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Endoscopic endonasal resection of nonfunctioning pituitary adenoma with radiological calcification

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Abstract

Objective Radiological calcification in nonfunctioning pituitary adenoma is scarcely rare, which appears in various formations and raises special diagnostic and therapeutic challenges. Here we present our experience about the clinical aspects and treatment of calcified nonfunctioning pituitary adenoma.

Methods A total of 145 patients who underwent surgical resection of nonfunctioning pituitary adenomas via endoscopic endonasal approach from February 2008 to December 2018 were reviewed. Among these patients, cases with radiological calcifications on preoperative imaging were included in this study. We analyzed these patients' records, radiological neuroimaging, endocrine evaluation, operative notes as well as intraoperative videos.

Results Calcification on preoperative neuroimaging was observed in only 7 patients with nonfunctioning pituitary adenomas. The study population consisted of these seven patients with intra-tumor calcification (n = 2), thin and egg shelf-like capsular calcification (n = 3), hard and armor-like capsular calcification (n = 2). In 85.7% of cases (n = 6), nonfunctioning pituitary adenomas with calcification were characterized by soft tumor texture. Evidences demonstrated apoplexy occurred in 71.4% of cases with calcified pituitary adenomas (n = 5). Patients with intra-tumor calcification as well as with thin and egg shelf-like capsular calcification underwent resection of both tumor and calcification through extra-pseduocapusual dissection via endoscopic endonasal approach. Besides, in the remaining 2 cases (28.6%), hard and armor-like capsular calcification was found surrounding a soft tumor component; however, it did not interfere with adequate removal of the soft part via endoscopic endonasal approach with the hard calcification untouched. Postoperative course of all patients was uneventful. Long term follow-up (median interval of 49 months, range 8–70 months) showed that no recurrence occurred.

Conclusions Although relatively rare, calcified nonfunctioning pituitary adenoma should be kept in mind to avoid making a wrong preoperative diagnosis. Given various calcification types, multiple surgical tactics is required accordingly. Extra-pseudocapusual resection via endoscopic endonasal approach is helpful for the resection of both adenoma and calcification.

Keywords Nonfunctioning pituitary adenoma · Calcification · Apoplexy · Endoscopic endonasal approach

Introduction

Radiological calcification of sellar lesions is most often found in craniopharyngioma, which contributes to the differential diagnosis [1, 2]. However, calcification can also be observed very rarely in pituitary adenomas with radiological frequencies of only 0.2% to 8%, most of which are functioning adenomas [3–5]. So far, there are little calcified nonfunctioning adenomas (NFPAs)documented in the English literatures [4, 6–9], the clinical aspects and treatment tactics of this rare pathology are far from understanding. Here we presented seven cases harboring calcified NFPAs who underwent resection of adenomas via endoscopic endonasal approach (EEA). Our case series highlight this imaging feature because either from the prognostic or therapeutic point of view distinction is important, considering the varied and more aggressive behavior of craniopharyngiomas as compared with NFPAs. Additionally, we discuss important clinical aspects and possible treatment tactics of such rare clinical phenomenon.

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Methods

Patients and calcification

After receiving ethics committee approval, we retrospectively analyzed our series of 145 consecutive patients who underwent endoscopic resection of NFPAs via EEA from February 2008 to December 2018. Inclusion criteria required primary NFPAs with calcification. Recurrent cases and patients with radiotherapy or medical therapy history as well as scans with artifacts or other non-calcified hyperdense materials were excluded. Informed consents were obtained from all the enrolled patients in the study.

Based on CT (axial, coronal or sagittal), calcifications were meticulously assessed by two senior imaging doctors who were blinded to the clinical data of the patients. Calcifications were interpreted according to the neuroimaging characteristics and included two major categories: (1) intra-tumor calcification (type1) and (2) capsular calcification (type2), the latter could be further classified into two subtypes: thin and eggshell-like calcification (type2A); hard and armor- like calcification (type2B). The classification of the calcification was shown in Fig. 1. All cases with radiological calcifications on preoperative imaging were included in this study. We reviewed these patients' records, radiological images, endocrine evaluation, operative notes as well as intraoperative videos.

