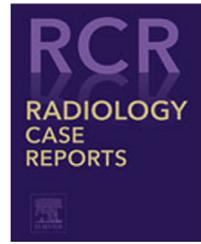


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Case report

The controversial entity of brain herniations into arachnoid granulations: A report of three cases with literature review ☆,☆☆

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ABSTRACT

Brain herniation into arachnoid granulation (BHAG) is a quite recently described controversial entity in terms of both etiology and clinical significance. It comprises a herniation of brain tissue into a presumed preexisting arachnoid granulation in dural venous sinuses, calvarium, meningeal or diploic veins. Most often described as an incidental finding in patients examined for unrelated pathologies, some BHAGs can possibly be related to headache, epilepsy or conditions with increased intracranial pressure such as idiopathic intracranial hypertension (IIH) or pseudotumor cerebri (PTC). The number of reported cases is low and there are only three more recently published observational studies on this subject with results lacking statistical significance due to relatively few BHAGs analyzed. Therefore, BHAGs still need an increased focus from both the radiologists and clinicians and more published studies and cases are necessary to help in understanding their factual meaning, clinical and treatment implications. In this article we describe three new cases of BHAGs to the literature, with patients presenting with different symptoms.

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Introduction

Brain herniations into arachnoid granulations (BHAGs) are rare findings of undetermined etiology and significance. The reported prevalence of BHAGs is 0.32% based on the work of Battal et al. where magnetic resonance imaging (MRI) scans of 6160 patients containing at least one high-resolution T1 or T2 sequence were examined retrospectively [1]. Children as

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young as 5 years old were included in studies on the subject [2], but the mean age was between 37.5 and 63 with women constituting between 66% and 69% of the patients [1–3]. The most common location of BHAGs was occipital squama (67% of all BHAGs described by Liebo et al. and 63% of all BHAGs in Malekzadehlashkariani et al.) and transverse sinus (62% of BHAGs, Battal and Hamcan et al.) [1–3]. The origins of herniated parenchyma described in the literature include cerebellar hemispheres, occipital lobes, inferior temporal gyrus, occipitotemporal gyrus, parietal cortex and superior frontal gyrus [3,4]. High-resolution volumetric T1 and T2-weighted MRI with maximum slice thickness of 1.5 mm, with or without contrast administration are necessary for full evaluation of BHAGs as standard, thick-sliced MRI sequences or computed tomography (CT) may be insufficient for assessment of their presence and continuity with brain parenchyma and cerebrospinal fluid (CSF) compartments [1]. In this article we describe three cases of BHAGs with different presentation followed by literature review.

Case 1

A 55-year-old man was referred for neurological evaluation due to a changed pattern in his chronic headache during the previous month. The patient was known with a twenty-year history of migraine and arterial hypertension diagnosed the year before. Until the actual presentation, the patient typically had a weekly migraine episode that could be controlled with sumatriptan intake. However, the headache pattern changed to a daily persistent unprovoked headache with sudden periodical exacerbations. The sumatriptan partly alleviated the pain, but the throbbing headache still persisted, a symptom which was never experienced before. The headache was additionally accompanied by visual disturbances in the form of shadowing and light flashes (photopsias) that presented frequently and spontaneously in the upper part of the left visual field. A regular short-termed loss of vision (obscurations) was not experienced, neither was double vision or pulsating tinnitus. The patient also denied generalized or partial seizures or changed level of consciousness.

Clinical examination showed a slightly overweight patient (body mass index, BMI 27) with blood pressure (BP) values between 173/106 mmHg and 165/117 mmHg. The rest of the physical and neurological examination was unremarkable.

A MRI scanning was ordered which showed a herniation of posterior aspect of the left inferior temporal gyrus into arachnoid granulation in the distal left transverse sinus close to the inflow of the vein of Labbé (Figs. 1 A–C). The herniated brain parenchyma was slightly atrophic, with gliosis at the edges, without signs of edema. The herniated sac was non-occluding to the sinus and flow could be seen in the involved sinus. No signs of intracranial hypertension were noted on imaging. The rest of the study was unremarkable. Retrospectively the finding could be visualized on a non-contrast CT from 10 years earlier (Figs. 1 D).

