





Original Article

## Surgical treatment of pituitary neuroendocrine tumors with coexisting intracranial lesions: A case series and review of the literature

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### ABSTRACT

**Background:** Pituitary neuroendocrine tumors (PitNETs) are a diverse group of benign neoplasms that account for a significant proportion of intracranial tumors (13%). The coexistence of PitNET with other intracranial lesions, such as meningiomas and intracranial aneurysms, has been constantly reported in the literature; yet, the pathophysiological mechanisms remain unknown, and the appropriate management is controversial. This study aims to describe the clinical characteristics, surgical treatment, and outcomes of patients with PitNET with coexisting intracranial lesions in a single healthcare center.

**Methods:** A retrospective analysis was conducted on 12 patients who underwent surgical treatment for PitNET and another intracranial lesion at our single tertiary referral center over 15 years from January 2008 to May 2023.

**Results:** Among these coexisting lesions, aneurysms were the most commonly found (41.67%), followed by meningiomas (33.33%). Surgical intervention for both lesions was performed in a single-stage procedure for most cases (75%), employing transcranial, endoscopic endonasal, and combined approaches. We found low preoperative Karnofsky Performance Scale scores in three patients, with significant differences in functional outcomes.

**Conclusion:** These findings contribute to the limited knowledge about PitNET coexisting with other intracranial lesions and emphasize the importance of patient-tailored, multidisciplinary management in these unusual scenarios.

**Keywords:** Aneurysm, Coexisting, Concomitant, Meningioma, Pituitary adenoma, Pituitary neuroendocrine tumor

### INTRODUCTION

Pituitary neuroendocrine tumors (PitNETs), previously named pituitary adenomas, represent a heterogeneous group of extra-axial benign tumors, which account for approximately 13% of all intracranial tumors,<sup>[38,42]</sup> with an annual incidence of 5.1 (3.9–7.4)/100,000.<sup>[10]</sup> The coexistence

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of PitNET with other intracranial lesions is considered an unusual event, without a clear pathophysiological mechanism, and sometimes even attributed to chance occurrence. Among these lesions, meningiomas<sup>[1,11,13,35,41,42]</sup> and intracranial aneurysms (IA)<sup>[17,19,27]</sup> are the most frequently reported.

Meningiomas are usually slow-growing tumors derived from the arachnoid cap cells, with an overall incidence of 8.3/100,000, and constitute the most common intracranial benign tumors.<sup>[7,42]</sup> While the occurrence of meningiomas induced by radiation therapy is well known,<sup>[23,29]</sup> the coexistence of PitNET with meningiomas in the absence of radiation history is uncommon. However, several case series have remarked the predilection for a perisellar location when associated with PitNET,<sup>[1,11,30]</sup> and even several physiopathological mechanisms have been proposed.<sup>[5,22,41,42]</sup> Moreover, the controversial association between IA in patients with PitNET, as well as their potential physiopathologic relationship, has been constantly described. Hu *et al.*<sup>[17]</sup> reported a higher prevalence of IA in patients with PitNET (8.3%) in comparison to general control subjects (2.4%), thus suggesting a causal relationship between them and raising doubts about the best therapeutic option in these scenarios.<sup>[24-26,33,36]</sup>

Different MESH terms have been employed to define the coexistence of more than one lesion in the intracranial space, such as “synchronous,” “concomitant,” “coexisting,” “coincidental,” and “collision tumor.” A distinction should be made in the case of collision tumors, which are defined as two or more histologically different neoplasms coexisting in the same area without histological admixture and, when involving the sellar region, common associations comprise PitNET along with Rathke cleft cysts (most frequent), craniopharyngiomas, metastatic brain tumors, gangliocytomas, and meningiomas, among others.<sup>[15]</sup> Conversely, “concomitant” or “coexisting” intracranial lesions involve lesions of different origins, such as tumoral (meningiomas) or vascular (aneurysms) ones, and located in the intracranial space, whether contiguous or far from each other.<sup>[15]</sup>

Even though the association between PitNET and other intracranial lesions has been well documented, the underlying pathophysiological mechanism remains unclear. Furthermore, there is no actual consensus about the best therapeutic option for such concomitant lesions; however, surgical treatment represents the best therapeutic option in those cases requiring intervention.<sup>[26]</sup> Some issues concerning the surgical treatment of these dual pathologies are whether they should be treated simultaneously (if technically feasible) or in a staged fashion, as well as the best surgical approach (transcranial [TC], endoscopic endonasal, or combined). In addition, there is a lack of information concerning the survival and functionality of this group of patients due to the rarity of these cases.

