Case report

Arteriovenous malformation within the velum interpositum

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We present a case involving a 70-year-old Latina woman who experienced a sudden onset of lightheadedness, diplopia, vertigo, and loss of balance. Imaging studies revealed a right thalamic intracerebral haemorrhage that obstructed the velum interpositum. Following unsuccessful embolisation, the thalamic region was surgically resected. Histopathological and immunohistochemical analyses of the resected brain tissue demonstrated abnormal blood vessels permeating through excessively cellular brain parenchyma, raising significant concern for a glial neoplasm. This case also illustrates a rare occurrence of an arteriovenous malformation within the velum interpositum, which, when acutely filled with blood, can expand the cavum and clinically present as a sudden onset of headache and vertigo.

Key words: arteriovenous malformation, pineal gland, oligodendroglioma, brain tumours.

Introduction

The velum interpositum is a triangular membranous structure formed by the invagination of the pia mater and is filled with cerebrospinal fluid. The apex of this triangle is oriented rostrally and is bound superiorly by the fornix and the hippocampal commissure; posteriorly, it is bordered by the splenium of the corpus callosum, and laterally, it extends into the bilateral thalami. It is positioned anterior and superior to the pineal gland and can expand to form a potential space known as the cavum velum interpositum. This cavum is typically present during foetal development but eventually obliterates in adulthood [1].

The pineal gland is an endocrine gland situated in the midline of the brain. Anatomically, it is located within the pineal recess, posterior to the third ventricle, superior to the tectum of the midbrain, inferior to the vein of Galen, and posterior to the splenium of the corpus callosum and the velum interpositum. The gland plays a crucial role in regulating circadian rhythms by secreting melatonin and modulating diurnal light signals received from the retina [2].

The most common pathologies of the velum interpositum include persistent cavum of the interpositum, arachnoid cysts, pineal cysts, and neoplasms. As space-occupying lesions, they often present with signs and symptoms of increased intracranial pressure. The persistent cavum typically manifests with psychosis, developmental delays, seizures, and hydrocephalus [3]. Due to its non-neoplastic nature, the cavum rarely requires surgical intervention. While conservative measures are sufficient for managing the cavum, neoplasms of the velum interpositum necessitate prompt surgical intervention. The most common neoplasms in this region include pineal germinoma, pineocytomas, pineoblastoma, pineal parenchymal tumours of

intermediate differentiation, choriocarcinoma, and both mature and immature teratomas [4]. Vascular lesions, such as arteriovenous malformations, aneurysms, cavernous malformations, and malformations of the vein of Galen, are rare [5–7] in proximity to the velum. When they do occur, these lesions can lead to bleeding and necrosis within the pineal gland parenchyma, resulting in pineal apoplexy. The clinical manifestations of apoplexy can go unnoticed or may present with severe vertigo, headache, nausea, and even memory loss or death. The most common causes of pineal apoplexy are pineal cysts [8, 9], with pineal tumours being less common [10]. Accurate histopathological differentiation between these two entities is crucial because it directs different treatment modalities. Herein, we present an uncommon case of a bleeding arteriovenous malformation within the velum interpositum that clinically presents as a haemorrhagic stroke, while histologically resembling a pineal tumour.

Case report

A 70-year-old Latina American female presented with a sudden onset of lightheadedness, diplopia, vertigo, and loss of balance, which were followed by falls. A non-contrast MRI of the brain revealed microvascular changes with haemorrhage within the right thalamus (Fig. 1A). An MRA of the brain demonstrated an incomplete circle of Willis without evidence of aneurysm or stenosis. Quantitative flow values indicated increased blood flow for her age (198 ml/min; reference value: 77–181 ml/min) in the posterior cerebral circulation and the right-sided dural sinuses. These changes were consistent with a Spetzler-Martin grade 3 velum interpositum arteriovenous malformation (AVM) (Fig. 1B). Following an attempted embolisation, her recovery was complicated by persistent diplopia and imbalance. A subsequent embolisation and total AVM resection were performed, resulting in significant improvement in her neurological condition.