After three weeks with maximally optimized antihypertensive therapy, the patient's BP was normalized, but his headache remained unchanged. Neurological examination was still normal and additional ophthalmic examination showed no papillary stasis and a normal optical coherence to-

mography (OCT) scanning. A supplementary lumbar puncture was ordered and showed slightly increased opening CSF pressure measuring 215 mm H₂O (normal values < 200 mm H₂O; abnormal >250 mm H₂O and equivocal: 200 to 250 mm H₂O [5]), otherwise normal cell counts, glucose and protein levels. The patient was discharged from the hospital and a follow-up in an outpatient clinic was ordered. At evaluation two months after discharge the headache was completely resolved and it was concluded that the headache resulted from insufficiently treated hypertension, and that BHAG was an incidental finding unrelated to the headache.

Case 2

A 21-year-old man was examined due to complaints of a pressure-like discomfort from the left ear during the past 6 months as well as nasal congestion during the past few years, normal hearing was preserved. He had used a xylomethazolin-based nasal spray without effects on the symptoms. There was no discharge from the nose or ears. Physical examination including otomicroscopy and tympanometry was unremarkable. Fiberoscopy revealed adenoid vegetations and was otherwise normal. Audiometry showed asymmetrical hearing loss on the left side, especially pronounced in the low sound frequencies. Weber and Rinne tests were normal. An MRI of the internal auditory canals (IACs) was ordered to rule out cerebellopontine (CP) angle tumor. The scan showed no pathology in the CP angles or IACs, but an arachnoid granulation in the distal left transverse sinus containing a herniation from the posterior part of the left inferior temporal gyrus measuring around 9 × 11 mm without signal abnormality or pathological contrast enhancement in the herniated brain and without evidence of sinus thrombosis (Figs. 2 A–E). A small amount of fluid in the left mastoid air cells and adenoid vegetations in the nasopharynx were noted. The patient's adenoid vegetations were subsequently removed surgically and the BHAG was considered as an incidental finding unrelated to the clinical presentation.

Case 3

A 25-year-old woman, known with paranoid schizophrenia (diagnosed in 2015, treated with Brexpiprazole and Quetiapine), was referred for neurological and cardiological evaluation due to episodes with loss of consciousness. Her medical history included three episodes with loss of consciousness during a period of seven to eight years. Two of the three episodes happened when she encountered new surroundings and felt nervous. She could only remember the details of the latest episode and described prodromes of sweating, accelerated respiration and feeling lethargic before fainting. Duration of unconsciousness lasted only seconds. She had a short re-orientation phase and no cramps, head turning, urine output or tongue bite was observed. When asked directly if she experienced absences during childhood, the patient described episodes of disorientation lasting a few seconds and occurring up to several times daily. This happened for as long as she can remember and was still present. Others observed her staring ahead but reacting when talked to without any automatisms.

