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# Intrasellar symptomatic salivary gland: case series and literature review

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## Abstract

**Purpose** Ectopic salivary glands have been found in both extracranial and intracranial locations, however, intrasellar symptomatic salivary gland is extremely rare and its clinical manifestation, radiological characteristics and outcome have not been systematically studied. Here we present a case series of intrasellar symptomatic salivary gland and perform a literature review to better characterize this disease.

**Methods** We retrospectively reviewed the data of three patients with intrasellar symptomatic salivary gland from our institutional and other cases available in literatures. Information for sex, age at diagnosis, clinical symptoms, radiological features, treatment strategy and prognosis were recorded.

**Results** A total of 11 cases (including our own) were identified. There were three men and eight women, with an average age at diagnosis of 28.3 years. The peak incidence was in the second and the third decade (72.7% of all cases). The most common symptom was headache (81.8% of all patients). About 63.6% patients had one or more abnormal hormone levels, and prolactin was likely the most vulnerable hormone. The radiological appearances of intrasellar salivary gland were various, and four cases mimicked pituitary adenoma radiologically. All patients underwent transsphenoidal surgery with no mortality.

**Conclusion** Although intrasellar symptomatic salivary gland is rare, it should be considered in the differential diagnosis of intrasellar lesions. Preoperative diagnosis is challenging since it mimics pituitary neoplasm in clinical and radiological manifestations, and confirmation for this disease could only be conducted through pathological examination. Transsphenoidal surgical resection is the preferred therapy and the patient prognosis is usually good.

**Keywords** Ectopic salivary gland · Intrasellar lesion · Pituitary gland · Transsphenoidal surgery

## Introduction

Ectopic salivary glands are known to develop both intracranially and extracranially. Sellar region is a common place where ectopic salivary glands take place, and approximately 3.39% of autopsy cases had ectopic intrasellar salivary gland, all of which appeared asymptomatic [1]. However, few cases of intrasellar symptomatic salivary gland have been reported [2–9]. Intrasellar salivary gland mimics pituitary adenoma in clinical and radiological manifestations, making it difficult to diagnosis before surgery [2, 7]. Here we report three patients with intrasellar symptomatic salivary glands that were diagnosed and treated at our institutional neurosurgery department from November 2008 to May 2018. We also review the literatures related to intrasellar salivary gland in the last 30 years and discuss the clinical manifestations, possible pathogenesis, radiological features, pathologic findings, treatment strategies for this rare disease.

## Case reports

### Case 1

A 57-year-old woman presented with 1-year headache. Neurologic examination and pituitary hormones tests were both normal. Magnetic resonance imaging (MRI)

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showed a mass (46 mm in diameter) in the sellar region, which was isointense on T1-weighted images (T1WI), iso-hyperintense on T2-weighted images (T2WI) (Fig. 1a) and heterogeneously enhancing after gadolinium administration (Fig. 1b). The initial diagnosis was chordoma. Subtotal excision was undergone for the patient through transsphenoidal surgery. Histological examination showed fragments of normal pituitary tissue mixed with salivary tissue, which organized in lobules of seromucous glands (Fig. 1c, d). Complete work-up of the surgical specimen did not give evidence of neoplastic lesion. The histological diagnosis was ectopic salivary gland. Postoperatively, plasma hormone levels of thyroid stimulating hormone (TSH), triiodothyronine, free triiodothyronine were transiently reduced. No progress had been observed in the one-year period after surgery.

## Case 2

A 36-year-old woman presented with 15-year headache. No other neuro-ophthalmological symptoms were present. Hormonal assays showed a high level of TSH, low levels of free tetraiodothyroxide and growth hormone (GH), and normal levels of other pituitary hormones, such as prolactin (PRL). MRI demonstrated 8 × 17 × 13 mm lesion in the posterior part of pituitary gland, which was hypointense