Surgical procedures

A standard binostril EEA was routinely used. The bone covering the anterior and inferior surfaces of the sella is removed to expose the margin of carvenous sinus and intercarvenous sinus. The dura mater is opened carefully with the below surface of the pituitary (the pituitary capsule) intact. After wide exposure of the sella turcica, the concept of extra-pseudocapsual dissection was implemented throughout the process of resection [10]. When the adenoma was too large for en block evacuation, internal debulking was typically required to facilitate the extra-pseudocapsual dissection. Our tactics to deal with the calcification was illustrated in Fig. 2. The closures were performed in a multilayer fashion. A pedicled nasoseptal flap was required for the case with intraoperative cerebrospinal fluid (CSF) leakage.

Diagnostic protocol of the included cases

The diagnosis of NFPAs was demonstrated by hormonal evaluation and histopathological as well as immunohistochemical studies. The apoplexy of the adenoma was evidenced by clinical manifestation, radiological imaging and histopathological evaluation [11].

Visual Assessment

Vision of each patent was assessed via visual impairment scores (VISs), which was developed by the German

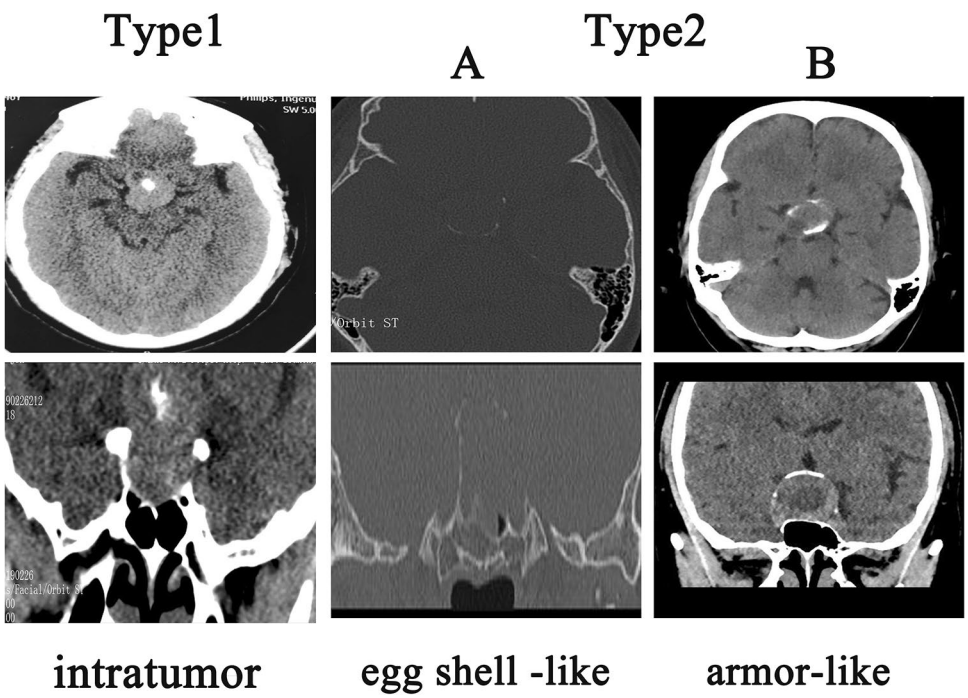

Fig. 1 Type of calcification

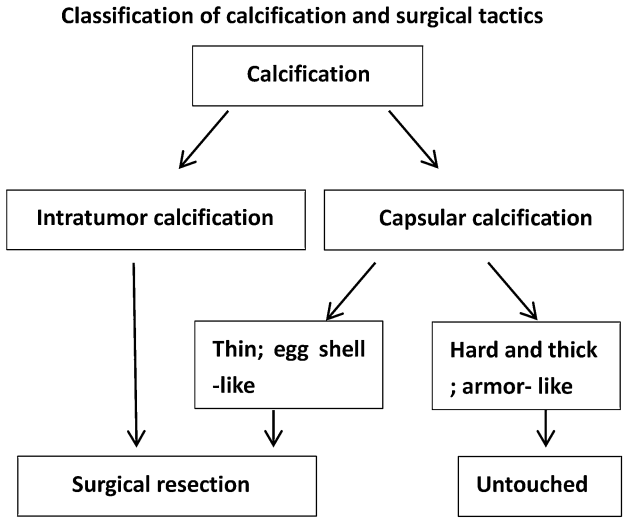

Fig. 2 The diagram shows surgical tactics for calcification

Ophthalmological Society [12]. According to the scores obtained (range 0–100), visual impairment could be further divided into the following 4 grades: grade 1 (score 0–25), no or minimal; grade 2 (score 26–50), moderate; grade 3 (score 51–75), severe; and grade 4 (score 76–100), subtotal or complete visual impairment.

Results

Patients and calcification

Following of inclusion and exclusion criteria, seven patients were enrolled in the study (Table 1); the mean age was 51 years (range 40–71 years). Patients presented with headache in five, visual lose in six, visual field defection in five patients. Acute aggravation in the course was recorded in 4 patients. Hypopituitary was found in one patient before operation. 2 patients exhibited intratumor calcification, while the remaining 5 cases were capsular calcification with eggshell-like calcification in 3 patients, armor- like calcification in 2 patients. Pituitary apoplexy was demonstrated in 5 patients. 85.7% of cases (n = 6) were characterized by soft tumor texture.