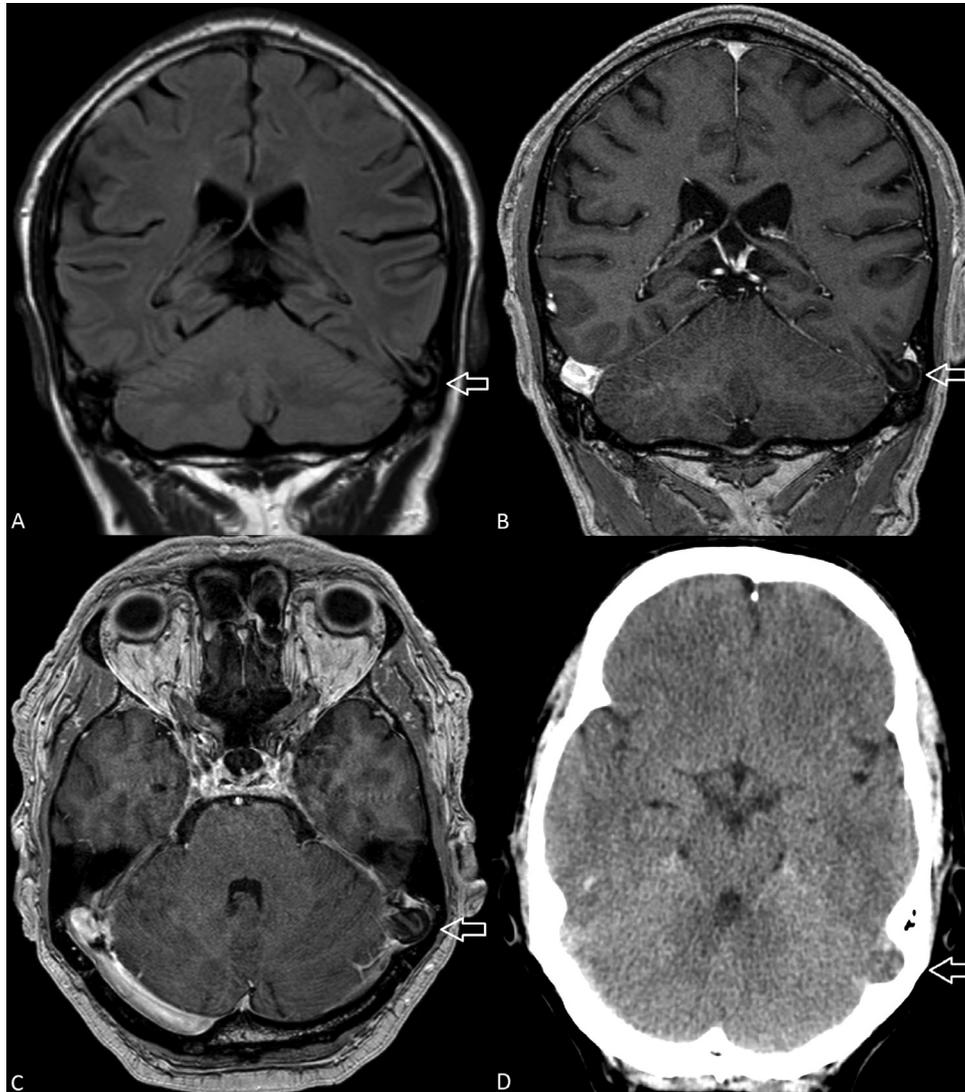


Fig. 1 – Imaging of patient described in Case 1. Coronal fluid-attenuated inversion recovery (FLAIR) MR (A) and gadolinium contrast-enhanced T1-weighted coronal (B) and axial (C) MR sequence showing a BHAG in the left transverse sinus with herniated brain tissue originating from the left inferior temporal gyrus (arrows). The herniated brain parenchyma appears atrophic, with a slight gliosis at the borders and without pathologic contrast enhancement. D: Axial non-contrast CT showing the same BHAG containing herniated brain isodense to the nonherniated brain parenchyma (arrow).

Physical and neurological examination was normal besides overweight (BMI 33). Cardiological evaluation included blood tests, electrocardiogram, 24 hours of Holter monitoring and orthostatic blood pressure measurement. Results were all unremarkable and no further cardiological assessment was needed.

Due to the non-specific episodes of disorientation since childhood the patient was referred to an MRI and electroencephalography (EEG). MRI showed a nonspecific punctate hyperintensity in the right frontal subcortical white matter. Additionally a herniation of the posterior aspect of the left inferior temporal gyrus into an arachnoid granulation located distally in the left transverse sinus was seen (Figs. 3 A-B). The

herniated brain tissue showed no signal abnormalities. There was no evidence of sinus thrombosis. Rest of the scan revealed no abnormal findings.

EEG performed afterwards was normal with no focal or epileptic activity. Since the standard EEG was normal, the patient was furthermore offered a longtime EEG with video recording to evaluate whether any EEG-correlate could be detected during the episodes of disorientation. The patient was, however, not interested since she herself did not find the episodes pathological, but simply due to being unfocused enhanced by her psychiatric disorder.

Based on the medical history, neurological and physical examination, MRI and EEG, there was only little suspicion of