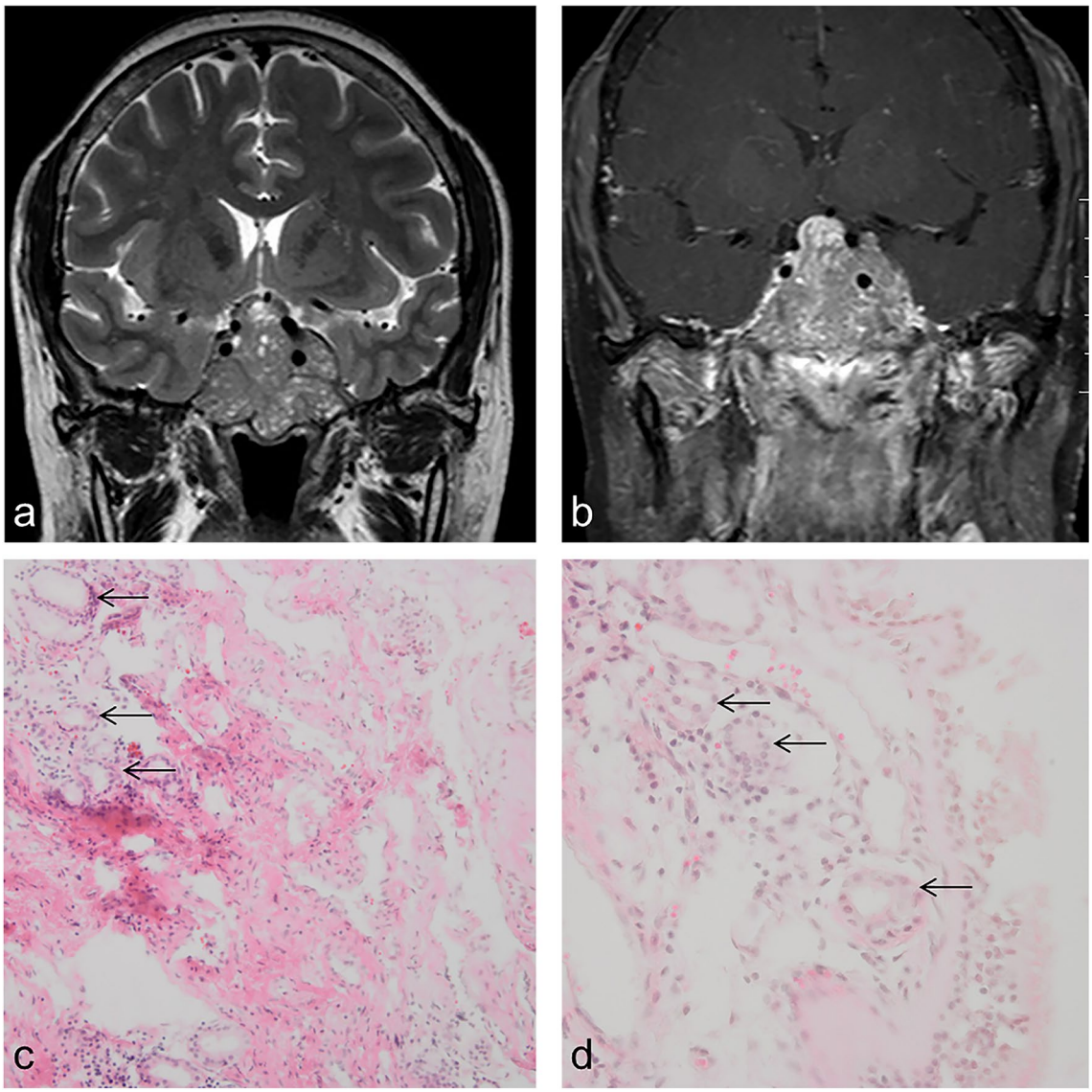


**Fig. 1** Magnetic resonance imaging (MRI) and histopathology of case 1. **a**, **b** Preoperative MRI shows a mass in the sellar region which surrounds bilateral internal carotid arteries on coronal T2-weighted image (**a**) and contrast-enhanced T1-weighted image (**b**). **c**, **d** Histological sections stained by hematoxylin and eosin (**c** original magnification × 200; **d** original magnification × 400). Black arrows point to salivary tissue organized in lobules of seromucous glands

