%), venous angioma (2%), and AVFs (4%). Clinical presentation varied from focal deficit to features of raised intracranial tension. CNS vascular system develops as a result of controlled interplay between mesodermal vascular cells and derivatives of neuroectoderm. Any disturbance in this regulated development causes malformations, which may involve arteries, capillaries, or the venous channels. [3] Majority of these lesions are congenital in origin and hence resemble early embryonic vasculature. In 1966, McCormick classified CNS VMs into four subtypes: AVMs, cavernous malformations, capillary telangiectasia, and venous malformations. Later, it was recognized that a proportion of these lesions show a combination of the subtypes with advancements in imaging techniques. VMs can be sporadic or familial and can also be associated with syndromes such as Osler–Weber–Rendu or hereditary hemorrhagic telangiectasia. Genetic alterations are being increasingly recognized in familial and syndromic associations of VM, which resulted in emergence of more detailed classification. [4] The International Society for the Study of Vascular Anomalies (ISSVA) classification recently adopted a classification scheme that separates "vascular tumours" secondary to active proliferation from "vascular malformations," due to developmental defects in vascular morphogenesis which differ in clinical profile, diagnostic, and therapeutic strategies. [11] Large series documenting the complete histological spectrum of VMs with clinicopathological details are scarce in literature. Most studies describe individual types of VMs in the context of seizure causation, neuroimaging, and treatment modalities. In this study, we documented the clinicopathological spectrum of surgically resected VMs over the last 10 years at our institute, a referral center that caters exclusively to patients with neurological and psychiatric disorders. We found only one other study that documented spectrum of 50 cases of VMs. [12]

Patients may present with seizure, focal neurologic deficits, or acute intracranial hemorrhage, depending on the site of involvement. Many small, cavernous malformations that present with large intracerebral hematomas may be excised at the time of hematoma resection. O Del Curling et al have noted seizures in 42% and focal deficits in 25%. [13] In our study, the focal deficits were seen most, followed by raised ICP and chronic seizures. Capillary telangiectasia was the most frequent VMs in the spinal region. They are most often congenital and maybe found in association with other VMs. There is invariably an incidental finding involving the pons. Most of the other studies have described the mean age of presentation as 5th decade with no obvious sex predilection. [14,15]

Conclusion

Vascular malformations of CNS are a diverse group of lesions, the clinical effects of which depend on its location, type (high flow vs. low flow) and associated hemorrhage. The reported spectrum of VMs documented in this study did not reflect population incidence, but the hospital-based incidence of malformations that were subjected to surgical excision. Several VMs maybe asymptomatic or incidental and others may be treated with noninvasive means with major advances in interventional radiology. Imaging and histopathology is critical for diagnosis, categorization, and management, which have an impact on patient prognosis.

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