# CT finding of ectopic pituitary adenoma: Case report and review of literature

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*Background.* Ectopic pituitary adenoma was first described by Erdheim in 1909, about 100 cases have been reported in literature, to the best of our knowledge, an ectopic pituitary adenoma located in the parapharyngeal space has not been reported thus far.

*Method.* A 59-year-old woman presenting with a neck lump, which was painlessness and growing, was without any neurological disorders or endocrine disorders. Auxiliary examinations included ultrasound, electronic nasopharyngolaryngoscopy, endocrine assessment, CT, and CT angiography.

*Results.* A CT scan showed a soft tissue density mass with clear boundary involving the carotid sheath area. The contrast-enhanced CT scan showed heterogeneous density. Tissues around the mass were pushed and displaced. CT angiography showed the mass was hypervascular and supported by the right internal carotid artery and branches of the external carotid artery. The tumor underwent a total removal and was confirmed as an adenoma with pituitary cells by histopathologic examinations, and postoperative recovery went well.

*Conclusion.* It is rarely seen that a pituitary adenoma is ectopic to the parapharyngeal space. Diagnosis is difficult and mainly depends on the postoperative pathological examination.  *Head Neck* **37**: E120–E124, 2015

**KEY WORDS: pituitary gland, ectopic, CT, adenoma, parapharyngeal space**

## INTRODUCTION

Pituitary adenoma is usually a benign intrasellar tumor, which could be observed in all ages. The incidence of pituitary adenoma is about 1 per 10,000 in the population. Ectopic pituitary adenoma is defined as adenoma that occurs outside the sella without any continuity with the normal pituitary gland.[1] Ectopic pituitary adenoma was first described by Erdheim in 1909, about 100 cases had been reported in literature, to the best of our knowledge, an ectopic pituitary adenoma located in the parapharyngeal space has not been reported thus far. We report 1 case of parapharyngeal space ectopic pituitary adenoma, mainly described by the CT findings, and a detailed review of the literature is included.

## CASE REPORT

A 59-year-old woman had noticed a painless lump on her neck for 2 years and found that it was gradually enlarging in recent days. General physical examination revealed a sharply demarcated, mobile, and nontender subcutaneous mass under the right earlobe, about 2.5 cm in diameter, without skin flush, tumefaction, macula, or canker. There were no neurological or endocrine disorders.

Color ultrasonography revealed an abnormal echo below the earlobe on the right side of the neck, which was adjacent to large vessels, with a size of 2.3 cm × 3.3 cm, ill-defined, mostly low echo levels (see Figure 1), and the color Doppler flow imaging showed abundant blood stream signal, therefore, the mass was considered to be a tumorous lesion (see Figure 2). Electronic nasopharyngolaryngoscopy found that the nasopharyngeal mucosa was smooth, and the infundibuliform recess was clear. The laryngeal mucosa was smooth and showed chronic congestion, both vocal cords were swelling, with a normal movement and closure, and the bilateral pyriform fossa were smooth. CT and CT angiography revealed a homogeneous soft tissue density mass with clear boundary involving the carotid sheath area, and the size of the mass was about 2.2 cm × 4.2 cm. The contrast-enhanced CT showed heterogeneous density. Tissues around the mass were pushed and displaced (Figures 3–6). CT angiography showed the mass was hypervascular and mainly supported by the right internal carotid artery and branches of the external carotid artery, and the major vessels were tortuous (Figure 7). The internal jugular vein was displaced posterolaterally and the internal carotid artery was displaced ahead and medially, which was considered as a neoplastic lesion in the carotid sheath area, likely to be a neurogenic tumor or neurilemmoma. Laboratory examination showed that the liver, kidneys, and blood coagulate functions of the patient were unremarkable, and a routine blood and electrolyte test showed negative findings. Thyrotropin-releasing hormone was 3.52 uIU/mL, and estradiol was <20 pg/mL, both were within the normal range.