The purpose of this study is to describe the clinical characteristics and our institutional experience in the management of PitNET coexisting with other intracranial lesions, emphasizing the surgical treatment employed and the long-term outcomes. Furthermore, we provide two illustrative cases and also present a literature review in an attempt to exemplify and discuss surgical decision-making.

## MATERIALS AND METHODS

### Patient population

We conducted a retrospective review of the medical records of all patients who were diagnosed with PitNET in coexistence with other intracranial lesions and who were surgically treated in our institution over 15 years (between 2008 and 2023). The review included demographic data, pre- and post-operative images, operative notes, histopathologic reports, and follow-up medical notes. Patients with a history of cranial radiotherapy and incomplete data in the medical records were excluded from the study. Institutional Review Board approval and informed consent were not required for the present study due to its retrospective design, without identifiable personal data.

PitNET were classified as non-functioning (NF) or functioning tumors. The hormonal type of the latter was further defined based on both hormonal profile results and clinical manifestations. The coexisting intracranial lesions were defined based on their histopathologic characteristics obtained from surgical samples; however, in those cases where the acquisition of tissue was not feasible (such as aneurysmal lesions), they were defined based on the preoperative images and intraoperative findings.

### Surgical procedures

All surgical procedures were authorized through written informed consent and performed by experienced skull base neurosurgeons. Surgical interventions were classified according to the number of procedures (one-stage vs. two-stage surgery) and the surgical approach(es) performed (TC, endonasal endoscopic, or both), which were further specified.

### Statistical analysis

Data are presented as means and standard deviations for continuous variables and as percentages for categorical variables. The Shapiro–Wilk test was used to determine distribution normality. Differences between categorical variables were determined with a Chi-squared test, whereas, for mean comparison of continuous variables, T and Wilcoxon tests were used, according to data distribution. Data were analyzed using STATA 17.

## RESULTS

A total of 1666 patients with the diagnosis of PitNET were operated on from January 2008 to May 2023 in our institution. Twelve patients with a coexisting intracranial lesion (0.72%) were included in our study. The mean (standard deviation [SD]) age of patients was 51.66 (5.416) (range 43–60) years, and 5 (41.67%) were men. Regarding PitNET, 10 (83.33%) were NF, and the remaining 2 (16.67%) were documented as growth hormone (GH)-secreting lesions. Aneurysms were the most common concomitant lesions, representing 5 (41.67%) of the total, followed by 4 (33.33%) meningiomas, 1 (8.33%) ependymoma, one cavernoma, and one arteriovenous malformation. As for the surgical approach chosen, 9 (75%) patients were intervened for both lesions in a single-stage procedure being the TC route performed in 4 (33.33%) patients; meanwhile, 1 (8.33%) patient was intervened through an endoscopic endonasal approach (EEA), and 7 (58.33%) with a combined TC/EEA combined approach. Three patients presented with low preoperative Karnofsky Performance Scale scores (70 or less) with a mean (SD) value of 79.16 (19.762) (range 30-90). The mean (SD) postoperative KPS was 67.5 (31.37). Significant differences were found among functional outcomes ( $P = 0.05$ ) [Table 1]. A detailed description of the patient's demographics, PitNET hormonal profile, associated lesions, and interventions performed are shown in Table 2.

### Representative cases

#### Case 1

A 54-year-old man with a 15-year history of acromegalic physical changes was referred to our emergency department due to the gradual onset of mental status and behavioral changes. On physical examination, the patient had evident acromegalic features; disorientation and inattention stood out on neurological examination. Fundoscopic examination revealed bilateral papillary atrophy. Eye movements were unrestricted, and his right pupil was mydriatic and with diminished response to light. The rest of the exploration was not assessable. Brain magnetic resonance imaging (MRI) with contrast revealed a large, homogeneously enhancing anterior skull base lesion originating from and conditioning hyperostosis of the planum sphenoidale, compatible with a meningioma. In addition, a homogeneously enhancing sellar lesion with some areas of T1-weighted imaging shortening, compatible with a PitNET, was observed [Figure 1]. Serum GH and insulin-like growth factor 1 (IGF-1) levels of 4.3 ng/mL and 527.4 ng/mL, respectively, were reported.

