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Short clinical case

Endoscopic endonasal resection of coexisting pituitary adenoma and meningioma: Two cases' report and literature review

Y.Y. Bao [1], X. Wu [1], H. Ding [1], T. Hong *

Department of neurosurgery, the First Affiliated Hospital of Nanchang University, 17, Yong Wai Zheng Street, Nanchang, China

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ABSTRACT

Introduction. – The coexistence of pituitary adenoma (PA) and para/suprasellar meningioma is an extremely rare event, which generally occurs in previous case reports. Literature on the endonasal endoscopic approach (EEA) to treat such synchronous tumours remains sparse.
Case description. – Two cases of concomitant sellar and supra/parasellar tumours are reported. A 62-year-old woman with a PA and a tuberculum sellae meningioma and a 56-year-old woman with a PA and a cavernous sinus (CS) meningioma. Both coexisting tumours were resected through a single extended EEA and achieved a good prognosis. To the best of our knowledge, endoscopic endonasal resection of coexisting PA and CS meningioma has not been previously reported in the literature.
Conclusion. – Our reports add to the literature two cases of coexisting PA and meningioma, with different consistence in sellar and para/suprasellar regions. Furthermore, the present case adds to the evidence that in the rare situation of coexisting sellar and suprasellar tumours located in the same sagittal plane, an extended EEA allows adequate exposure and safe removal of both tumours. However, for tumours coexisting in the sellar and parasellar region in the same coronal plane, we should draw attention to this rare situation for differential diagnosis of synchronous PA and CS meningioma to avoid unnecessary surgery and to decide the best strategy for treatment.

1. Introduction

Pituitary adenomas (PAs) and meningiomas are two types of common benign intracranial neoplasms. The former represents 10% to 15% of all intracranial tumours [1], while the latter comprises 15–25% of all primary intracranial neoplasms [2,3]. Nevertheless, the coexistence of PA and meningioma is an extremely rare clinical scenario with no previous known risk factors for either tumour [3–8]. Both lesions can reach a large size and cause similar signs and symptoms, which make the diagnosis and treatment of this coexisting tumour difficult [9–11]. Therefore, clinical awareness and recognition of such a rare condition before surgery is of great importance when surgical removal is necessary. Today, with the increased use of endoscopic techniques and the progression of the extended approaches, it is now possible to safely resect coexisting PA and meningioma through a single-staged endoscopic endonasal approach (EEA). Although a small number of cases have been reported in the literature describing the simultaneous coexistence of PA and meningioma, as well as the methods of treatment, literature on technical aspects of EEA for treatment of such concomitant tumours remains sparse [11–14]. Herein, we present two cases of coexistent tumours, including a PA and a tuberculum sellae meningioma, as well as a PA and a cavernous sinus (CS) meningioma, both of which were diagnosed and resected through a single extended EEA. To our knowledge, endoscopic endonasal resection of coexisting PA and CS meningioma has not been previously reported in the literature. In addition, a systematic review of the relevant supporting literature was provided.

2. Case report

2.1. Case 1

2.1.1. History and examination

A 62-year-old woman presented with progressive visual loss in her left eye for two years. Contrast-enhanced magnetic resonance imaging (MRI) demonstrated a homogenously enhancing sellar mass and was thought to be a pituitary microadenoma. Additionally, immediately adjacent to it, a homogenously enhancing extra-axial lesion with a "dural tail" was found and was supposed to be a tuberculum sellae meningioma (Fig. 1A and B). Preoperative

* Corresponding author.
E-mail address: ht2000@vip.sina.com (T. Hong).
[1] These authors contributed equally to this work.