on T2WI (Fig. 2a) and mild hyperintense on T1WI. There was no enhancement after gadolinium administration (Fig. 2b). The diagnosis before surgery was pituitary adenoma or Rathke's cleft cyst. Gross total resection via an endoscopic transnasal approach was performed. Intraoperatively, the lesion presented as cystic mass, which was filled with translucent gelatinous content. Histological examination showed scattered islands of seromucous glands mixed with fragments of simple columnar epithelium, constituting the lining of the Rathke's cyst (Fig. 2c, d). The histological diagnosis was ectopic salivary gland accompanied by Rathke's cleft cyst. Postoperatively, no further neurological deficits were present and repeated. MRI examination documented the absence of evident abnormalities. There was no recurrence during the four-year follow up.

## Case 3

A 48-year-old woman presented with 8-month nausea accompanied by progressively blurred vision in both eyes for 1 year. Endocrine evaluation revealed a low level of testosterone (T). MRI showed a mass (17 mm in diameter) in the sellar region, which was isointense on T1WI and

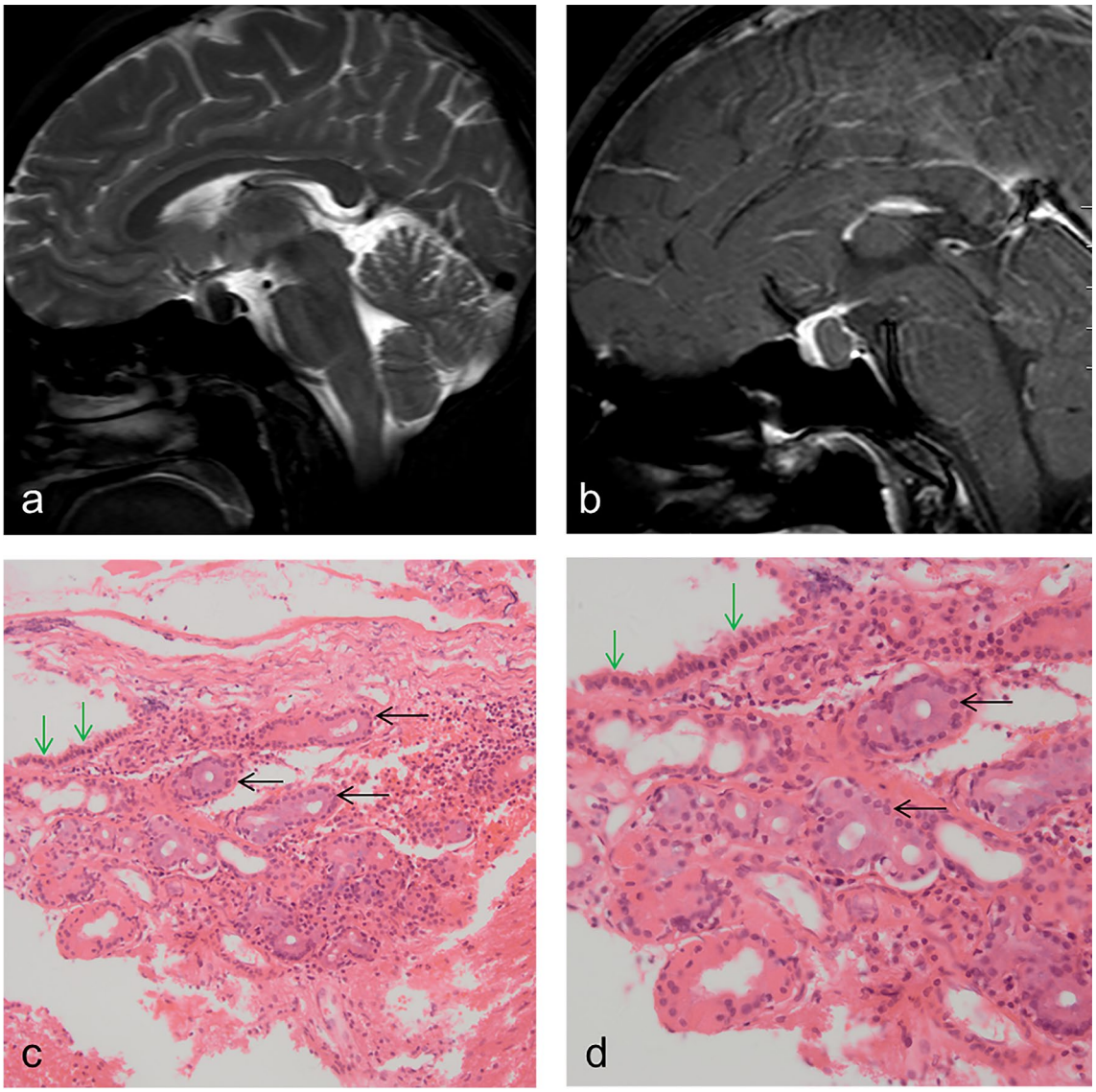