The patient underwent a resection of the right parapharyngeal space tumor while under general anesthesia. Intraoperatively, there was an inverted cone, toughness, well-

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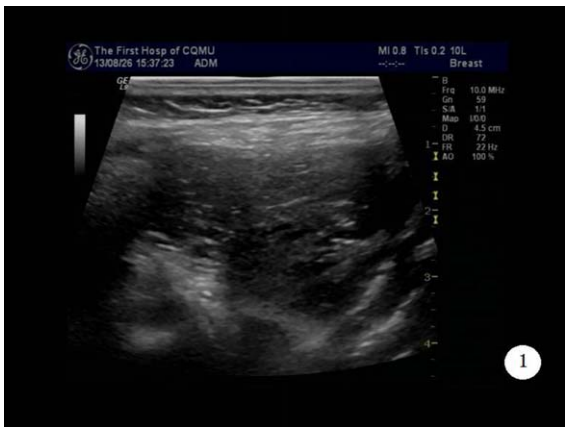


FIGURE 1. Color sonogram showing abnormal echo under the right ear, which is adjacent to the great vessels, with a size of 23 × 33 mm, ill-defined, and showed mostly low echo levels.

defined, and mobile mass, about 20 mm × 50 mm, longitudinally growing, coming from the vagus nerve, while the high bound arrived from the jugular foramen, the low bound reached the carotid body. Moreover, the mass was adherent to the carotid sheath, then the mass was completely excised along the vagus nerve.

The pathological examination showed that the right parapharyngeal space had an ectopic pituitary adenoma (Figure 8). Immunohistochemistry results showed GH(+),S100(+), Ki67 2%(+), SMA(-), CK(-), EMA(-), LCA(-), CD3(-), CD20(-), CD38(-), CD138(-), GFAP(-), TSH(-), ACTH(-), and PRL(-).

## DISCUSSION

### Overview

Ectopic pituitary adenoma is distinctly rare and it was first reported by Erdheim in 1909. With the development of imaging technology, the incidence of ectopic pituitary adenoma is increasing, about 100 cases have been reported in literature so far.[2,3] According to different locations, ectopic pituitary adenoma is divided into intracranial and

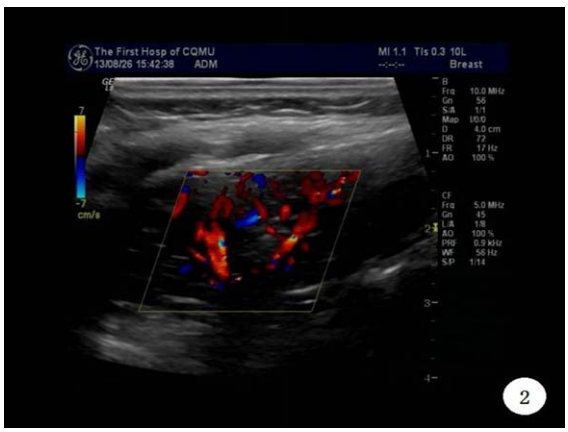


FIGURE 2. Color Doppler flow imaging showing abundant blood stream signal.

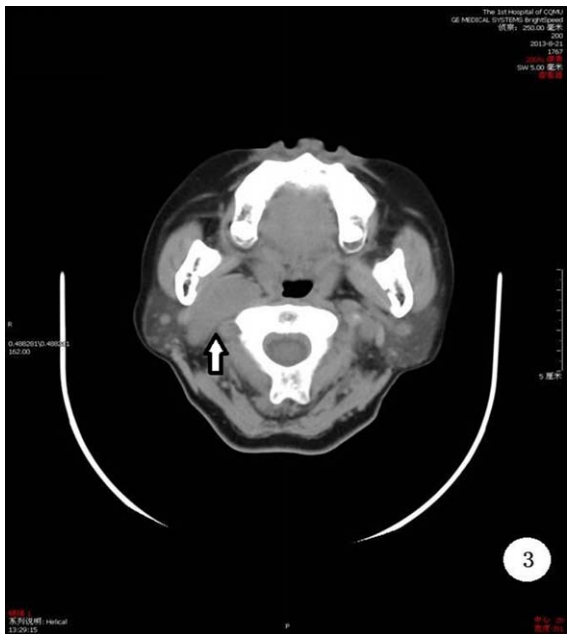


FIGURE 3. CT scan showing a soft tissue density mass (marked with white arrow) with a clear boundary involving the carotid sheath area, with a size of 22 × 42 mm. The contrast-enhanced CT had heterogeneous density.