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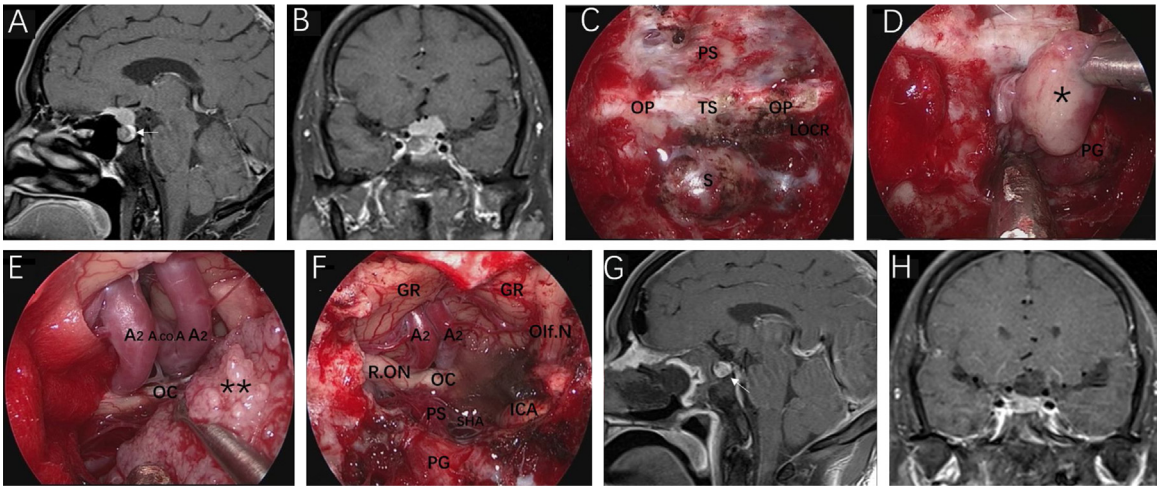

Fig. 1. Illustrative case 1. A and B. Preoperative (A) sagittal, and (B) coronal Gd-enhanced MRI demonstrated coexistent microadenoma and tuberculum sellae meningioma. The white arrow represents the residual pituitary gland. C–F. Intraoperative images. C. After bone removal and before dural opening. D. Removal of the soft and pale PA with suction. E. Sharp dissection of the meningioma away from the neurovascular structures. F. Final endoscopic view after complete tumours removal. G and H. Corresponding postoperative MRI showed that the suprasellar meningioma and the adjacent pituitary adenoma (PA) were completely removed, and the residual pituitary gland could be seen within the sella. OP = optic protuberance; PS = planum sphenoidale; S = sella; TS = tuberculum sellae; LOCR = lateral optocarotid recess; * = pituitary adenoma; ** = meningioma; A.co.A = anterior communicating artery; OC = optic chiasma; ICA = internal carotid artery; L.ON = left optic nerve; R.ON = right optic nerve; Olf.N = olfactory nerve; PG = pituitary gland; PS = pituitary stalk; GR = gyrus rectus; SHA = superior hypophyseal artery.

visual examination showed visual acuity of 20/20 in the right and 20/400 in the left eye, accompanied by a left temporal visual field defect. Preoperative serum hormone levels were normal. The risks associated with craniotomy and EEA were informed to the patient and her family, and finally the patient decided to undergo a single-stage endoscopic surgery.

2.1.2. Surgical operation

The standard endonasal endoscopic surgical approach to the sphenoid sinus is performed as described elsewhere [13,15]. The bones overlying the sella, tuberculum sellae, and planum sphenoidale were removed. After a cruciate incision was made over the sella and planum dura, two clearly separate intrasellar and suprasellar masses with distinct consistence were exposed. Bleeding from the superior intercavernous sinus during the removal of tuberculum sellae can be readily controlled with the use of hemostatic agents or with the bipolar coagulation and transected. The soft and pale intrasellar tumour was removed with suction, and the squeezed normal pituitary gland was preserved (Fig. 1D). Next, the prechiasmatic cistern was opened and the suprasellar tumour was fully exposed. The relatively tough tumour was removed by progressive debulking and careful dissection from the adjacent vital neurovascular structures (Fig. 1E). Finally, the tumour in the left optic canal was explored and removed. Cranial base reconstruction was performed in a multilayered fashion with the fascia lata and the vascularised pedicled nasoseptal flap made at the beginning of the procedure.

2.1.3. Postoperative course

Contrast-enhanced postoperative MRI within 24-hours post-operation showed gross total resection (GTR) of the lesions (Fig. 1G and H). The patient experienced improvement of visual acuity, and the pituitary function remained at the preoperative level. The left temporal visual field defect has been partially improved during the 6-month follow-up period. There was no postoperative cerebrospinal fluid (CSF) leakage, and the pathological results confirmed the diagnosis of the two distinct entities, a non-functioning adenoma and a meningioma (Fig. 2).