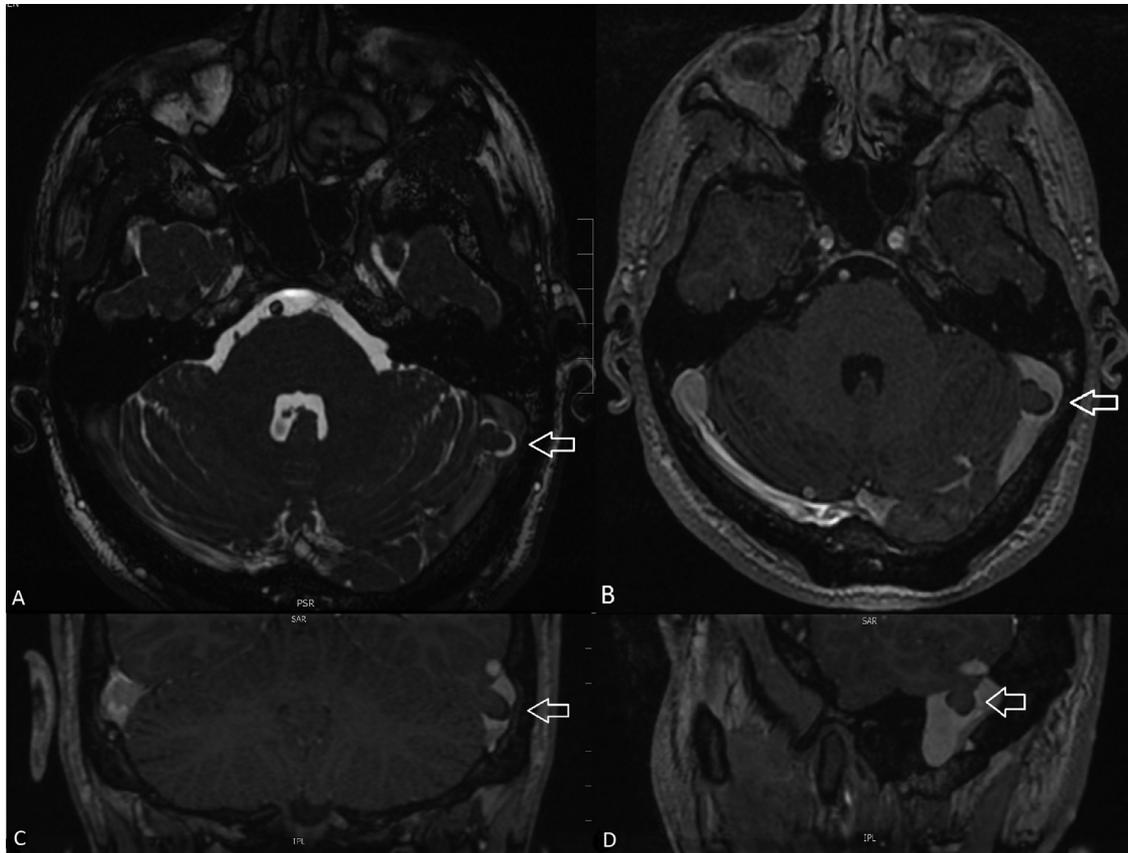


Fig. 2 – MR scan of the patient described in Case 2. Axial T2-weighted Fast Imaging Employing Steady-state Acquisition (FIESTA) sequence (A), axial (B), coronal (C) and sagittal (D) gadolinium-enhanced T1-weighted sequence showing a BHAG in the left transverse sinus with the herniated brain tissue extruding from the posterior part of the left inferior temporal gyrus (arrows). No signal or structural abnormalities can be seen.