**Fig. 2** Magnetic resonance imaging (MRI) and histopathology of case 2. **a**, **b** Preoperative MRI displays a lesion in the posterior part of pituitary gland on sagittal T2-weighted image (**a**) and contrast-enhanced T1-weighted image (**b**). **c**, **d** Histological sections stained by hematoxylin and eosin (**c** original magnification × 200; **d** original magnification × 400). Black arrows point to scattered islands of seromucous glands, and green arrows point to simple columnar epithelium constituting the lining of the Rathke's cleft cyst

mild hyperintense on T2WI (Fig. 3a). Rim enhancement was found after gadolinium administration (Fig. 3b). Pituitary adenoma was suspected through preoperative imaging. The patient underwent transsphenoidal excision of the lesion. Upon microscopy, there were some fragments of squamous and ciliated columnar epithelium, constituting the lining of the Rathke's cyst (Fig. 3c, d). In addition, scattered islands of seromucous glands were also found. Therefore, the histological diagnosis was ectopic salivary gland accompanied by Rathke's cleft cyst. The patient showed improved symptom without hormonal deficiency after surgery. No recurrence was observed after the one-year follow up.

## Literature review

The literature review was conducted on MEDLINE and EMBASE databases with the following keywords: salivary gland, sella turcica, and pituitary gland. A total of 11 cases (including our own) with intrasellar symptomatic salivary gland were identified since 1988 (Table 1). In the present