2.2. Case 2

2.2.1. History and examination

A 56-year-old woman presented with 1-year history of headache and progressive bilateral visual loss for more than 1 month. On admission, contrast-enhanced MRI revealed a $2.8 \times 2.0 \times 1.6$ cm moderate inhomogeneous enhancement intra- and suprasellar mass with involving the right CS and completely encasing the right internal carotid artery (ICA), which was suspected to be a pituitary macroadenoma (Fig. 3A and B). Preoperative visual examination demonstrated visual acuity of 20/80 in the right and 20/50 in the left eye, but her visual field remained full. Preoperative serum hormone levels were normal. The patient refused a transcranial approach, but agreed to endoscopic endonasal resection of the lesion.

2.2.2. Surgical operation

Due to the lesion involved the lateral compartment of the CS, an initial transmaxillary–transpterygoidal approach was performed. This approach has been well described in our previous literature [16]. The sella and CS were identified, and the overlying bones were removed using a high-speed curved endonasal diamond drill. After opening the dura of the sella, we can see the normal pituitary gland and the closely adjacent pink and fragile intrasellar tumour (Fig. 3D). This soft tumour was separated and completely removed with suction. Next, the tumour of the CS was explored. After location of the exact course of the intracavernous ICA with image guidance and intraoperative Doppler probe, the dura of the CS was opened with a retractable blade or hook blade from the medial margin of the CS segment of ICA to the lateral margin. To obtain proximal and distal ICA control, the C-shaped parasellar ICA within the CS was fully exposed. Partial pituitary transposition was performed so that has more surgical space for CS tumour. When the medial wall of the CS was opened, unexpectedly, we found that the CS component had a harder consistency than the sellar tumour, which led us to suspect different histological lesions. A rapid frozen pathological examination was performed, which confirmed that the lesion was coexisting PA and meningioma. A subtotal resection (STR) was performed via the medial and lateral corridors. The

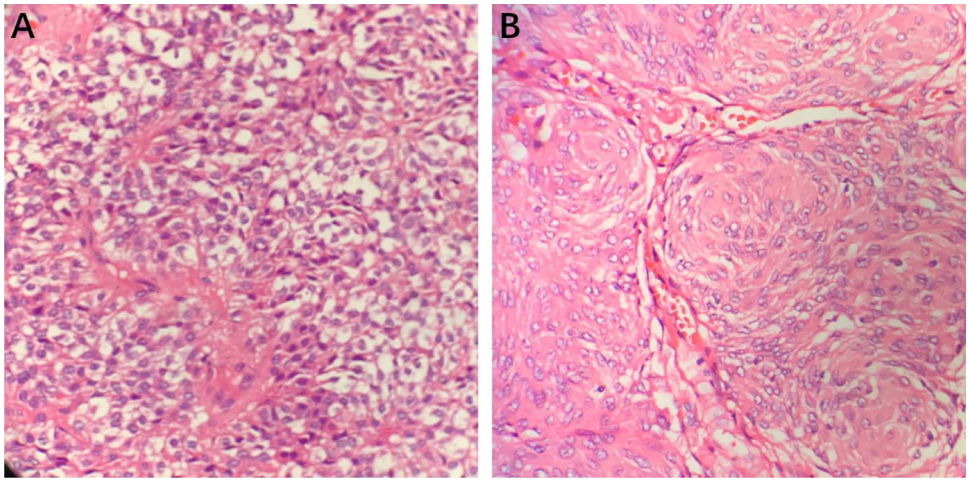

Fig. 2. Histological examination (case 1). A. The adenoma component consisted of uniform cells with rounded nuclei and eosinophilic cytoplasm. Immunohistochemical results showed GH (−), LH (−), TSH (−), ACTH (−), FSH (−), PRL (−). B. High-power hematoxylin and eosin (H&E) stained micrograph demonstrated a marked characteristic pattern of meningioma with whorl formation. Immunohistochemical results revealed EMA (++), Vimentin (+), PR (+), CD34 (−), stat6 (−), and Ki-67 (index approximately 5%).