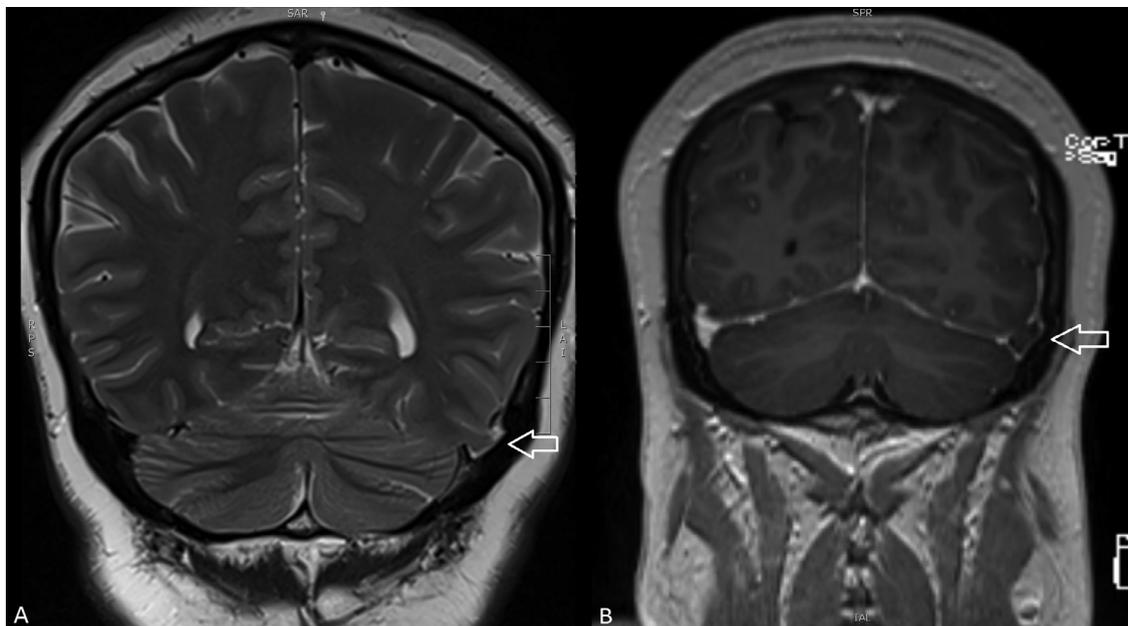


Fig. 3 – MR imaging of the patient described in Case 3. Coronal T2-weighted (A) and gadolinium contrast-enhanced T1-weighted sequence (B) showing a BHAG in the left transverse sinus with the herniated brain tissue originating from the posterior part of the left inferior temporal gyrus (arrows). No signal or structural abnormalities can be seen in the herniation.

epileptic seizures and thus, vasovagal syncope was considered the most plausible diagnosis, and the BHAG was considered an incidental finding unrelated to the loss of consciousness and episodes of disorientation.

Discussion

Brain herniation into arachnoid granulation (BHAG) is the brain tissue present in or in the vicinity of a presumed pre-existing arachnoid granulation (AG), with the latter being a protrusion of arachnoidea into dura mater or intracranial venous sinus containing cerebrospinal fluid (CSF), sometimes with addition of vessels and loose connective tissue. The role of AGs is probably CSF absorption into the venous system acting as a one-way valve, although other theories on the mechanism of CSF drainage have been proposed [6-8]. They increase in number and size with the person's age and are almost never seen in youngest children [9]. AGs may be found anywhere in relation to dural venous sinuses, most commonly in or close to transverse or sigmoid sinuses [10,11]. They originate from arachnoid villi on the visceral surface of arachnoid membrane probably due to CSF pulsations, the same mechanism that also can force the brain tissue into AG thus resulting in BHAG [3]. Malekzadehshkariani et al. and Liebo et al. proposed the theory of brain parenchyma herniating into preexisting AGs secondary to their observation that BHAGs were most commonly found at the most frequent location of AGs and due to the fact that brain parenchyma in BHAGs was surrounded by CSF [2,3]. However, other authors claim that a brain herniation could possibly be formed without preexisting AG through dural defects or localized dural weakness [1,12]. Other proposed etiologies include spontaneous origin, origin resulting from normal pia-arachnoid bridges between the brain and AG, hydrodynamic constraints on the brain and AG, chronically or periodically elevated intracranial pressure (ICP) like in meningitis, intracranial tumors with mass effect or head trauma [2,3,12-14]. Pia-arachnoid bridges were described as digitations of pia mater on the brain surface entering into the AGs, pulling the brain tissue and anchoring it into the dura which could possibly explain cerebellar tissue herniations into the transverse and sigmoid sinus apparently against gravity or CSF pulsation forces [3,13].

The fact that some people have multiple BHAGs (between 25% and 100% of the patients [2,3,13]) could support the theory for a causative factor in BHAGs' formation. Increase in size of BHAGs was observed in patients with space-occupying lesions and aggravated perifocal edema [2] justifying the role of ICP in formation of BHAGs. All patients described by Wolbach had autopsy findings suggesting increased ICP and all had multiple BHAGs [13]. However, in other reported patients the size of BHAGs remained unchanged despite imaging signs of ICP drop or conditions with transient increase in ICP [2]. Nevertheless, measurement of ICP was not performed in any of the studies in literature and thus the definite relationship between ICP and progression or regression of BHAGs cannot be confirmed.

Another controversial issue associated with BHAGs is the symptoms they potentially may cause. In our article we have described three different presentations of patients carrying