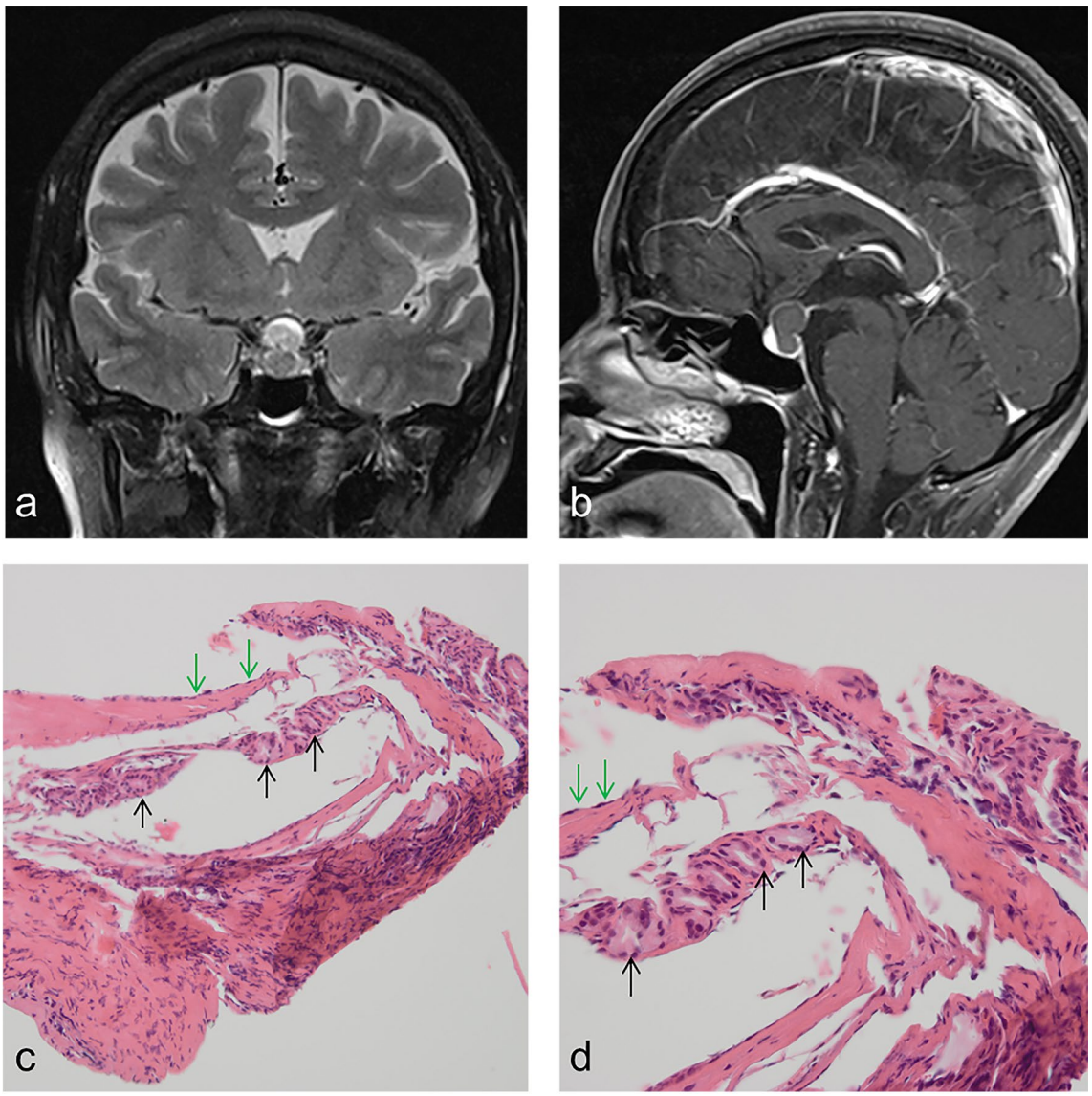


**Fig. 3** Magnetic resonance imaging (MRI) and histopathology of case 3. **a**, **b** Preoperative MRI shows a mass mimicking pituitary adenoma in the sellar region on coronal T2-weighted image (**a**) and sagittal contrast-enhanced T1-weighted image (**b**). **c**, **d** Histological sections stained by hematoxylin and eosin (**c** original magnification × 200; **d** original magnification × 400). Black arrows point to scattered seromucous glands, and green arrows point to squamous epithelium constituting the lining of the Rathke's cleft cyst

series of 11 patients, there were 3 male (M) patients and 8 female (F), whose ages ranged from 11 to 57 years, with an average age at diagnosis of 28.3 years. The peak incidence was in the second and the third decade (72.7% of the cases). The most common presenting complaint was headache, accounting for 81.8% (9/11) of all patients. Among the women in the third decade, 75% (3/4) developed galactorrhea and menstrual irregularities with different degrees, and two of them had mild hyperprolactinemia which might be caused by compression of pituitary stalk. Other symptoms including visual deficit, nausea and growth retardation had also been reported. About 63.6% (7/11) had one or more abnormal hormone levels. PRL was likely the most vulnerable hormone in intrasellar salivary gland, accounting for 57% (4/7) in patients with hormone abnormality. Besides, abnormal levels of TSH and GH had also been reported.