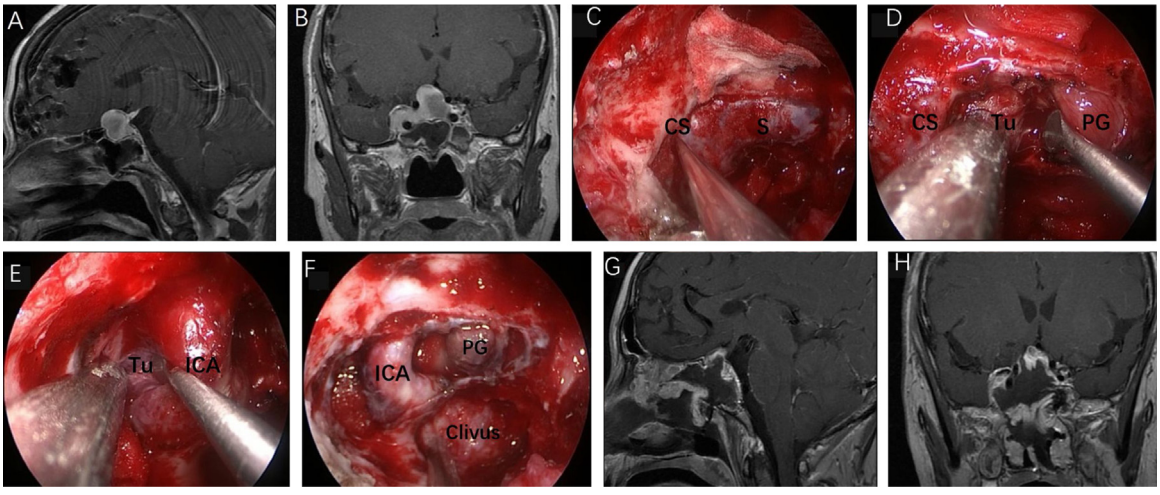

Fig. 3. Illustrative case 2. A–B. Preoperative (A) sagittal, and (B) coronal, Gd-enhanced MRI demonstrated an intra- and suprasellar tumour with right cavernous sinus (CS) invasion. C–F. Intraoperative images. C. Locating of the exact course of the intracavernous ICA with image guidance. D. Separation and removal of tumor tightly adhered to the normal pituitary gland. E. Resection of tumour in the CS through the lateral corridors. F. Endoscopic view after tumour resection. G–H. Corresponding postoperative MRI showed subtotal resection (STR), with part of the tumour remaining in the right CS and suprasellar. Tu = tumour.

skull base dural defect was repaired with an autologous fascia lata inlay graft followed by a vascularised pedicled nasoseptal flap.

2.2.3. *Postoperative course*

Contrast-enhanced postoperative MRI demonstrated STR of the tumour with part of the tumour remaining in the right CS and suprasellar (Fig. 3G and H). The patient experienced resolution of the headache and improvement in visual acuity, and postoperative hormone levels were still within the normal range. Postoperative CSF leakage did not occur, but experienced a transient diabetes insipidus (DI). The pathologic examination of the sellar tissue showed a non-functioning adenoma and the parasellar tumour proved to be a meningothelial meningioma WHO I (Fig. 4). Gamma knife radiosurgery has been recommended for treatment of residual tumour. No tumour-related symptoms were found in telephone follow-up 6 months after radiotherapy.

3. Discussion

The coexistence of PA and meningioma is an uncommon phenomenon, especially in patients who have not received radiotherapy for a pituitary mass [3–8]. This rare entity deserves our serious consideration in the aspects of the pathogenetic relationship, the imaging and pathological diagnosis, as well as the surgical indications and approach.

We performed a systemic search in the PubMed databases to find any publication presenting patients with coexisting PA and para/suprasellar meningioma. The search strings included the following criteria: “coexist tumo(u)r”, or “synchronous”, or “concomitant”, or “collison”, or “sellar”, or “parasellar”, or “intracranial”, or “suprasellar”. The literature review was extended for references cited in these reports, and only publications reporting synchronous PA and para/suprasellar meningioma were included. We identified 17 patients in 15 publications on sellar and para/suprasellar synchronous tumours that were published between 1956 and

Table 1
Literature review of coexisting PA and para/suprasellar meningioma.

