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Review Article:

Arachnoid Granulations: An Overview

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Abstract

Arachnoid granulations are cerebrospinal fluid (CSF)-filled protrusions with meningothelial lining extending through a dural opening into the venous sinuses. These structures filter and drain the CSF into central venous circulation across a lining of arachnoid cells. Detection of defects in these regular fillings within intracranial dural sinuses decreases the erroneous diagnosis of the existence of an intrasinus pathological process. It is essential for clinicians as well as forensic pathologists to be aware of unusual intracranially morphologies existing, especially intrasinus arachnoid granulations, as it is significant for clinical diagnosis, accurate treatment, and even in the postmortem examination in determining the cause of death. This article aims to provide an overview of arachnoid granulations in the medical literature.

INTRODUCTION

Antonio Pacchioni initially described arachnoid granulations (AGs) more than 300 years ago [1]. Arachnoid granulations are outpouchings of the arachnoid meningeal membrane extending into the dural sinuses or calvarium, surrounded by dense connective tissue capsule, that allow the cerebrospinal fluid (CSF) absorption into the venous system from the space between Arachnoid and Piamater, i.e., subarachnoid space. Within dural sinuses, these appear as well-defined focal localized nodular, oblong, or rounded structures [2,3]. Arachnoid villi are microscopically visible, whereas arachnoid granulations representing distended villi are visible to the naked eye [4]. Its function is to drain CSF to the lower-pressured venous system. AGs grow in numbers and size with age in response to increased CSF pressure from the subarachnoid space. They usually measure a few

millimeters but may enlarge to penetrate the inner table of the skull, most commonly adjacent to the midline of the posterior frontal or anterior parietal area [5].

Literature Review

Age: In a study by Yew M et al., all subjects were older than 30 years, with 50% of subjects aged 55 years or older. The prevalence of AGs expanding into the temporal bone was twenty-eight percent among the subjects aged 50 years or above [6]. Autopsy-based studies on giant arachnoid granulations (GAGs), generally occurring as a rare incidental finding, are common in adults, especially in elders over 65 years of age [7]. GAGs in a 6-year-old girl child with benign intracranial hypertension are also reported [8].

Size: The average size of the AGs was 8.1 x 9.4 x 10.0 mm (ranging from 4 –19 mm) in a study pertaining to the dorsal superior sagittal sinus [9]. In the elderly, it can reach a remarkable size (up to 25 mm and more in diameter) [7].

Locations: AGs are primarily located beneath the superior sagittal sinus (SSS) and the venous lacunae in the parasagittal region and communicate with the SSS [2, 10]. In decreasing order of frequency, it is thought to be present maximum in the transverse sinus, then the cavernous sinus, the superior petrosal sinus, and least in the straight sinus [11]. Occasionally, they are also seen at the posterior portion of the temporal bone wall [12]. In a study by Yew M et al., AGs demonstrated a greater tendency to occur at the middle cranial fossa compared to the temporal bone's posterior cranial fossa surfaces. AGs were often found to enter the temporal bone at the tegmen mastoideum and tegmen tympani. Additionally, they were observed within the posterior view of the petrous pyramid, the internal auditory canal, and the cochlear aqueduct's inferior aperture at the jugular foramen's superior extent [6].

Diagnosis: The diagnostic proof of AG was the radiological appearance on multiple modalities with an unchanged appearance over the long term. A non-contrast computed tomography (CT) of the head executed to rule out intracranial hemorrhage disclosed a tubular and elongated lesion within the posterior SSS. Magnetic resonance imaging (MR) revealed the lesion resembling CSF appearance, i.e., hyperintense on T2-weighted MRI and hypointense without any appreciable enhancement on T1-weighted MRI. MRI also

demonstrated a T2-hypointense flow void above the lesion and vascular bundle entry into the neck of the lesion's superior end. In T2-weighted Fluid-attenuated inversion recovery (FLAIR) imaging, the lesion demonstrated suppression of signal similar to CSF [2]. AGs are generally hypointense but occasionally mild hyperintense compared with CSF without gadolinium enhancement [13]. A cerebral digital subtraction angiography disclosed bilateral non-flow signal focal areas protruding into both sinus's lumen at the transverse sinus-sigmoid sinus junction compatible with GAGs and left transverse sinus hypoplasia [14]. On high-resolution computed tomography (HRCT) of the temporal bone, AGs appeared as erosions in the wall of the posterior temporal bone, without any mass, often presented as a lobulated surface, and with an attenuation varying from CSF and brain tissue [12]. On high-resolution T2- T2-weighted images, a linear hypointense constituent of the internal fibrous structure of the AG can be visualized [10]. AGs in the cerebral dural sinuses can also be revealed in contrast-enhanced 3D MR venography.