## Discussion

Ectopic salivary glands have been found in various extracranial and intracranial locations, including larynx, esophagus, large intestine, middle ear, chest wall, optic nerve sheath, cerebellopontine angle [10–16]. Schochet found that salivary gland tissue fragments in the posterior lobe of pituitary gland in 78 of 300 (3.39%) serial necropsy cases [1]. Then Rittierodt got a higher rate in pituitary slides

**Table 1** Summary of Patients with intrasellar symptomatic salivary gland in last 30 years

| Author and year | Sex/age (years) | Symptom | Abnormality of hormone | MRI | | | | Therapeutic method | Outcome |
|---|---|---|---|---|---|---|---|---|---|
| | | | | Size, cm | T1WI | T2WI | Enhanced | | |
| Kato et al. (1988) [9] | M/11 | Growth retardation | GH↓ | NS | Hyperintense | Hypointense | NS | Transsphenoidal | Diabetes insipidus |
| Tatter et al. (1995) [8] | F/22 | Headache, galactorrhea menstrual irregularities | PRL↑ | 1.2 | Isointense | Iso-hypointense | No enhancement | Transsphenoidal | Uneventful |
| Kim et al. (2007) [6] | F/19 | Headache, nausea, visual deficit | None | 1.8 | Hyperintense | NS | Show enhancement | Transsphenoidal | Diabetes insipidus |
| Chen et al. (2007) [7] | F/28 | Headache, galactorrhea menstrual irregularities | PRL↑ | 0.6 | Isointense | Isointense | Less enhancement | Transsphenoidal | Diabetes insipidus |
| Ranucci et al. (2013) [3] | M/17 | Headache, nausea | PRL↑ | 1.9 | NS | NS | No enhancement | Transsphenoidal | Uneventful |
| Stefanits et al. (2013) [2] | F/23 | Headache, galactorrhea menstrual irregularities | None | 1.5 | Hyperintense | NS | No enhancement | Transsphenoidal | Diabetes insipidus, hypopituitarism |
| Hwang (2013) [5] | F/26 | Headache | None | 1.9 | Hyperintense | Hypointense | No enhancement | Transsphenoidal | Diabetes insipidus |
| Tanaka et al. (2015) [4] | M/24 | Headache, visual deficit | TSH↓, PRL↓ | 1.6 | Hyperintense | Hypointense | Rim enhancement | Transsphenoidal | Diabetes insipidus |
| In present | F/57 | Headache | None | 4.6 | Isointense | Heterogeneous (iso-hyperintense) | Heterogeneous enhancement | Transsphenoidal | Hypopituitarism |
| In present | F/36 | Headache | TSH↑,GH↓ | 1.7 | Hyperintense | Hypointense | No enhancement | Transsphenoidal | Uneventful |
| In present | F/48 | Nausea, visual deficit | T↓ | 1.7 | Isointense | Hyperintense | Rim enhancement | Transsphenoidal | Uneventful |

*MRI* magnetic resonance imaging, *T1WI* T1-weighted images, *T2WI* T2-weighted images, *M* male, *F* female, *TSH* thyroid stimulating hormone, *GH* growth hormone, *PRL* prolactin, *T* testosterone, *NS* not stated

cut sagittally, around 8.8% (20 of 228 cases) had salivary gland cell groups in the pars intermedia of pituitary gland [17]. To our best knowledge, only 8 cases of symptomatic ectopic salivary glands within the pituitary gland have ever been reported, and some cases are complicated by Rathke cleft cyst [2, 3]. Among the 3470 sellar lesions at our department in the last 10 years, there are only 4 cases with intrasellar symptomatic salivary gland, and one was excluded for failing to be followed up. Meanwhile, there was a female preponderance for intrasellar symptomatic salivary gland. In the present series, 72.7% of the patients with intrasellar symptomatic salivary gland were female.

The presence of salivary gland tissue in the sellar region may involve the development of the pituitary gland. Embryologically, Rathke pouch migrates from the primitive oral cavity towards the base of the brain and fuses with an extension of the third ventricle to form pituitary gland. Meanwhile, salivary gland which develops from primitive oral cavity epithelium is transferred to the sellar region within the wall of Rathke's pouch. Therefore, the ectopic salivary gland tissue is probably the direct transfer of preexisting seromucous glands from the primitive oral cavity to the sellar region, driven by the Rathke's pouch migration. This is why Rathke's cleft cyst is often complicated with intrasellar salivary gland, which usually communicates with the cystic cavity. An alternative explanation is the differentiation from primitive pituitary epithelium to salivary gland tissue. Kusakabe et al. reported that during the organogenesis of the mouse's anterior pituitary, there was a developmental stage when pituitary epithelium could respond to the heterotopic submandibular gland mesenchyme, leading to subsequent development of a submandibular gland-like tissue [18]. Thus, it is possible that during human embryogenesis, salivary gland mesenchyme which is accompanied by the migration of Rathke's pouch, could induce primitive pituitary epithelium to differentiate towards salivary gland tissue.