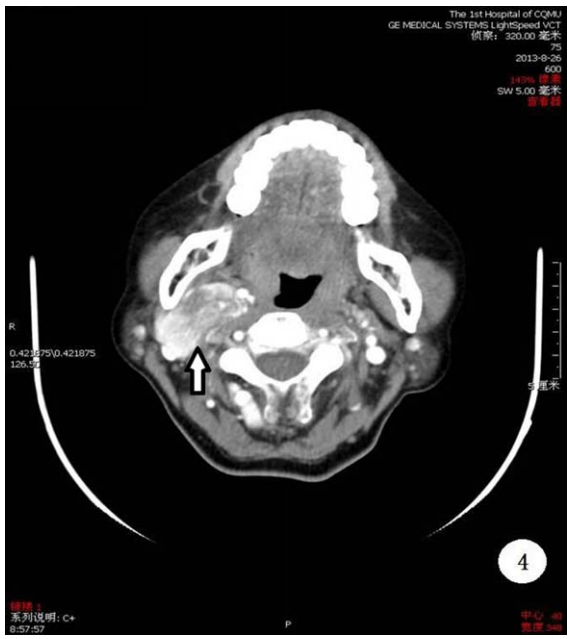


FIGURE 4. CT scan showing a soft tissue density mass (marked with white arrow) with a clear boundary involving the carotid sheath area, with a size of 22 × 42 mm. The contrast-enhanced CT had heterogeneous density.

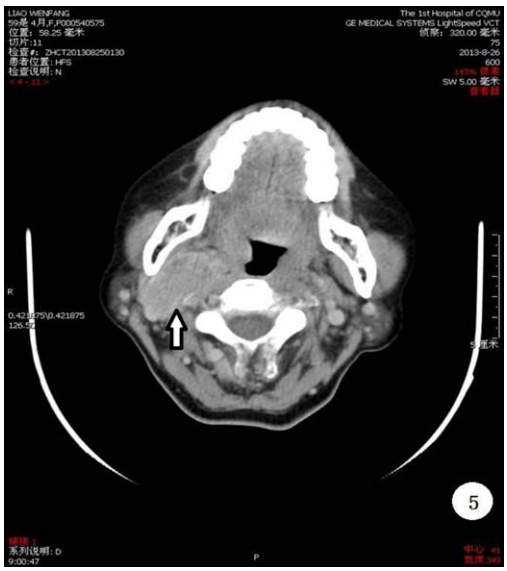


FIGURE 5. CT scan showing a soft tissue density mass (marked with white arrow) with a clear boundary involving carotid sheath area, with a size of 22 × 42 mm. The contrast-enhanced CT had heterogeneous density.