Patient outcomes

Patients with intra-tumor calcification and with thin and egg shell-like capsular calcification underwent resection of both tumor and calcification. We suggested extra-pseudocapsual resection had its advantage in the resection of the calcification. Besides, in the remaining 2 cases (28.6%), evidence of hard and armor- like capsular calcification were seen surrounding a soft tumor component; however, it did not interfere with adequate removal of the soft part with the hard calcification intact. The surgical course was uneventful. Four patients were gonadotrophic adenomas while the remaining patients were null-cell adenomas. After operation, 3 patients underwent transient diabetes insipidus and recovered before discharging. Intraoperative cerebral spinal fluid leakage occurred in five patients, which disappeared post operation through careful repair of sella turcica with vascularized nasal septal flap. Neither infection nor death occurred after operation. Obvious decreasing of VISs was found in five patients and VISs grade improved in four patients after operation. No patients experienced persistent hypopituitary after operation. Long term follow-up (median interval of 49 months, range 8–70 months) indicated that no recurrence occurred.

Case presentation

A 43-year-old male patient was admitted with complaints of headache and blurred vision for 3 years. Paranasal CT scans revealed a well-circumscribed calcified mass lodged in the sellar region (Fig. 3a, b); Its CT value was approximately 350 Hounsfield units, whereas that of cranial bone was about 500 Hounsfield units. MR images of the patient revealed a contrasting, heterointensity, well-circumscribed lesion in the same area (Fig. 3c, d). The tumor expanded

Table 1 Data of enrolled calcified nonfunctioning pituitary adenoma

Case	Age	Gender	Type	Headache	VISs		Evidence of apoplexy	Consistency	Hardy score	Hypopituitary	
					Preop.	Postop.				Preop.	Postop.
1	59	M	1	Y	12	12	N	Soft	B	N	N
2	71	F	2A	Y	59	33	Y	Soft	B	N	N
3	43	M	2B	Y	74	50	Y	Soft	B	N	N
4	58	M	1	Y	87	85	Y	Soft	C	Y	N
5	40	F	2B	N	50	20	Y	Soft	B	N	N
6	44	M	2A	N	68	51	Y	Soft	B	N	N
7	42	F	2A	Y	35	15	N	Hard	B	N	N