The radiological appearance of intrasellar salivary gland can be quite variable. The three patients in our department present hyperdensity on CT, which is consistent with previous literatures [5, 9]. MRI commonly reveals well-defined, intrasellar masses with or without compression of optic chiasm, which are hyperintense or isointense on T1WI, and hypointense or isointense on T2WI. Typically, there was no enhancement or just rim enhancement after gadolinium administration. All reports mentioned the size of the lesion through MRI except one case. The average diameter was 1.85 cm, ranging from 0.6 cm to 4.6 cm. However, these radiologic features are nonspecific and could be found in other sellar lesions, especially pituitary adenoma. Pituitary adenoma typically shows hypointense or isointense signal on the precontrast T1WI, variable signal on T2WI and decreased degree of enhancement compared with the normal pituitary gland [19, 20]. Therefore, it is difficult to distinguish intrasellar salivary gland from pituitary adenoma through the image. In the present series of 11 patients, four cases mimicked pituitary adenoma radiologically, which led to preoperative misdiagnosis. Besides, one case in our department has predominantly isointense T1WI signal, hyperintense T2WI signal and heterogeneous enhancement with bone destruction, which makes it very similar to chordoma radiologically [21, 22].

Intrasellar salivary gland is typically benign and self-limiting, but the disease may be persistent and progressive. Stefanits et al. concluded that the progressive growth is due to active mucous secretion within the ectopic glands, which might be driven by parasympathetic innervation [2]. Moreover, it is possible that intrasellar salivary gland undergoes neoplastic transformation, giving rise to salivary gland-like tumor [23–27]. Based on our experience and review of the literature, surgery is the preferred method to make a diagnosis and achieve rapid improvement of neurologic symptoms. In the present series of 11 patients, all underwent transnasal transsphenoidal surgery to remove the lesion, and none received postoperative chemotherapy or radiotherapy. Intraoperatively, the 11 lesions are all cystic and filled with gelatinous fluid, which can be white, yellow, or gray substance. Additionally, all 11 cases were histologically confirmed and seemed to show similar features: there were scattered islands of seromucous glands filled with mucus. In some cases, the glandular lumina is communicated with a cystic cavity., and the cells lining the cyst walls can be ciliated or nonciliated columnar epithelium, or squamous epithelium, which is compatible with Rathke's cleft cyst. There was no mortality in 11 cases after surgery. One significant postoperative complication is diabetes insipidus, which could be found in more than half of the patients. Two patients had hypopituitarism and received replacement therapy. In our 3 patients, clinical symptoms resolved postoperatively, and no recurrence occurred for at least a 1-year follow up.

## Conclusion

Intrasellar salivary gland, although rarely symptomatic, should be taken into consideration in the differential diagnosis of intrasellar lesions. It mainly involves females and can cause symptoms such as headache, galactorrhea, menstrual irregularities and visual deficit, mimicking pituitary neoplasm in clinical and radiological manifestations. The diagnosis of ectopic salivary gland could only be confirmed by pathological examination. Transsphenoidal surgical resection appears to be an adequate treatment for this disease and the patient prognosis is often good.

**Author contributions** ZL participated the study conception, performed the literature search and revised the manuscript. YZ participated the study conception, collected data and drafted the manuscript. RF performed the literature search and data analysis. ZT collected the image data. YR and YL collected and analyzed the pathological pictures of patients. JX participated the study conception and manuscript revision.

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## Compliance with ethical standards

**Conflict of interest** The authors declare that they have no conflict of interest.

**Ethical approval** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

**Informed consent** Informed consent was obtained from all individual participants included in the study.

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