We decided to approach both lesions through a combined EEA and TC approach in one surgical stage. Initially, an EEA trans-tuberculum/ trans-planum was performed for both resection of the sellar lesion and vascular control of

**Table 1:** Demographic and operative characteristics.

<u>CLINICAL VARIABLES</u>	
Gender – n (%)	
- Male	5 (41.67)
- Female	7 (58.88)
Mean age – mean (S.D.)	51.66 (5.416)
<u>SURGICAL VARIABLES</u>	
PitNET secretory status – n (%)	
- Secretory	2 (16.67)
- Non-secretory	10 (83.33)
Concomitant lesion – n (%)	
- Aneurysms	5 (41.67)
- Meningiomas	4 (33.33)
- Others*	3 (25)
Surgical stages – n (%)	
- Single-stage	9 (75)
- Multi-stage	3 (25)
Surgical approach – n (%)	
- EEA	1 (8.33)
- TC	4 (33.33)
- Combined (EEA+TC)	7 (58.33)
<u>FUNCTIONAL VARIABLES (p=0.05)</u>	
Preop. KPS – mean (SD)	79.16 (19.762)
Postop. KPS – mean (SD)	67.5 (31.37)

EEA: endoscopic endonasal approach; KPS: Karnofsky Performance Scale; PitNET: pituitary neuroendocrine tumor; Postop.: postoperative; Preop.: preoperative; TC: transcranial; SD: standard deviation  
\*1 ependymoma, 1 cavernoma, and 1 arteriovenous malformation

the meningioma by coagulation of the posterior ethmoidal arteries. Once the endoscopic stage was concluded, a transbasal approach was performed, achieving a Simpson I resection. The anterior skull base was reconstructed with fat graft and pedicled pericranium, and the sellar floor was reconstructed in a multilayered fashion employing inlay fascia lata, fat graft, onlay fascia lata, and a previously harvested nasoseptal flap. Transient diabetes insipidus and hypernatremia arose postoperatively, which were managed satisfactorily, and the patient was discharged after two weeks. At follow-up, biochemical remission was demonstrated; however, visual acuity remained severely impaired.

#### Case 2

A 55-year-old female with no relevant medical history presented to our department with a 6-year history of headache, joint pain in both hands, as well as acral and facial enlargement. Decreased visual acuity (20/60 bilaterally) and bitemporal hemianopsia were found on ophthalmologic evaluation. Endocrinological testing was relevant for a GH level of 24 ng/mL and IGF-1 of 770 ng/mL (index 3.83). Brain MRI revealed an isointense T1- and T2-weighted imaging sellar lesion, with heterogeneous contrast enhancement, extending upward into the third ventricle and with para

**Table 2:** Main characteristics and surgical treatment of the 13 cases of PitNET coexisting with other intracranial lesions.

