CASE REPORT
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Ectopic Growth Hormone-Secreting Pituitary Adenoma of the Clivus

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Ectopic pituitary adenoma, occurring outside the sella turcica without any continuity with intrasellar pituitary gland is very rare. So far, less than 90 such cases have been reported in the literature. Regarding to ectopic locations, suprasellar region, sphenoid sinus and clivus have been reported in decending order of frequency. To our best knowledge, growth hormone-secreting ectopic pituitary adenoma in the clivus has never been reported. With the pertinent literature review, we present our unique case with its characteristic magnetic resonance imaging and immunohistochemical features.

KEY WORDS : Ectopic adenoma · Growth hormone secreting · Pituitary gland · Clivus · Sphenoid sinus.

Introduction

Pituitary adenomas are the most common pituitary neoplasms, which constitute 10% to 20% of primary brain tumors. Ectopic pituitary adenoma, occurring outside the sella turcica without any continuity with intrasellar pituitary gland is very rare. Ectopic pituitary adenoma was first reported by Erdheim in 1909[2]. Since then about 90 cases has been reported[1,3,5,7,9,10]. We report a case of ectopic growth hormone (GH)-secreting pituitary adenoma of the clivus.

Case Report

A 44-year-old man was presented with progressive acromegalic feature and headache (Fig. 1). Polydipsia and bilateral palm paresthesia was also complained. Blood pressure was 160/100mmHg on admission. Electrocardiography showed left ventricular hypertrophy by voltage. He was diagnosed as to have secondary hypertension by cardiologist. Endocrinological study on admission revealed increased serum GH level, 27.39ng/ml and IGF-1, 1553ng/ml (Table 1). Growth hormone level was not suppressed in oral glucose tolerance test(OGTT) (Table 2). Other serum hormonal levels were within normal limits.

A plain sella cone down view showed a decreased density on upper clivus, and a magnetic resonance imaging(MRI) of brain showed isosignal mass on T1WI at the upper clivus just below the sellar turcica, which was ovoid in shape with 1.5×1.2×1cm size, showing mild inhomogenous enhancement. The seemingly normal pituitary gland was seen anterosuperiorly

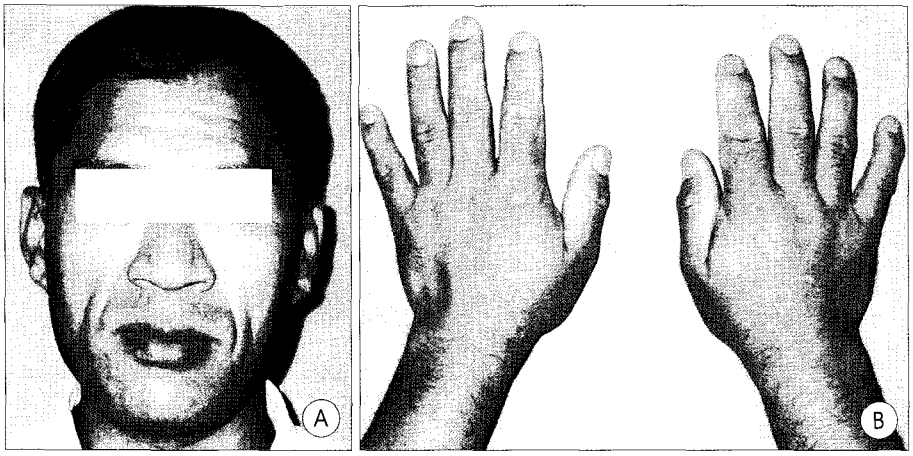

Fig. 1. A : Thickening of facial skin fold with mild mandibular enlargement. B : Typical acromegalic hands are shown.

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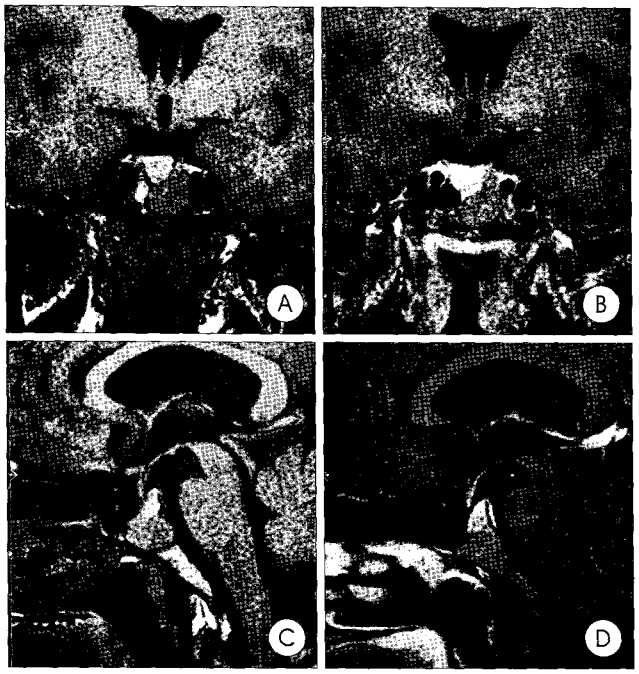