Authors & Year	Sex/Age	PA	Meningioma	Clinical Presentation	Surgical approach	Degree of tumour Resection	Outcomes
O'Connell. 1956 [21]	F/47	Inactive/intra-suprasellar	Suprasellar	Visual loss, frontal headaches	Right subfrontal approach	NS	Improvement of visual acuity
Probst. 1971 [6]	M/48	ACTH/intrasellar	Suprasellar	Visual loss	TSS for adenoma + craniotomy for meningioma	NS	NS
Yamada K et al., 1986 [19]	F/52	Inactive/intrasellar	Parasellar	Visual loss, headache and galactorrhea	Right frontal osteoplastic approach	STR	Relieved of headache and visual loss, blood prolactin was controlled satisfactorily with drug treatment
Zentner J et al., 1989 [5]	M/46	PRL/intra-suprasellar	Planum sphenoidale	Right oculomotor paresis	Medication for prolactinoma + left pterional approach for both tumours	NS	Postoperatively course was uneventful
Laun A et al., 1993 [7]	F/61	GH/intrasellar	Tuberculum sellae	Vision loss, bitemporal hemianopia	Left pterional approach	GTR	No tumour recurrence was seen 2 years after operation
Abs et al., 1993 [2]	F/47	PRL/intrasellar	Tuberculum sellae	Aphasia, right temporary hemiparesis	Subfrontal approach for meningioma + TTS for adenoma 3 months later	GTR	NS
Gorge et al., 1993 [8]	M/53	PRL/intrasellar	Para-suprasellar	Impotence, decrease of libido and vision loss	Left frontolateral approach	NS	Left sided vision improved slightly
Prevedello et al., 2007 [13]	F/52	Inactive/intrasellar	Tuberculum sellae	Right temporal visual field loss, headache	EEA	GTR	Headache relieved and visual acuity recovered completely, but CSF leakage occurred after negative re-exploratory surgery
Basu A et al., 2010 [22]	M/39	PRL/intra-suprasellar	Parasellar	Frontal headaches, erectile dysfunction with loss of libido	Medication for prolactinoma + Left frontotemporal approach 5 year later	NS	Normal life
Mahvash et al., 2014 [12]	F/36	Inactive/intrasellar	Tuberculum sellae	Right visual field loss, headache	EEA	GTR	Visual field and visual acuity recovered completely, but developed continued hormonal dysregulation during the 6-week follow
Karsy M et al., 2015 [18]	F/70	Inactive/intrasellar	Suprasellar	Gradual decrease inmental status and increased confusion	TTS	NS	The patient could not be weaned from the extra-ventricular drain and a permanent VP shunt was placed
Amirjamshidi et al., 2017 [17]	F/37	PRL/intrasellar	Suprasellar	Headache, diplopia, visual loss and persistent oligomenorrhea	Right pterional approach for meningioma + medication for prolactinoma	GTR	Remarkable improvement of visual acuity and further medical treatment was needed
	M/42	Inactive/intrasellar	Suprasellar	Bitemporal hemianopia	TTS + Right pterional approach	GTR	Remarkable improvement of visual acuity
Zhao Y et al., 2017 [20]	F/58	GH/intrasellar	Parasellar	Acromegalic appearance, snoring and headache	TSS for adenoma + craniotomy for meningioma 3 months later	GTR	NS
	F/58	GH/intrasellar	parasellar	Acromegalic appearance and snoring	TSS for adenoma + Craniotomy for meningioma 3 months later	GTR	NS
De Vries F et al., 2019 [11]	F/75	Inactive/intrasellar	Suprasellar	Depression, fatigue weight loss and temporal visual field defect	EEA	STR	Visual fields had improved, but severe epistaxis occurred on day 12
Roethlisberge M et al., 2019 [14]	F/54	GH/intra-suprasellar	Suprasellar	Visual loss, headache and dizziness	EEA	STR	Improvement of bilateral visual field and residual tumor will receive radiosurgical treatment
Present cases	M/62	Inactive/intrasellar	Tuberculum sellae	Visual loss, left temporal visual field defect	EEA	GTR	Normal life
	F/56	Inactive/intrasellar	Cavernous sinus	Visual loss, headache	EEA	STR	Transient DI and no changes in residual tumor with GKS