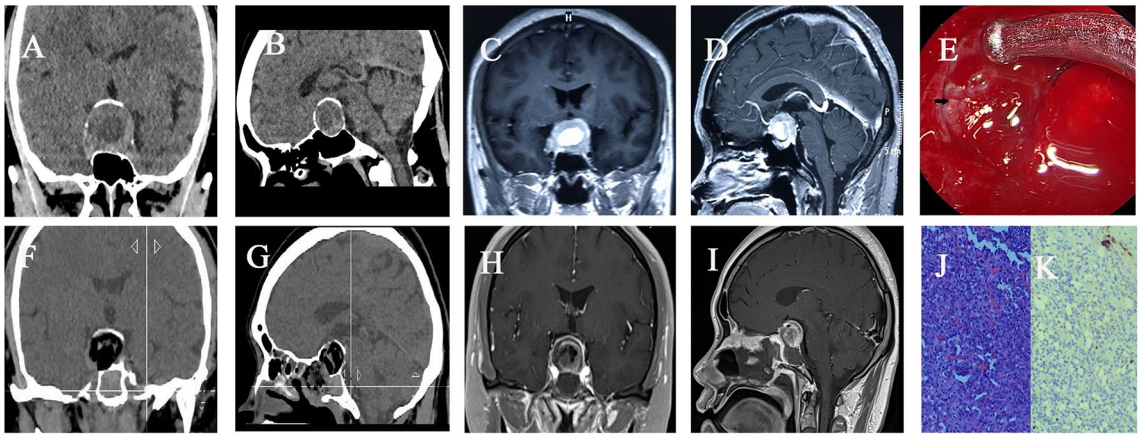

Fig. 3 The patient is a 43-year-old man with hard and armor-like capusual calcification. **a**, **b** calcification in axial and coronal CT imaging before operation; **c**, **d** MR images of the patient revealed a contrasting, heterointensity, well-circumscribed lesion in the same area. **e** Intraoperative imaging indicates armor-like capusual calcification(arrow); **f–i** Postoperative CT and MR imaging indicated residual calcification; **j**, **k** Postoperative pathology demonstrated a nonfunctioning pituitary adenoma

into suprasellar region with less lateral expandation, and compressed the chiasma. It was thus classified into armor-like capsular calcification (type2B). Clinical examination of the patient revealed bitemporal hemianopsia and vision loss without any other positive neurological signs. His hormonal evaluation is normal.

The patient underwent operation via EEA. The solid portion of the adenoma was soft while the calcification was hard and adherent to surrounding structure, which corresponded to the armor-like calcification in our classification. So we resected the solid portion of the adenoma via extrapseudocapsule dissection with calcification untouched after balancing against functional compromise (Fig. 3e), which was demonstrated by postoperative imaging (Fig. 3f–i). Postoperative histopathology demonstrated a null cell adenoma (Fig. 3j, k). His VISs decreased from 74 (grade 3) to 50 (grade 2) after operation and no recurrence was confirmed during his follow-up for 28 months.

Discussion

At present, only 9 studies of calcification in NFPAs have been documented in English literatures [4, 6–9, 13–16]. However, all these studies are case report. We here present a relatively large series of calcified NFPAs focused on the clinical aspects and possible surgical tactics. Our present study confirmed the possible occurrence of NFPAs with radiological calcification and highlighted the importance of endoscopy in resection of such lesions. To the best of our knowledge, our cases are the largest series about the calcification in NFPAs. Compared with the previous case report, our case series offered good illustration and detailed classification as well as subsequent surgical tactics of calcified NFPAs.

The calcification of pituitary adenoma raises special diagnostic challenges, which often masquerades as craniopharygioma. Compared with hormone-secreting pituitary adenoma, calcified nonfunctioning pituitary adenoma is more difficult to differentiate from craniopharygioma, because of less distinctive clinical evidences. Given the origination of pituitary adenoma, the sella turcica of the case with pituitary adenoma usually extends and the remaining normal pituitary gland is displaced to the posterior or lateral side of the adenoma instead of the bottom of sella turcica. These may help to differentiate calcified NFPAs from craniopharyngiomas. As little information is helpful for the differential diagnosis, therefore, we suggest that clinical vigilance is of critically importance.