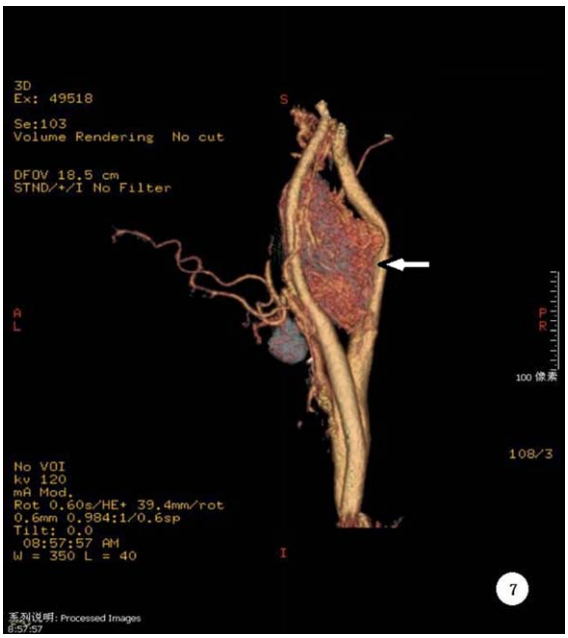


FIGURE 7. CT angiogram showed the mass was hypervascular and supported by the right internal carotid artery and branches of external carotid artery, and the major vessels were tortuous. The internal jugular vein was displaced posterolaterally and the internal carotid artery was displaced ahead and medially.

extracranial types, about 35 cases had been reported in the first mentioned of 2,[4] 27 cases were located in the suprasellar cistern, 2 cases were in the wings of the sphenoid bone, 3 cases were in the third ventricle, 2 cases were in the cavernous sinus, and 1 case was in the interpeduncular cistern. As the majority, the extracranial type came to 73% in total cases, which is most common in the sphenoid sinus, ectopic pituitary adenoma in the nasal cavity, petrosal, and jugular foramen also could be observed, but an ectopic pituitary adenoma located in the parapharyngeal space has not been reported thus far. Ectopic pituitary adenoma could be classified into either functional or nonfunctional types on account of the occurrence of endocrine disorder. The incidence of the functional type was relatively high. In the research of over 80 ectopic pituitary

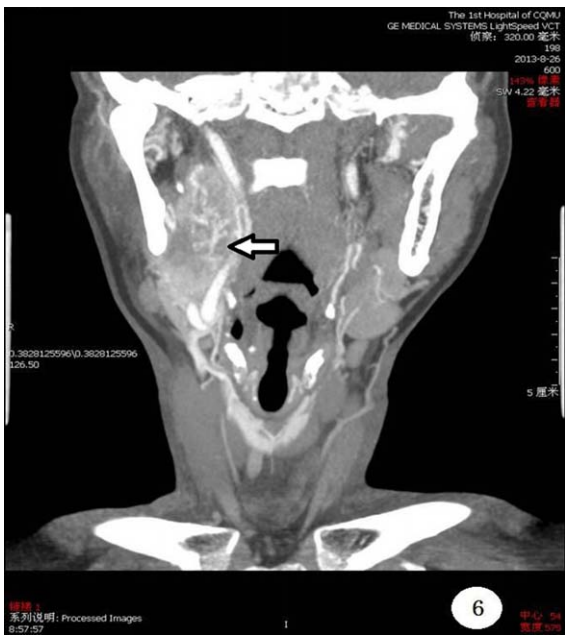


FIGURE 6. Appearance of lesion ectopic pituitary adenoma at the arterial phase in enhanced scanning at the coronal position.

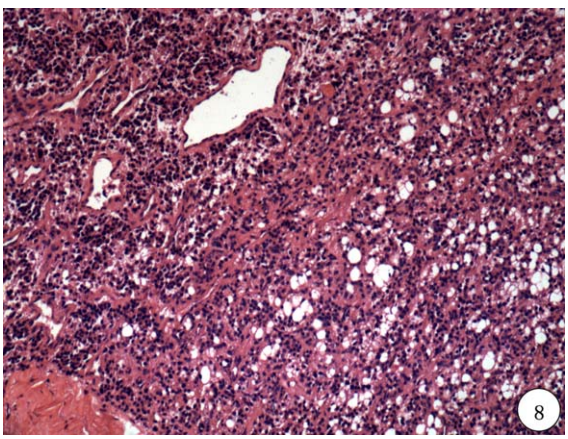


FIGURE 8. The pathological examination showed (the right parapharyngeal space) ectopic pituitary adenoma (hematoxylin-eosin stain, original magnification ×100). Immunohistochemistry results showed GH(+), S100(+), and Ki67 2%(+).