PA = pituitary adenoma; F = female; M = male; NS = not stated; TSS = trans-sphenoidal microscopic; STR= subtotal resection; GTR= gross total resection; EEA = endoscopic endonasal approach; CSF = cerebrospinal fluid; VP = ventriculoperitoneal; DI = diabetes insipidus; GKS = Gamma knife surgery.

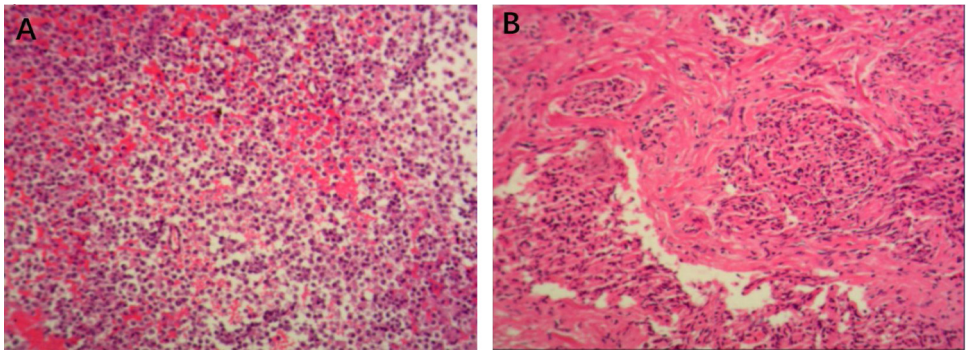

Fig. 4. Histological examination (case 2). A. The cells of adenohypophyseal component were arranged as sheets, the nucleus was round and a small amount of eosinophilic secretion can be seen. Immunohistochemical results showed GH (+), LH (−), TSH (−), ACTH (−), FSH (−), PRL (−), PR (−), P53 1% (+), EMA (−), and Ki-67 (index approximately 2%). B. High-power H&E stained micrograph showed round or oval tumour cells, and some of them were arranged in an irregular whorl formation, consistent with meningothelial meningioma. Immunohistochemical results revealed EMA (+), PR (−).