BHAGs – an incidental BHAG finding without any confirmed association with the first patient's headache (case 1), another BHAG possibly as incidental finding unassociated with the second patient's asymmetrical hearing loss (case 2) and the third patient's syncope (case 3). Three more recently published observational studies on this subject showed that most of BHAGs are incidental findings with no relation to symptoms, but a smaller part of BHAGs might be symptomatic (29% of patients with BHAGs and conditions leading to increased ICP described by Malekzadehshkariani et al., 25% of patients with signs or symptoms that might be explained by the BHAGs and 63% with imaging or clinical signs of raised ICP described by Liebo et al.) [2,3]. Battal et al. found a tendency towards the occurrence of BHAGs in patients with headache compared with the general population, though without reaching statistical significance [1]. BHAGs originating from inferior temporal lobe could potentially result in epilepsy. Demonstrating this correlation can be difficult due to the known undersampling of this region by bipolar EEG montage [15]. Additionally, it has been shown that epilepsy can result from temporal lobe encephalocoeles [16]. All patients in autopsy series described by Wolbach died with signs of increased ICP and all had multiple BHAGs [13]. Patients with BHAG containing left temporal lobe tissue located in transverse and sigmoid sinus described by Coban and Karatag, presented with headaches, dizziness, imbalance and pressure sensation in the ear [17,18]. Liebo et al. described a case of a woman with CSF otorrhea from a BHAG eroding the left posterior petrous bone [2]. The occurrence or absence of symptoms from BHAGs may be associated with eloquence of herniated brain tissue [2]. Indeed, most of the reported BHAGs in literature occurred in the posteroinferior parts of cranial cavity and contained non-eloquent brain tissue that hardly can cause any symptom [2,3]. Venous hypertension from BHAG could also explain symptoms in some of the patients, similarly to some symptomatic AGs leading to venous outflow obstruction from stenosis or occlusion of the sinus they protrude into [3]. Overall, the number of published BHAG cases is low and the number of analyzed BHAGs in the three recent observational studies was not sufficient to make any definite conclusion (Malekzadehshkariani et al. analyzed 68 cases in 38 patients, Battal og Hamcan et al. - 21 BHAGs in 20 patients, and 21 BHAGs in 16 patients identified by Liebo et al.) [1-3].

Signal and structural changes of the herniated brain tissue in the form of vasogenic edema, blood-brain barrier breakdown, focal pachymeningitis, infarction, gliosis or encephalomalacia could explain the presence of symptomatic BHAGs. Such signal and structural changes could result from tethering, inflammation or strangulation of the herniated brain tissue [2,3]. These changes were observed in 46% of BHAGs in the cohort analyzed by Malekzadehshkariani et al. (100% of them contained cerebellar tissue) and in 33% of patients described by Liebo et al. [2,3]. In 29% cases with signal abnormalities described by Liebo et al., BHAGs could be associated with the patients' signs and symptoms [3]. No signal changes were seen in the cohort analyzed by Battal and Hamcan [1]. However, there were described symptomatic BHAG cases without any visible signal abnormalities in the herniated brain, a possible explanation of which could be milder grades of signal changes undetectable by routine 1.5 or 3 Tesla MRIs [3]. On

the other hand, the majority of BHAGs with signal or structural abnormalities in the study by Liebo et al. had no associated symptoms [2]. The studies on pathological correlation between MR signal changes and cellular changes in potentially symptomatic BHAGs are lacking.

The rarity of BHAGs and their potential relation with symptoms in some of the patients makes them an important entity to be identified by the radiologists. It is important to recognize both AGs and BHAGs correctly and avoid confusing them with normal filling defects of dural sinuses such as septae or fat, or with pathological conditions including sinus thrombosis, malignancy or encephalocele which have different clinical consequences for the patient [19–21]. Contrary to sinus thrombosis, AG or BHAG protruding into an intracranial sinus causes a localized, well-defined filling defect in the sinus without involvement of the whole sinus and the draining cortical veins. Space-occupying lesions in dural sinuses are typically irregularly shaped, contrast-enhancing findings infiltrating underlying brain tissue and causing lytic changes in the surrounding bone. Encephalocele is a protrusion outside the outer skull layer containing brain herniation, while BHAG does not extend outside the skull, though it may cause a lytic defect in the inner, diploic or even outer skull layer with extracranial CSF extrusion [3]. If the BHAG is suspected to have a relation with the patient's symptoms, control imaging or even surgical decompression may be considered [3]. If no relation with the symptoms is suspected, regardless the presence or absence of parenchymal abnormality of the herniated brain or in the underlying parenchyma, no follow up may be needed [3].

Conclusion

BHAGs are herniations of brain tissue into a presumably pre-existing AG. Their etiology is not completely understood and many theories can be found in the literature. Most of BHAGs are asymptomatic incidental findings, but a part of them can potentially be linked to particular symptoms probably due to eloquent brain tissue found in the herniation. Studies analyzing enough cases allowing statistically significant results are needed to conclude on BHAGs' clinical significance, but this may be difficult due to their rare occurrence.

Patient consent

Written, informed consent for publication of the described cases was obtained from the patients.

Declaration of Competing Interest

All authors have no conflict of interest to declare.

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