In many cases, AG identification is facilitated by their characteristic appearances, i.e., oval or rounded-shaped, well-defined outlines with homogenous intensity. The cortical vein adjacent to it is considered a supplementary supportive element [15]. MRI evaluation of cerebral AGs in venous sinus using 3D T2 CUBE and 3D contrast-enhanced BRAVO sequence can also be demonstrated. MRI showed these entities as largely hypointense with CSF in T1, hyperintense with CSF in T2 sequences, isointense on FLAIR, hypointense on DWI, and seen as filling defects on BRAVO. Septations as linear variations of signal intensity were seen within the granulations. Altered MR signal intensity was noted occasionally when calcifications existed. The AGs disclose as filling defects at MR angiography (MRA). They appear elliptical on oblique MRA images [16].

Microscopy: Transmission electron microscopy analysis showed that the structure of AG has a reticular conglomerate with endothelial cells that resemble lymphatic linings. Immunohistochemistry and immunoelectron microscopy revealed the expression of molecules specific to lymphatic endothelial cells [17]. Scanning electron microscopy demonstrated the tridimensional architecture of the collagen element in the AGs. It revealed a pedicle, body, and apex,

surrounded by a capsule of connective tissue composed of collagen fiber bundles that line pores of different sizes and shapes. Tiny bundles line the smaller pores at the apical region of AG, and thicker bundles line the larger pores at the lateral regions. In the body, the bundles of collagen fibers compose a fibrous meshwork, and in some areas, these bundles have a circular orientation, forming pores similar to those found at the region of the capsule [18].

Histology: AGs observed in a study by Yew M et al. revealed the following histologic features: 1) consistent with typical arachnoid cells i.e. nests of small nucleated cells that are organized loosely or densely in a webby pattern with prominent extracellular channels: 2) an outer fibrous layer of AG lining the bony defect; 3) dura mater dehiscence placing the AG in direct contact with the bone; and 4) bone erosion to varying depths. Cells that line the AGs were often noticed clustered at the tips of AGs and were accompanied by concentric calcifications or psammoma. Cortical erosion was found in all cases, with about 50% of AGs penetrating air-filled spaces or marrow. Brain tissue accompanied AGs and was observed extending through the defects in the dura mater and into the bony defects [7].

Proteins: Arachnoidal cells on confluent cultures expressed Cytokeratin intermediate filaments and the intermediate filament protein vimentin. These cells also express a few cytoskeletal proteins and junctional proteins like connexin43 involved in the formation of gap junctions, desmosomes desmoplakin 1 and 2 (a structural protein that links the desmosome to intermediate filaments), epithelial-specific adherens junctions like E-cadherin, as well as tight junctions like zonula occludens 1. In particular, these junctional proteins may be essential for allowing the arachnoidal cells to regulate CSF outflow [19].

Complications: AGs and the lymphatic system have a role in the pathophysiology of idiopathic intracranial hypertension (IIH) by restricting the absorption of CSF from the venous system and or congestion and overflow of the glymphatic system [20, 21]. Presentation of symptoms of progressive bifrontal headaches with a GAG at posterior SSS is also noted [22]. An MRI study also observed AGs bulging into the sigmoid sinus, transverse sinus, straight sinus, and confluence sinuum [23].

Controversial entity: Brain herniation into arachnoid granulations (BHAGs) comprises a brain tissue herniation into a presumed preexisting AG in the calvarium, dural venous sinuses, and meningeal or diploic veins. Some BHAGs can possibly cause headaches, epilepsy, or increased intracranial pressure conditions like IIH or pseudotumor cerebri (PTC) [24]. A study conducted by 68 BHAG was observed, with increasing order of frequency, in occipital squama, transverse sinus, lateral lacuna of the SSS, and straight sinus, and the most frequent involvement of the cerebellar tissue in BHAG. Parenchymal signal and structural changes were demonstrated in 46% of BHAG, of which 100 % were cerebellar [25].

Protective Effect: AGs may have a protective effect against the development of shunt-dependent chronic hydrocephalus following aneurysmal subarachnoid hemorrhage [26].