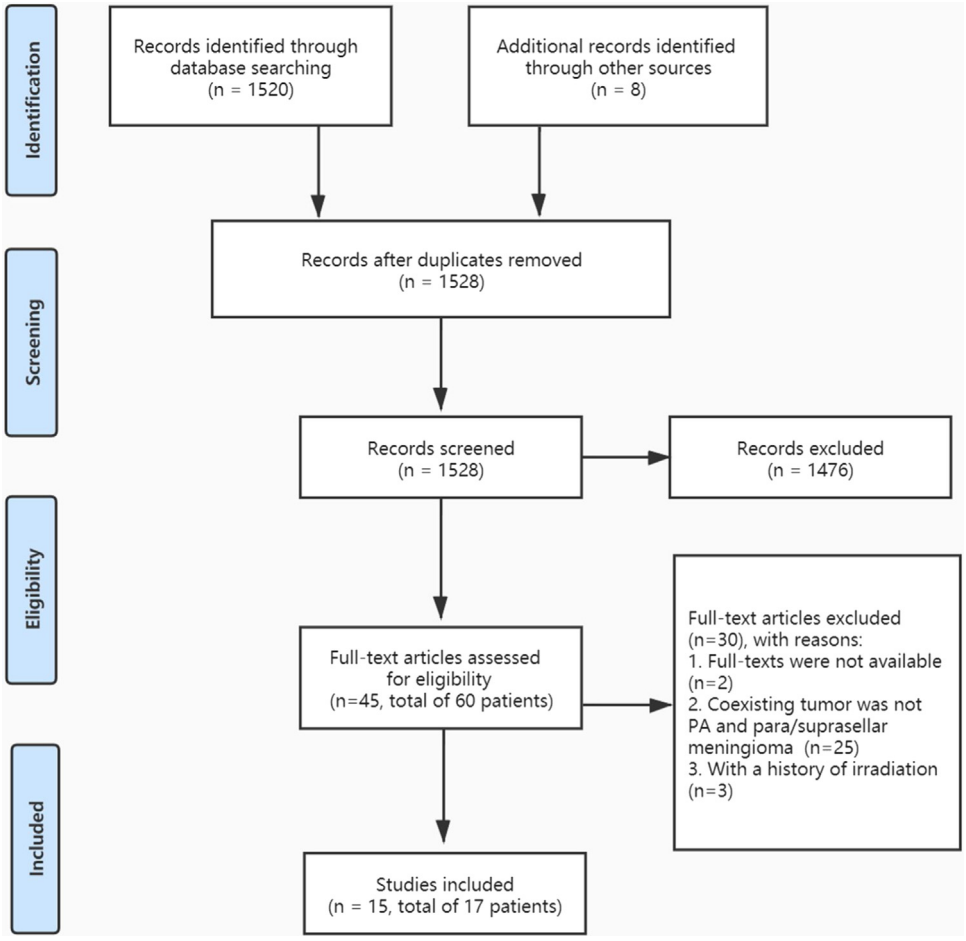

Fig. 5. Article selection process.

December 2019 (Fig. 5)[2,3,5–8,11,14,17–22]. Including the present cases, all patients had a synchronous PA and a para/suprasellar meningioma without a history of irradiation. Among these cases, the number of women was overwhelmingly majority. In classifying these cases according to the type of PA. There were 5 cases of PRL-secreting adenomas, 4 cases of GH-secreting adenoma, 1 case of ACTH-secreting adenoma and 9 cases of non-functioning adenoma. The clinical characteristics, treatment strategies and postoperative results of all patients were shown in Table 1.

The association between PAs and meningiomas has been widely explored. Several underlying pathophysiological mechanisms have been proposed to trigger the occurrence of PA with meningioma in a single patient, but the etiology is still unclear. Among them, the risk of developing a meningioma after radiotherapy for PA has been well established [23–29]. Characteristic features of these meningiomas include the localisation within the radiation field and a minimal latent period of 5 years between the irradiation and diagnosis of meningiomas. In all reported cases, although prolactinomas are general the most common PA, the GH-secreting adenomas are the most frequent coexisting with meningiomas [2,4,7,14,20,23,30,31]. Therefore, some authors thought that the GH-secreting adenoma induces the growth of meningioma, which might lead to the

transformation of arachnoid cap cells into meningioma [32–34]. However, this theory is debatable and cannot explain the occurrence of non-functioning adenomas in coexisting, as happened in our two cases [11,13,19,21,35]. Another hypothesis is that the concomitant adjacent tumours are caused by the activation of the signal pathway of receptor tyrosine kinases [3,34]. Additionally, some believed that this coexistence can be considered a pure coincidence [4,17].

Given the clinical and imaging similarities to the coexisting PA and para/suprasellar meningioma, a correct preoperative diagnosis is difficult to make based on MRI alone, especially in the cases of contiguous tumours mimicking a single tumour [9–11]. Recently, De Vries et al. [11] reported a case of a patient with unexpected concomitant PA and suprasellar meningioma. The initial MRI suggested two separate tumours on the basis of differing signals, but this distinction was disappeared during follow-up. This rare condition brought great confusion to our preoperative diagnosis. Although sometimes diagnosing the two tumours as a single entity may not result in different treatment strategies and surgical outcomes, it is important to predict this rare combination of tumours before surgery when surgical resection is necessary. In case 1, the coexisting PA and meningioma was correctly diagnosed by preoperative MRI, which showed different radiological features of the two locations. The intrasellar lesion showed a faint enhancement and displacement pituitary gland to the left, but the suprasellar lesion had a slightly higher enhancement with the broad-based, which can reach above the tuberculum sellae and planum sphenoidale (Fig. 1A and B). However, for our case 2, the simultaneous occurrence of a PA with a CS meningioma created diagnostic confusion due to the similar radiological characteristics and “encasing” with each other (Fig. 3A and B). Before the operation, we routinely considered a solitary Knosp grade IV PA invading the right CS, but during the operation, we found that there was a great difference in the tumour consistency between the sellar and CS region. The CS component had a harder consistency than the sellar tumour, and it was likely to be two different tumours. The postoperative pathological results confirmed the coexistence of PA and meningioma (Fig. 4).