adenoma cases located in the parallel sella turcica by Mitsuya et al,[5] about 70% of ectopic pituitary adenoma were functional, and the adrenocorticotropic hormone-secreting adenoma was the most common type, second was the prolactin (PRL)-secreting adenoma, with an obviously incensement of adrenocorticotropic hormone and PRL.[5]About 58% of patients were accompanied with endocrine abnormality when they came to the hospital,[6] including acromegaly, hyperparathyroidism, and Cushing's syndrome. In another retrospective analysis of 75 ectopic pituitary adenoma cases done by Thompson et al,[7] they found that luteotropin was expressed mostly in immunohistochemistry.

## Pathogenesis

Several hypotheses have been proposed to explain the origin and pathogenesis of the ectopic pituitary adenoma, the exact reason remains uncertain. One proposal suggested a derivation from residual cells of Rathke's pouch, which is thought to eventually form the anterior pituitary gland,[8] while the posterior pituitary gland originates from the infundibulum. During the embryonic development, the Rathke's pouch migrates upward, and is separated from the oropharyngeal ectoderm because of the closure of skull, leaving a few pituitary cells in its path, and then the residual cells may be retained in the sphenoid sinus, sphenoid bone, or possibly within the sella turcica separated from the normal pituitary gland. Adenomatous change of these ectopic pituitary tissues would lead to the formation of ectopic pituitary adenomas. Hori[9] found that sporadic pituitary cells located in the meningioma around the pituitary stalk and suprasellar in the entire fetus and 75% in adults, the ectopic cells were not continued with the pituitary pars tuberalis, which were the same with anterior pituitary cells in immunohistochemistry. Another theory is that of tumor dissemination. Most pituitary adenomas are benign in theory, but the minority may spread with blood metastasis, meningeal, or cerebrospinal fluid spreading.[10] The resection of adenoma also provided an opportunity to implantation metastasis.[11] Some scholars supposed ectopic pituitary adenoma might be oriented from the craniopharyngeal canal during intrauterine life.[12] The case we present was located in the right parapharyngeal space, there was no pituitary adenoma-relevant history at the time, and we think it is closely associated with the remnant tissues during the migration of Rathke's pouch.

## Clinical manifestation

Endocrine disorder and focal neurological disturbance are the most common findings clinically, whereas few cases are symptomless. The performance of endocrine disorder is associated with the tumor type, menostasia, lactopoiesis, hypertrichosis, Cushing's syndrome, acromegaly, agnogenic weight gaining, insipidus, and diabetes could be observed, which are similar to the typical intrasellar adenoma.[13] Focal neurological disturbance perform as nonspecific headache, visual disorder, intracranial hypertension, encephalic nerves disturbance, and hydrocephalus. Nasal occlusion and hemorrhinia could be observed in the cases that occurred in the pharynx nasalis. The case we report had no symptoms, as mentioned before.

## Immunohistochemical studies

Similar to the normal pituitary adenomas, most ectopic pituitary adenomas showed a variable cellularity, with polygonal, plasmacytoid, granular, and oncocytic tumor cells. With a very low proliferation index (Ki-67 <3%), synaptophysin, CD56, neurone specific enolase, chromogranin, and cytokeratin were positive, CD7 and CD5/6 were negative. Reactivity with pituitary hormones was not limited to 1 hormone, and some cases were nonreactive. Additional immunohistochemistries, such as TTF-1, desmin, myogenin, EBER, SMA, HMB-45, and GFAP, were all negative. In the case we report, with the growth hormone positive, but the patient without any endocrine disorder, the reason may be owing to the serum hormone that was secreted by the ectopic pituitary adenoma was too little or without biologic activity. Otherwise, it was notable that the keratin was negative in our case, which was characteristic of paraganglioma. In the retrospective research of 32 ectopic sphenoid sinus pituitary adenomas by Lester[12], it was found that pan-cytokeratin was positive in 79%, in other words, some ectopic pituitary adenoma might be keratin negative, too. However, paraganglioma would be positive with tyrosine hydroxylase while negative for both pituitary hormones and pituitary transcription factors, and glial fibrillary acidic protein positive or NSE, Syn, and CgA positive.[7,10,11,14]