No.	Age/ Sex	PitNET Subtype	Coexisting lesion	Location	Type of intervention	No. Approaches	Surgical Approach
1	60/F	NS	Aneurysm	LT paraclinoid (ophth. segment)	One-stage	1	TC: LT lateral supraorbital (for both lesions)
2	45/M	NS	Aneurysm	LT ICA bifurcation	One-stage	1	TC: LT Pterional (for both lesions)
3	55/F	NS	Aneurysm	Bil. paraclinoid	One-stage	1	TC: RT Pterional+intradural clinoidectomy (for both lesions)
4	54/F	GH	Aneurysm	LT paraclinoid (ophth. segment)	One-stage	2*	1°:TC: LT Pterional (aneurysm clipping) 2°:EEA (PitNET resection)
5	55/F	NS	Aneurysm	LT ICA, comm. segment	Two-stage	2	1°: LT Pterional (aneurysm clipping) 2°: EEA (PitNET resection) TC:
6	43/F	NS	Cavernoma	RT Frontomedial	One-stage	2*	1°:EEA (PitNET resection) 2°:TC: Anterior interhemispheric approach (cavernoma resection)
7	52/M	NS	Supratentorial Ependymoma (WHO II)	LT lateral ventricle	One-stage	2*	1°:EEA (PitNET) 2°:TC: LT Pterional+Endo port assisted (ependymoma resection)
8	49/F	NS	Arteriovenous Malformation	LT frontal (SM II)	One-stage	1	TC (for both lesions)
9	51/F	NS	Meningioma (Fibroblastic, WHO I)	LT Parietal convexity	Two-stages	2	1°:EEA (PitNET) 2°:TC: LT centered temporoparietal craniotomy (meningioma resection)
10	55/M	GH	Meningioma (Meningothelial, WHO I)	Planum sphenoidale	One-stage	2*	1°: EEA (PitNET and partial meningioma resection) 2°:TC: LT Pterional craniotomy (to complete meningioma resection)
11	57/F	NS	Meningioma (Meningothelial, WHO I)	Planum sphenoidale	One Stage	1	EEA (for both lesions)
12	44/F	NS	Meningioma	LT tentorial incisura Meningioma	Two-stage	1	1°: EEA (PitNET resection) 2°: SRS 16 Gy single dose

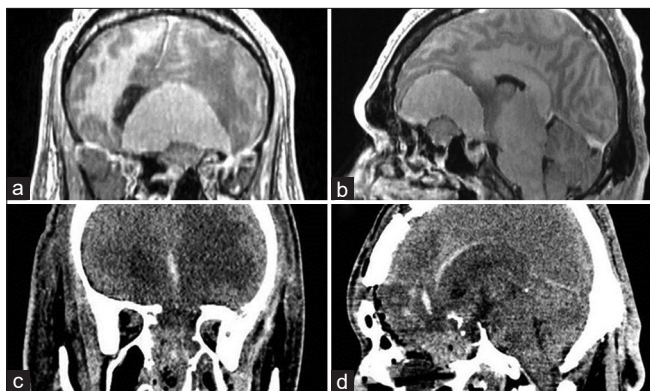
Abbreviations: bil.: bilateral; comm.: communicating; EEA: endonasal endoscopic approach; F: female; GH: growth-hormone; Gy: Gray; ICA: internal carotid artery; LT: left; M: male; NS: non-secretory; Ophth.: ophthalmic; PitNET: pituitary neuroendocrine tumor; RT: right; SM: Spetzler-Martin; SRS: Stereotactic radiosurgery; TC: transcranial

\*Both lesions were treated in one surgical stage through two different surgical approaches

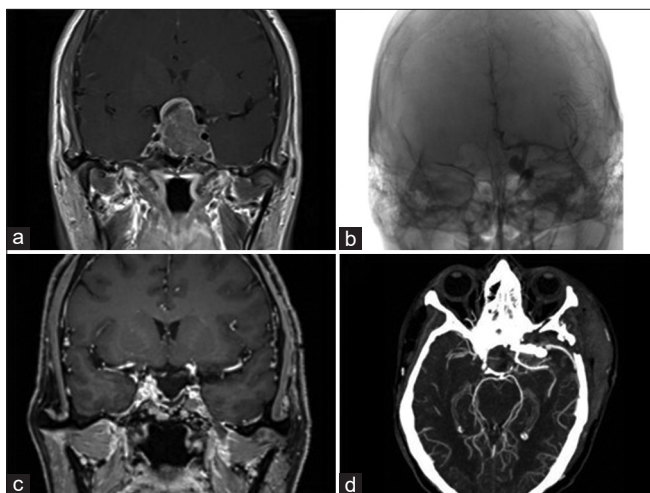
seller extension into the right cavernous sinus [Figure 2]. In addition, the MRI disclosed a left paraclinoid aneurysm, which was further assessed with a digital subtraction angiography (DSA), which reported left ophthalmic aneurysm.