For surgical removal of coexisting PA and para/suprasellar meningioma, different techniques and approaches have been described. However, any of these strategies imply a significant increase in the risk of morbidity as compared to the surgical treatment of a single PA or meningioma. In most reported cases, the coexisting tumours were treated independently, usually managing the PA first with either medical therapy or a transphenoidal approach, and then at the same time or a few months later with a transcranial approach for meningioma [2,5,6,17,20,22]. Additionally, some authors used a single transcranial (pterional, subfrontal, frontotemporal) approach for both tumours [7,8,19,21]. However, whether transcranial or trans-sphenoidal approach with microsurgery, the maneuverability and exposure of the surgery under the microscope are limited. It makes the GTR of the tumours extremely challenging to neurosurgeons. Today, endoscopy, which offers the wider close-up view of the surgical field, is widely used in the minimally invasive surgical approach for resection of sellar and suprasellar lesions (i.e., PAs, meningiomas and craniopharyngiomas). Although it has the disadvantage of increasing the rate of CSF leakage, potential advantages provided by EEA including avoiding brain retraction, improved visualisation, better protection of surrounding neurovascular structures, and shorter hospital stay [36–39]. Those advantages can also apply to the coexisting PA and suprasellar meningioma. Moreover, endoscopy may have the potential of providing a closer inspection of the tumours, which may promote the detection of different types of lesions intraoperatively [11,40]. To our best knowledge, only four previous cases of coexisting PA and suprasellar meningioma successfully resected through a pure EEA have been reported so far [11–14]. Our cases presented herein include the first example of PA coexisting with CS meningioma, also included a PA with a tuberculum sellae meningioma. Two coexisting tumours underwent an extended EEA. The former was completely resected and the latter was STR, followed by stereotactic radiotherapy (SRT) 4 weeks after the operation to prevent further tumour growth.

For the CS meningiomas, radical resection is always difficult, because it entails the risk of injury or occlusion of the ICA and may aggravate already present cranial nerve (CN) deficits or cause new ones.

At present, general consensus is that CS meningiomas should be operated on only if they have extracavernous extensions, and only these extensions should be excised surgically [41,42]. In this paper, we performed selective decompression of the CS meningioma and removed intrasellar PA as completely as possible. Although partial resection of CS meningioma helps to enhance the safety and efficacy of SRT [43,44], the risks of removing CS meningioma far outweigh the advantages. Fortunately, our case 2 has a good prognosis. Here, I hope that this case can give a warning to other neurosurgeons that in the future, when coexisting CS meningiomas and PA are encountered, the resection of CS meningioma should be suspended in time, and the patient should be recommended with Gamma knife radiosurgery after operation.

4. Conclusion

In conclusion, although very rare, the coexistence of two different tissue types of intracranial tumours has been described in patients who had not received head radiotherapy. Our reports add to the literature two cases of coexisting PA and meningioma, with different consistence in sellar and para/suprasellar regions. Furthermore, the present case adds to the evidence that in the rare situation of coexisting sellar and suprasellar tumours located in the same sagittal plane, an extended EEA allows adequate exposure and safe removal of both tumours. However, for tumours coexisting in the sellar and parasellar region in the same coronal plane, we should draw attention to this rare situation for differential diagnosis of synchronous PA and CS meningioma to avoid unnecessary surgery and to decide the best strategy for treatment.

Ethical approval

This study was approved by the ethical review committee of the First Affiliated Hospital of Nanchang University.

Human and animal rights

The authors declare that the work described has not involved experimentation on humans or animals.

Informed consent and patient details

Informed consent was not required for the studies reported in this manuscript. The authors declare that this report does not contain any personal information that could lead to the identification of the patient(s) and/or volunteers.

Disclosure of interest

The authors declare that they have no competing interest.

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Author contributions

All authors attest that they meet the current International Committee of Medical Journal Editors (ICMJE) criteria for Authorship.

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