## Imaging features

Ectopic pituitary adenoma has no characteristic imaging features, the ectopic lesions presented as well-defined soft tissue masses with homogeneous isodensity or slightly high density (compared to the brain parenchyma), calcifications were seldom, and they showed mild to moderate enhancement with gadolinium in a contrast-enhancing CT scan. Ectopic pituitary adenoma lesion located in the Sella turcica region was accompanied with the compression, absorption, thinning, or destruction of bone, and the tumor was separated from the intrasellar content by the intact dura mater, and some cases were associated with a partial or complete empty sella. MRI demonstrated slightly hypointense or isointense signal in T1-weighted images, hyperintense or isointense signal in T2-weighted images, and inhomogeneous signal within the lesion. Some ectopic pituitary adenomas could suffer with sacciform, hemorrhage, or necrosis. In the research of imaging findings of 8 ectopic sphenoid sinus pituitary adenomas by Yang et al,[15] found that MRI demonstrated a specific bubble-like and thin hyperintense signal, and cribriform appearance in an enhanced scan, because the adenoma was formed of abundant epithelioglandular cells, which had formed plenty of acinus in unequal size. They also thought that the empty sella was important evidence to identify ectopic pituitary adenoma. Because of the special location, the case we reported appeared with nonspecific CT findings, as the literature described, so the preoperative diagnosis was difficult.

## Differential diagnosis

As to the ectopic pituitary adenoma with secretory function, the combined use of clinical situation, laboratory tests, and imaging examinations can make a definite

diagnosis. However, it is difficult to diagnose the cases without secretory function, like the ectopic adenoma located in the parapharyngeal space, as we present. Therefore, in our opinion, the possibility of ectopic pituitary adenoma should be considered when the common types of occupying lesion in the parapharyngeal space have been ruled out. Following are some usual tumors located in the parapharyngeal space.

**Schwannoma.** Schwannoma can be expressed as round or oval with periphery smooth, and has an intact capsule, which is derived from Schwann cells. The tumors have necrosis in the sac variable area. Patients have no rational symptoms, and it could cause a sensation disorder or corresponding pain and numbness where the tumor encroaches the nerve. A CT scan would show a vertical and elliptical soft mass with inhomogeneous and slightly lower density, and it grows along the direction of the nerve. Schwannoma contains 2 cellular components, the sarciniform (A zone) cells, which have an enhancement effect and the reticulate cells (B zone), so the tumor has a typical feature with hyperdensity involving the low intensity.

**Neurofibroma.** They are multiple benign neoplasms of the peripheral nervous system, arising from mesodermally derived Schwann cells, it could cause sensation disorder when the nerves are involved. On a CT scan, it would appear as a homogeneous low-density mass, with lower density of cystic structures, and nonobvious enhancement.

**Paraganglioma carotid body tumor.** A paraganglioma carotid body tumor is the most commonly type, its main clinical manifestation is a painless and benign neoplasm located under the angle of jaw, which could grow quickly in size when malignant change happens. CT shows a well-defined circular or elliptic soft tissue mass with attenuation similar to that of muscle. A CT enhancement scan shows intense enhancement, the boundary and shape of the tumor becomes clearer. Circuitous and serpiginous vascular changes could be observed, as the arteries and veins around tumor are displaced.

**Aneurysm of carotid artery.** The main manifestation is a pulsating mass on the neck. A CT scan could discover the calcifications within the tumor, and could show an obviously intralesional enhancement. Moreover, ultrasonic inspection could appear as abnormal hemodynamics that contributes to correct diagnosis.

**Branchial cleft cyst.** A painless soft mass in the parotid region or neck that grows gradually. A CT scan could show a circular or elliptic and tunicary mass with homogeneous and nonenhanced low density, while the capsule wall could have a well-defined enhancement. Ultrasonography shows an encapsulated mass with anechoic and back increased echo.