Due to the presence of an aneurysm in the para sellar region and the potential risk of rupture during the EEA resection of the GH-secreting PitNET, we decided to initially perform a microsurgical clipping of the aneurysm through a pterional approach and, subsequently, perform an EEA in a single surgical stage. The treatment of both lesions transcranially was also considered, but due to the enhanced visualization of the sellar region provided by the endoscope and the better

tumoral and hormonal control associated, an EEA was favored. During the microsurgical stage, a left extradural anterior clinoidectomy and unroofing of the optic canal were performed to gain access to the distal dural ring and carotid cave for proximal control. Afterward, a left paraclinoid Barami IA, with a dorsomedial projection, was visualized. After thorough dissection, the aneurysm was finally excluded with two clips. Intraoperative fluorescence angiography confirmed the complete exclusion of the aneurysm as well as the hemodynamic integrity of the related vessels. Subsequently, the sellar lesion was resected through an EEA. After opening the sellar dura, a soft tumor was visualized, and



**Figure 1:** (a and b) Coronal and sagittal T1-post contrast magnetic resonance imaging demonstrated a homogeneously enhancing anterior fossa lesion, dependent on the planum sphenoidale, which conditioned significant hyperostosis of the sphenoid bone. The lesion extended dorsally, leading to a right subfalcal herniation and compression of the frontal horns of the lateral ventricles and corpus callosum. In the sagittal projection, a hyperintense sellar mass confined to the sella turcica was also noted. (c and d) Coronal and sagittal postoperative non-contrast computed tomography revealed total tumoral removal of both meningioma and PitNET, associated with a significant anterior skull base bony defect, which was repaired as mentioned above.



**Figure 2:** (a) Coronal T1-post contrast magnetic resonance imaging (MRI) demonstrated a heterogeneously enhancing sellar lesion, with suprasellar extension into the third ventricle and parasellar extension into the left cavernous sinus. (b) An anteroposterior angiogram of the left internal carotid artery showed a left paraclinoid aneurysm with a dorsomedial projection. (c) Coronal T1-weighted post-contrast MRI obtained two months after surgery revealed a gross total resection of the pituitary neuroendocrine tumors with a small remnant at the left cavernous sinus. (d) Postoperative computed tomography angiography demonstrated total aneurysm occlusion with preservation of the parental vessels and branches

gross total resection was performed. A similar reconstruction as the one described in Case 1 was performed. The

postoperative course was uneventful. Biochemical remission was achieved, and her vision gradually improved.

## DISCUSSION

The coexistence of PitNET with other intracranial lesions is unusual, especially when patients with previous irradiation therapy for pituitary tumors have been excluded from the study. However, in the current medical literature, there are several case reports of PitNET associated with other intracranial lesions, such as craniopharyngiomas,<sup>[15]</sup> lymphomas,<sup>[32]</sup> gliomas,<sup>[4]</sup> aneurysms,<sup>[17,19,24-27,33,36]</sup> and meningiomas<sup>[1,5,11,13,22,30,35,41,42]</sup> among others. However, it should be noted that both aneurysms and meningiomas are the most consistently reported ones and even several pathophysiologic theories have been proposed to explain their association.<sup>[17,26,27,41,42]</sup> The higher prevalence of aneurysms and meningiomas in this population of patients was also noted in the present study, where both the former (five cases [41.6%]) and the latter (four cases [33.3%]) comprised three-quarters of the total number of cases; therefore, they are the main subject of this discussion.

The association of IA with PitNET has been constantly reported<sup>[9,17,19,26,27]</sup>; however, the reported prevalence of this association is greatly variable, ranging from 0.5% to 8.3% in different series.<sup>[9,16,17,27,28]</sup> In addition, data variability between countries has also been noted; Hu *et al.*<sup>[17]</sup> reported an overall prevalence of 8.3% of unruptured IA among 434 Chinese patients with PitNET, whereas Oh *et al.*<sup>[27]</sup> reported this association only in 2.4% of Korean patients. Despite this variability, the literature suggests that the prevalence of IA is higher in patients with PitNET compared to the general population and in patients with other benign intracranial tumors.<sup>[3,9,19,27,37]</sup> The underlying mechanisms for this association remain unknown; therefore, many theories have been postulated to explain the development of aneurysms in patients with PitNET, such as mechanical disturbances, hemodynamic changes, direct tumoral infiltration, hormonal alterations, and increased levels of vascular endothelial growth factor.<sup>[17,19,26,36]</sup>