The exact mechanism involved in the calcification of pituitary adenoma remains totally obscure and controversial. As most calcified pituitary adenomas in the literature are hormone-secreting adenomas and nonfunctioning adenomas are considered to be seldom calcified [6], many scholars believe the increased serum level of hormone produced by the adenoma plays an important role in calcification [6, 17–20]. Prolactinomas tend to be calcified more often, which were reported to account for 76.9% of pituitary adenomas with radiological calcification [21]. It is obviously that different underlying pathologies leads to the development of calcification in NFPAs. Some studies believed insufficient tumor blood supply may trigger osteoid metaplasia [6, 22]. Clinical manifestation and evidences from pathological studies demonstrated the occurrence of pituitary apoplexy in most of our cases, so we suggest massive degeneration secondary to pituitary apoplexy may have an important role in the calcification

in these NFPAs. The macroadenoma seems to be more susceptible to calcification than the microadenoma in NFPAs. However, the diagnosis of NFPAs may be delayed because of more insidious presentation than hormone secreting pituitary adenomas, which may result in more calcification in macroadenomas.

Extra- pseduocapusual dissection of the tumor from the surrounding gland and dura is a great progress in the surgical tactics of pituitary adenomas which allows safe dissection and prevention of unnecessary manipulation that can damage the normal adenohypophysis and the arounding nerves and vessels [23]. Growing evidences have demonstrated that extra-pseduocapusual resection improves the rate of gross total resection, remission rates, as well as the resolution of preoperative visual impairment [24, 25]. So the concept of extra-pseduocapusual resection has been recommended for all the pituitary adenomas and throughout the course of resection of the tumor. However, the narrow operative field and compromise visibility under microscope limited the application of extra-pseduocapusual resection especially in macroadenoma. Instead, endoscope results in improved visibility of the tumor margins as the tumor is centrally decompressed and the remaining tumor descends and the normal gland expands. This advantage, particularly during surgery for macroadenomas, facilitates the extrapseduocapusual dissection via endoscope. Moreover, endoscopic endonasal approach allows for the creation of a pedicled nasoseptal flap for repair of cerebrospinal fluid (CSF) leakage, which creates a durable, vascularized barrier and is effective in preventing postoperative CSF fistulas. So, we generally recommend that endoscopic surgery be undertaken preferentially over microscope.

Whether the calcification can be removed depends largely on its type, not only its quality. We found intratumor calcification were relatively easy to be removed via extra-pseduocapusual resection, while resection of capsular calcification is generally considered to be challenging, which should be balanced with the risk of the management. Our experience indicates it is possible to resect the thin and eggshell-like capsular calcification through extra-pseduocapusual resection via EEA, which might be dissected as a part of pseudocapsual. As for hard and armor-like calcification, we propose to resect the solid portion of the adenoma and leave the hard and adherent calcification intact to avoid subsequent potential complications. Rasmussen et al. [5] believed that pituitary calcifications represent a benign and regressive process with less concern of recurrence, which was content with other studies [17, 19]. Although follow-up of our two cases with hard and armor-like calcification for 28 months and 49 months respectively indicates no sign of recurrence, the concerns about the recurrence caused by the residual calcification still remains, which requires more cases and longer follow-up.

Conclusions

Although scarcely rare, calcified NFPAs should be taken into account to make the correct preoperative diagnosis for proper management. The radiological assessment of the type and the quality of the calcified NFPAs plays an important role in predicting the feasibility of tumor removal. Depending on the results of the preoperative evaluation, the extra-pseduocapusual resection via EEA could be an effective, feasible option for removing such tumors.

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Compliance with ethical standards

Conflict of interest The authors declare there is no conflict of interest that would prejudice the impartiality of this scientific work.

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