**Neuroendocrine tumor.** A neuroendocrine tumor, usually occurs in the stomach, pancreas, or intestinal tract. On the basis of different locations, the neuroendocrine tumor could express relevant hormones. Metastatic neuroendocrine neoplasms located in the parapharyngeal space may also be difficult to differentiate from actual pituitary adenomas. However, generally, these tumors will have a known history of a primary tumor elsewhere. A CT scan could show a soft tissue density mass, with an obscure boundary, and shows heterogeneous enhancement in contrast scanning. In immunohistochemistry, the metastatic neuroendocrine tumor would be positive with chromogranin A and synaptophysin, which was apart from the ectopic pituitary adenoma.

## REFERENCES


1. Matsuno A, Katayama H, Okazaki R, et al. Ectopic pituitary adenoma in the sphenoid sinus causing acromegaly associated with empty sella. *ANZ J Surg* 2001;71:495–498.
2. Ali R, Noma U, Jansen M, Smyth D. Ectopic pituitary adenoma presenting as midline nasopharyngeal mass. *Ir J Med Sci* 2010;179:593–595.
3. Ghazi AA, Amirbaigloo A, Dezfooli AA, et al. Ectopic acromegaly due to growth hormone releasing hormone. *Endocrine* 2013;43:293–302.
4. Li-Jun L. Two cases of ectopic pituitary adenoma and review of literature. *Clin Med J* 2013;33:62–63.
5. Mitsuya K, Nakasu Y, Nioka H, Nakasu S. Ectopic growth hormone-releasing adenoma in the cavernous sinus – case report. *Neurol Med Chir (Tokyo)* 2004;44:380–385.
6. Madonna D, Kendler A, Soliman AM. Ectopic growth hormone-secreting pituitary adenoma in the sphenoid sinus. *Ann Otol Rhinol Laryngol* 2001; 110:99–101.
7. Thompson LD, Seethala RR, Müller S. Ectopic sphenoid sinus pituitary adenoma (ESSPA) with normal anterior pituitary gland: a clinicopathologic and immunophenotypic study of 32 cases with a comprehensive review of the English literature. *Head Neck Pathol* 2012;6:75–100.
8. Bhatoe HS, Kotwal N, Badwal S. Clival pituitary adenoma with acromegaly: case report and review of literature. *Skull Base* 2007;17:265–268.
9. Hori A. Suprasellar peri-infundibular ectopic adenohypophysis in fetal and adult brains. *J Neurosurg* 1985;63:113–115.
10. Rasmussen P, Lindholm J. Ectopic pituitary adenomas. *Clin Endocrinol (Oxf)* 1979;11:69–74.
11. Yang L, Zou Y, Xia OC, Lu Z. Diagnosis and treatment of ectopic pituitary adenoma: a report of 3 cases and literature review. *Chinese J Neuroscience* 2012;5:516–518.
12. Lester DR, Thompson.Raja R. Ectopic Sphenoid Sinus Pituitary Adenoma (ESSPA) with Normal Anterior Pituitary Gland: A Clinicopathologic and Immunophenotypic Study of 32 Cases with a Comprehensive Review of the English Literature. *J Head and Neck Pathol* 2012;6:75–100.
13. Kaushik C, Ramakrishnaiah R, Angtuaco EJ. Ectopic pituitary adenoma in persistent craniopharyngeal canal: case report and literature review. *J Comput Assist Tomogr* 2010;34:612–614.
14. Luk KH, Lam KS, Kung AW, Fung CF, Leung SY. Suprasellar ectopic pituitary adenoma presenting as cranial diabetes insipidus. *Postgrad Med J* 1992;68:467–469.
15. Yang BT, Chong VF, Wang ZC, Xian JF, Chen QH. Sphenoid sinus ectopic pituitary adenomas: CT and MRI findings. *Br J Radiol* 2010;83: 218–224.