Microscopically, the resected specimen exhibited numerous prominent blood vessels of variable thickness within the brain tissue, accompanied by areas of increased cellularity (Fig. 2). While regions of moderate cellularity (Fig. 2A) were consistent with gliotic brain tissue, areas with higher cellularity (Fig. 2B, C) contained foci of dystrophic calcification and were predominantly composed of cells with round nuclei, inconspicuous nucleoli, and focally prominent perinuclear clear halos (Fig. 2B, C). These findings prompted a differential diagnostic consideration of an oligodendroglioma-like neoplasm or architecturally distorted normal pineal gland tissue. Numerous prominent blood vessels were present, including histologically normal arteries and veins interspersed with some focally atypical vasculature. The atypical features were characterised by duplication (Fig. 3A – red arrows) or absence (Fig. 3A – blue arrows) of the internal elastic lamina (Fig. 3A). These findings were consistent with an arteriovenous malformation (AVM). Some blood vessels exhibited evidence of previous surgical em-

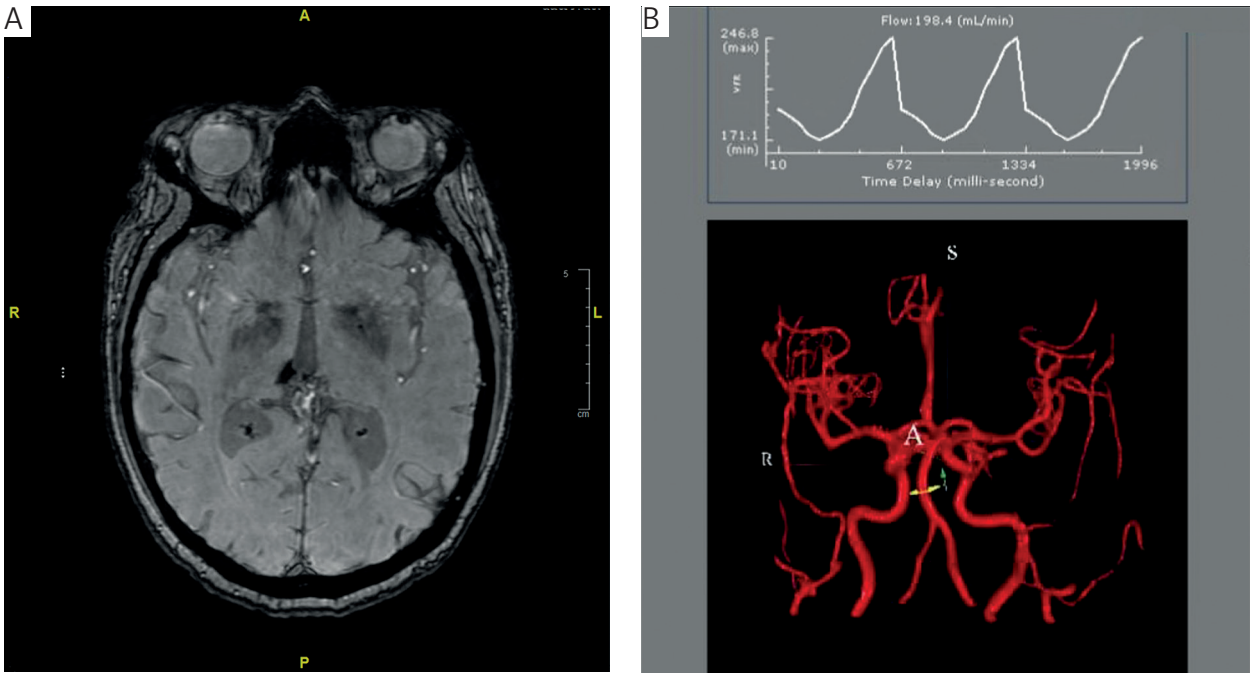

Fig. 1. A) MRI image of the brain shows right thalamic ischaemia due to AVM in the velum interpositum region. **B)** Quantitative studies showed increased blood flow in the basilar circulation