The pattern of distribution of the IA has also been a matter of debate, and a predilection for the anterior circulation has been advised.<sup>[3,16,17,21,28,39]</sup> Based on the previous case series, those aneurysms associated with PitNET are located predominantly on the internal carotid artery (ICA) (69%), followed by the anterior cerebral artery-anterior communicating artery (ACA-AcoA) complex (19%), vertebrobasilar system (9.5%), and middle cerebral artery (MCA) (2.5%).<sup>[9,27]</sup> This pattern of distribution differs significantly from that reported in the general population (ICA [35%], ACA-AcoA complex [30%], MCA [20%], and vertebrobasilar system [5%]).<sup>[9,17,27,34]</sup> In the present series, all the aneurysms originated from the ICA, especially from its ophthalmic segment (60%). In this regard, Locatelli *et*

*al.*<sup>[21]</sup> proposed the participation of the ICA and ACoA in the blood supply of the sellar region as a possible explanation for this distribution. Yet, three large case series by Hu *et al.*,<sup>[17]</sup> Oh *et al.*<sup>[27]</sup> and Kim *et al.*,<sup>[20]</sup> the pattern of distribution of the IA did not differ from that of the control patients.

Another controversial association is the hormonal secretion of PitNET and its role in the development of IA. The secretion of GH by the tumor has been proposed as a risk factor for the development of IA.<sup>[2,19,26,36,37]</sup> Jakubowski and Kendall<sup>[19]</sup> reported the presence of silent IA in 13.8% of GH-secreting PitNET, compared to 5.1% in NF tumors; however, this association has been reported to be as high as 50%.<sup>[3]</sup> Some theories to explain this association include the increased level of GH and IGF-1, which may contribute to the development of IA through atherosclerotic and/or degenerative changes of the arterial wall, as well as changes in collagen biosynthesis.<sup>[2,19,26,36,37]</sup> Nevertheless, this association is inconsistent and, thus, remains controversial. On the other hand, it is worth mentioning that age ( $P = 0.002$ ) and cavernous sinus invasion ( $P = 0.019$ ) have been found as independent risk factors for IA development in patients with PitNET.<sup>[17,27]</sup> In the present case series, there was one case of GH-secreting PitNET out of five cases associated with IA (20%). However, no association could be assessed due to the limited number of cases.

The diagnosis of IA associated with PitNET is usually an incidental finding while carrying out preoperative image studies, and most of the IA are silent and unruptured; therefore, the clinical manifestations of the patients are usually due to the mass effect or hormonal secretion of the pituitary tumor.<sup>[24,27,36]</sup> However, there have been reports of fatal epistaxis and pituitary apoplexy secondary to the rupture of these aneurysms.<sup>[18,39]</sup> Hence, the misdiagnosis of these conditions may lead to the accidental rupture of IA during tumoral resection, leading to lethal hemorrhagic consequences. DSA is the gold standard for diagnosis of IA; however, due to the low prevalence of this association and the risks associated with this procedure, routine preoperative DSA is not advised in patients with PitNET.<sup>[9]</sup> Nevertheless, MRI angiography and computed tomography angiography (CTA) are less invasive alternatives, especially CTA, which is more accessible, quick, and has higher sensitivity than MRA.<sup>[17,24,27,39]</sup> In our institution, we routinely perform preoperative CTA and MRI for patients with PitNET with significant suprasellar and/or parasellar extension for both assessing the perisellar vasculature as well as for neuronavigation.

Different therapeutic options and protocols have been proposed for the management of PitNET coexisting with IA. Based on the current literature and our institutional experience, it is advisable to treat the IA at the first stage (whether with microsurgical or endovascular procedures) and then proceed with the tumoral resection.<sup>[9,24,25,36]</sup> Both treatments may be performed in one or two surgical stages,