Differential Diagnosis: It may be misdiagnosed for venous sinus thrombosis with risks of unnecessary anticoagulation, intravascular thrombolysis or thrombectomy, or invasive intracranial pressure monitoring [2]. Due to the elliptical shape of oblique MRA images, they could be mistaken for Thrombus [16]. On HRCT, differentiation should be initially made from papillary endolymphatic sac tumor. The characteristic CT appearance is an aggressive soft-tissue tumor mass eroding the surface of the posterior temporal bone at the endolymphatic sac location and containing bone spicules with a peripheral rim of calcifications [27, 28]. T1- and T2-weighted images are characterized by heterogeneous signal intensities with typically focal high T1 signal intensities due to hemorrhagic and proteinaceous components [27]. Broad differential diagnosis of giant AGs in the dural venous sinuses other than dural venous sinus thrombosis also include metastases, meningiomas, arachnoid cysts, calvarial osseous lesions, dermoids, epidermoids, and extra-axial hemangiomas, including the papillary endothelial hyperplasia [29, 30]. These lesions demonstrate a more aggressive appearance locally than AGs. Further, chondromatous tumors are situated more anteriorly in the temporal bone at the petro-occipital synchondrosis and chordoma at the petrous apex or in paraganglioma, more posteriorly at the jugular foramen [31]. Occasionally, AGs even penetrate the diploic space and eventually

expand into the outer table, mimicking osteolytic lesions [5].

Conclusion: Medical professional, as well as forensic pathologists, needs to be aware of unusual intracranial morphologies existing, particularly intrasinus arachnoid granulations, as it is significant for clinical diagnosis, accurate treatment, and even in the postmortem examination in determining the cause of death. It is essential to be aware of the variability in the presentation of AGs to correctly identify them and distinguish them from other dural sinus pathology. Further, the radiologist, neurosurgeon, and autopsy surgeon should know its existence because they can be incidentally noted. This distinction of arachnoid granulations can be brought up by meticulously considering its CT and MR imaging characteristics and other required diagnostic procedures.

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Declaration of competing interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this paper.

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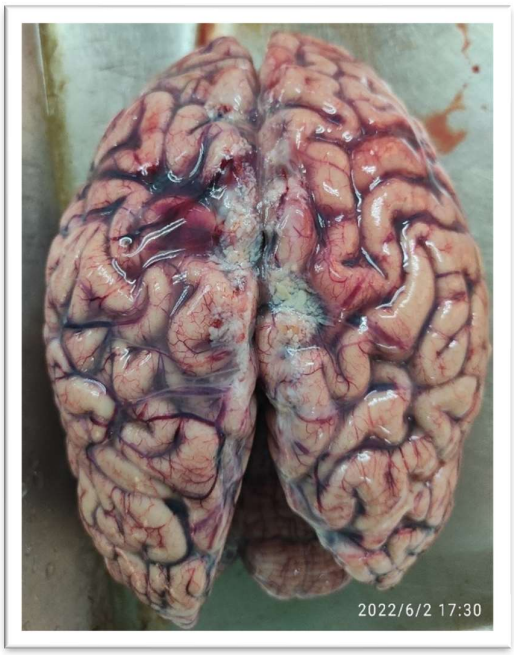
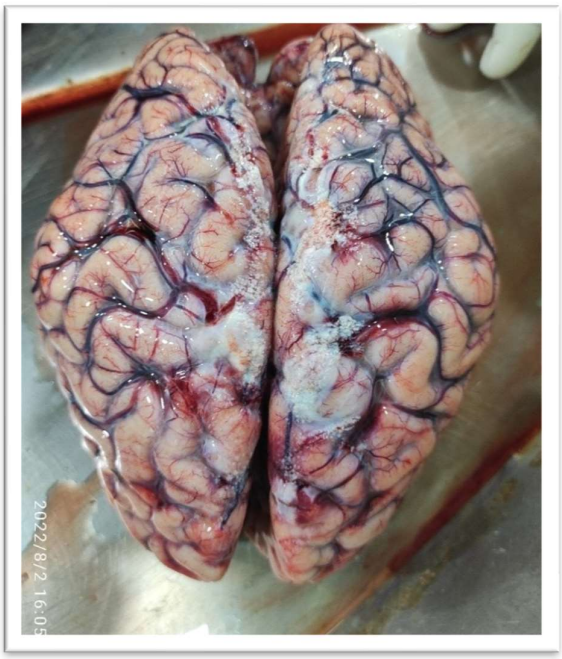


Picture A: Showing Gross image of Brain with Arachnoid Granulations in a case of sudden death of 50-year-old male



Picture B: Showing Gross image of Brain with adherent Arachnoid Granulations in a case of electrocution of 30 year old male