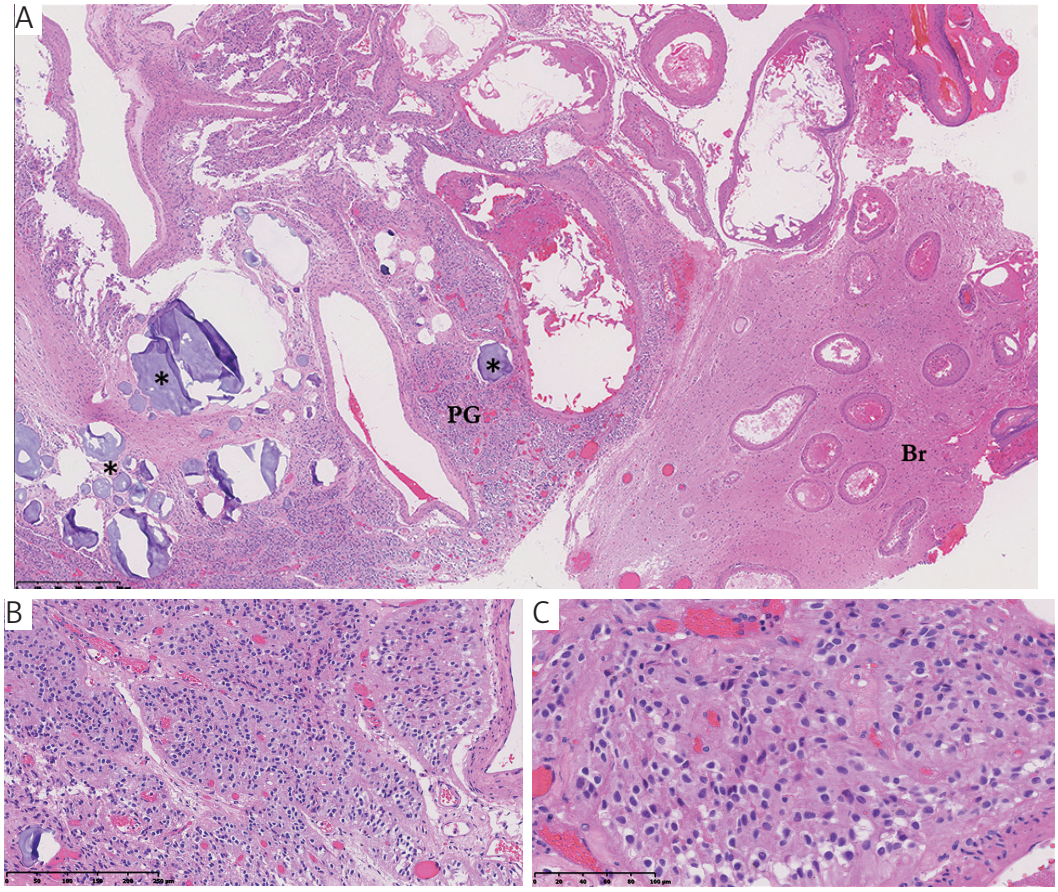

Fig. 2. A) The HE image of the resected pineal specimen (10×). Numerous prominent blood vessels of variable thickness penetrate brain tissue of high cellularity (marked PG) and moderate cellularity (marked Br). Areas of dystrophic calcification are noted (*). **B)** (20×) and **C)** (40×). Higher magnifications of area with higher cellularity (PG) populated by cells with round nuclei, inconspicuous nucleoli, and focally prominent perinuclear white halos

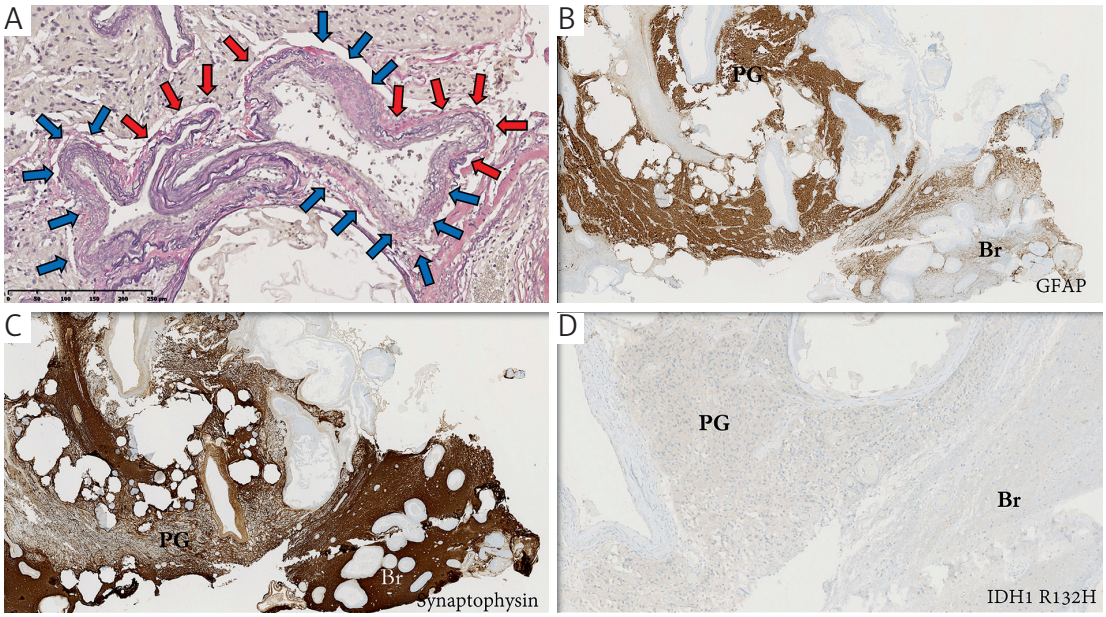

Fig. 3. A) Lesional blood vessels with focally prominent and duplicated (red arrows) or absent (blue arrows) internal elastic lamina (elastic stain). **B)** Synaptophysin immunostain highlights pineal gland tissue (PG) and to a lesser extend adjacent brain parenchyma (Br). **C)** GFAP immunostain highlights brain tissue and focally pineal gland. **D)** Pineal gland and brain tissue are both negative for IDH1 R132H protein expression by immunohistochemistry