but always securing the IA before the tumoral resection to avoid potential catastrophic hemorrhages, especially when both lesions are close to each other.<sup>[9,24,25,33]</sup> The planning of the surgical strategy must be tailored to the patient, and several factors should be considered for treatment selection, especially the spatial arrangement between the IA and the PitNET. A reasonable approach consists of the preoperative endovascular occlusion of the IA before surgical resection of the pituitary tumor.<sup>[9]</sup> In a case series by Raper *et al.*,<sup>[31]</sup> the management included staged coiling or carotid sacrifice before endonasal endoscopic resection of the PitNET. In cases of fusiform IA, flow-diverting stenting may represent a safe and minimally invasive alternative; however, the requirement of dual antiplatelet therapy and the resulting associated risk of hemorrhagic pituitary apoplexy must be considered.<sup>[25]</sup> Another rational option is to treat both lesions through a microsurgical approach, whether in two surgical stages or through a simultaneous treatment of both pathologies in a single surgical stage (when anatomically feasible) through a TC pterional, supraorbital, or front-orbital approach or an EEA.<sup>[14,24,33,36,37]</sup> In the present study, 4 out of 5 cases (80%) were treated in one surgical stage, one of which was treated through a combined approach (TC and EEA) in one surgical stage. The pterional approach was the preferred one due to its versatility and the satisfactory exposure of the sellar and perisellar region. A less invasive alternative might have been the endovascular occlusion of the aneurysm in the first stage, followed by tumoral resection; however, a TC approach was decided due to the favorable anatomy and experience of the skull base neurosurgeon, offering the patients a more definitive treatment of the IA at a lower economic burden.

On the other hand, meningiomas comprised one-third (33.3%) of the intracranial lesions associated with PitNET in the present series, representing the second most frequent lesion. This association in patients with a previous history of intracranial radiation therapy is well known<sup>[23,29]</sup> However, in the absence of this medical background, their association is unusual. Although these two neoplasms do not share a well-known etiological origin, some authors have suggested that their association is higher than expected in the general population.<sup>[11,41]</sup> In the literature, it has been suggested that GH hypersecretion by the pituitary tumor may play a role in the development of meningiomas. De Vries *et al.*<sup>[11]</sup> reported that, compared with other types of PitNET, the association with meningiomas is most frequent with GH-secreting PitNET, while Friend *et al.*<sup>[12]</sup> found the expression of IGF-1 and GH receptors in 75% of meningiomas. On the other hand, some studies have proposed a common genetic mechanism leading to both neoplasms, such as MEN1 gene mutations and the resultant PI3K/AKT/mTOR signaling pathway dysregulation.<sup>[13,41,42]</sup> Besides, it is worth mentioning that the reported cases of meningiomas coexisting with

PitNET tend to demonstrate a predilection for the para sellar region in as high as 44% of the cases<sup>[5,11]</sup>, which is consistent with our findings, where planum sphenoidale meningiomas represented 2 out of 4 cases (50%). However, despite the numerous pathophysiological mechanisms proposed in the literature, there is still no clear evidence of a causal effect between both neoplasms, and there remains the possibility of representing just an incidental finding.

The presence of a PitNET coexisting with a distally located meningioma may have several therapeutic options, and they are usually treated independently and according to the presence of symptoms, hormonal secretion, response to medical treatment (prolactinomas), as well as the treatment goals, being the expectant management sometimes the best option.<sup>[6]</sup> However, when both lesions are closely located, they represent a real therapeutic challenge, with the resultant increased risk of surgical morbidity compared with the treatment of either lesion alone. There are different approaches for these unusual scenarios, and some authors have recommended the resection of both tumors in one surgical stage (if feasible).<sup>[5,6,35]</sup> For this purpose, some authors have employed a single TC (pterional, subfrontal, and frontotemporal) approach for resection of both lesions.<sup>[1,5,8,40]</sup> However, with the recent advancements in endoscopic techniques and instrumentation, in addition to the great exposure of the anterior skull base provided by EEA, the resection of both lesions through an endoscopic approach has been reported as a good and safe alternative in selected cases and centers with experienced endoscopic surgeons.<sup>[1,6,11,22,30]</sup>

## CONCLUSION

Although unusual in occurrence, the coexistence of PitNET with other intracranial lesions has been described, representing both IA and meningiomas, the most frequent ones. Despite the low incidence and absence of a clear causative factor for these concomitant lesions, the possibility of this association must be taken into account as part of the preoperative differential diagnosis, and the surgical approach must be tailored to the patient's symptoms, anatomical location of both lesions, and the suitability for treating both lesion in one surgical stage. Likewise, the present case series provides valuable information to the little knowledge about these unusual concomitant lesions.

## Ethical approval

The Institutional Review Board approval is not required.

## Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Nil.

## Conflicts of interest

There are no conflicts of interest.

## Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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