bolisation. Areas of high cellularity showed no signs of increased mitotic activity or rosette formations. The cells in these regions expressed synaptophysin (Fig. 3B) and, focally, glial fibrillary acidic protein (GFAP; Fig. 3C), while lacking expression of IDH1 R132H, p53, or Ki67 proteins (Fig. 3D). Collectively, these findings are indicative of an AVM involving the pineal gland and adjacent brain tissues, and do not support the diagnosis of an oligodendroglial neoplasm with prominent vascularity.

Discussion

Arteriovenous malformations (AVMs) of the brain are developmental anomalies of the cerebral blood vessels that result in the premature shunting of arterial blood into the venous system, subsequently preventing normal oxygenation of brain tissue [11]. Although AVMs are often clinically silent, they can present with symptoms such as cerebral bleeding, seizures, focal neurological deficits, and headaches [12]. The most serious complication of a brain AVM is rupture, which can lead to life-threatening cerebral haemorrhage and a rapid increase in intracranial pressure. It is estimated that the prevalence of AVMs among healthy young individuals is approximately 1–2% [13].

Vascular anomalies of the pineal region are rare and include aneurysms of the pineal gland region, AVMs, vein of Galen aneurysms, and cavernous malformations [14]. Aneurysms of the pineal gland region can originate from either the superior cerebellar artery or the posterior cerebral artery, constituting approximately 3% of all intracranial aneurysms [14]. Clinically, pineal region AVMs can present in various ways, depending on whether they have ruptured. Unruptured pineal AVMs may manifest as visual impairment, acalculia, dyslexia, or even metabolic disorders. In contrast, ruptured pineal AVMs are associated with intraventricular haemorrhage and can lead to the rapid development of acute hydrocephalus due to increased intracranial pressure [15–17].

Our case reveals numerous vascular channels of varying thickness embedded within a monotonous population of cells characterised by uniform, rounded nuclei, an increased nuclear-cytoplasmic ratio, and perivascular clearing. This uniform cell population raised the possibility of an underlying astrocytic process. However, no mitotic activity was observed in the haematoxylin-eosin staining, which would suggest a high cell turnover. This possibility was further excluded by GFAP and synaptophysin staining, which highlighted reactive astrocytes in the vicinity of the abnormal vasculature, as well as the absence of mutant IDH R132H staining (Fig. 3). Among all intracranial neoplasms, lesions in the pineal gland region are found in only up to 1% of cases [18]. Most of these tumours are pineal parenchymal tumours (up to 42%) and other neoplasms like meningioma, choroid plexus papilloma, and craniopharyngioma. Most of these tumours are pineal parenchymal tumours (up to 42%), along with other neoplasms such as meningioma, choroid plexus papilloma, and craniopharyngioma [19]. Only a few cases of pineal gland oligodendrogliomas have been reported, and most of them were high-grade. Low-grade oligodendrogliomas are exceedingly rare entities [20].

The aetiology of brain AVMs remains unclear, as more than 95% of AVMs do not exhibit any genetic alterations. The most common genetic association with AVMs is hereditary haemorrhagic telangiectasia, which involves mutations in the transforming growth factor β (*TGF-β*) family of receptor genes, specifically the activin receptor-like kinase 1 gene (*ALK1* or *ACVLR1*) and the endoglin (*ENG*) gene [21, 22]. In studies conducted by Hong *et al*. [23], brain AVMs demonstrated an 81% prevalence of *KRAS*/*BRAF* somatic gene mutations. The patient samples revealed activating mutations in *BRAF* and *KRAS* (p.G12A and p.S65_A66insDS). To date, no genetic alterations have been reported in pineal gland AVMs.

The treatment of brain AVMs includes microsurgery, endovascular procedures, radiosurgery, embolisation, and conservative management [5]. Clinical decision-making is based on the size, location, and vascular anatomy of the AVMs. While asymptomatic or minimally symptomatic patients are typically monitored, those who experience significant or recurrent haemorrhages require more active intervention. Microsurgical resection of pineal AVMs results in the complete removal of the lesion and carries a minimal risk of future haemorrhages [5]. The Spetzler-Martin classification and subsequent classifications of AVMs serve as valuable evaluation tools for assessing the risk of postoperative functional outcomes in these patients [24, 25].

Disclosures

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4. Conflicts of interest: None.

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