Fig. 2. Preoperative magnetic resonance imaging of brain shows a 1.5 ×1.2×1cm sized mass in the upper clivus, separated from the normal pituitary gland at T1 weighted coronal image (A) and sagittal image (C). The mass is isosignal in T1-weighted image and enhanced inhomogeneously at gadolinium-enhanced coronal (B) and sagittal image (D).

to the clival mass (Fig. 2).

Operation was done via a wider than usual transsphenoidal approach(TSA) to expose the upper clivus. The tumor was friable and removed carefully by curette. The sellar floor was removed and the dura mater of the pituitary gland was confirmed intact. Sphenoid sinus was filled with fat tissue obtained from abdominal wall and the wound was closed as usual.

The patient's postoperative course was uneventful. The baseline level of serum growth hormone dropped to 3.78ng/ml at the 14th postoperative day. In OGTT, GH was suppressed normally (Table 2). The postoperative MRI was taken one day after operation and showed no evidence of remaining tumor. Histopathological examination revealed GH-immunopositive pituitary adenoma. The endocrinological tests performed 6 months after surgery revealed normal basal pituitary hormones with normal suppression of GH level with OGTT.

Table 1. Baseline level of serum anterior pituitary hormones

Hormone(normal)	Preoperative	Postoperative (14 days after)
TSH(0.4~4.1μIU/mℓ)	1.12	1.07
Prolactin(1.41~19.45ng/mℓ)	8.08	11.49
hGH(0~8ng/mℓ)	27.39	3.79
Cortisol(5~25μg/dℓ)	9.57	23.42
LH (0.63~7.89mIU/mℓ)	6.84	5.3
FSH(1.3~22.2mIU/mℓ)	8.99	7.04
IGF-1(SM-C)(62~350ng/mℓ)	1553	117.51

Abbreviations : FSH, follicle-stimulating hormone; GH, growth hormone; LH, lutenizing hormone; PRL, prolactin; TSH, thyroid-stimulating hormone; IGF-1, insuline-like growth factor

Table 2. Oral glucose tolerance test

hGH(normal)	Preoperative	Postoperative	
		14 days after	6 months after
basal(0~8ng/mℓ)	27.39	3.79	0.77
30min(0~8ng/mℓ)	27.04	3.67	0.59
60min(0~8ng/mℓ)	29.83	4.33	0.52
90min(0~8ng/mℓ)	22.32	3.82	0.53
120min(0~8ng/mℓ)	28.35	3.85	0.53

Discussion

Ectopic pituitary adenomas have been reported about 90 cases[1,3,5,7,9,10]. They have variable hormonal activities and anatomic distributions (Table 3). Regarding to anatomic lo-

Table 3. Reported cases of ectopic pituitary adenoma

Location	Hormone									Total
	GH	ACTH	PRL	ACTH/TSH	GH/PRL	FSH	LH	Inactive	ND	
Suprasellar	1	12	8	1	0	0	0	9	0	31
Sphenoid sinus	7	7	9	1	1	0	0	6	0	31
Cavernous sinus	1	6	0	0	0	0	0	0	1	8
Clivus	1*	0	6	0	0	0	0	1	0	8
Nasopharynx	0	1	0	0	0	1	0	2	0	4
Superior orbital fissure	0	2	0	0	0	0	0	0	0	2
Sphenoid wing	0	0	0	0	0	0	0	1	0	1
Petrous temporal bone	0	0	0	0	0	0	0	1	0	1
Third ventricle	0	0	0	0	0	0	1	0	0	1
Sellar floor	1	1	0	0	0	0	0	0	0	2
Temporal lobe	0	1	0	0	0	0	0	0	0	1
Total	11	30	23	2	1	1	1	20	1	90

Abbreviations : ACTH, adrenocorticotropic hormone; FSH, follicle-stimulating hormone; GH, growth hormone; LH, lutenizing hormone; ND, not described; PRL, prolactin ; TSH, thyroid-stimulating hormone. * : present case

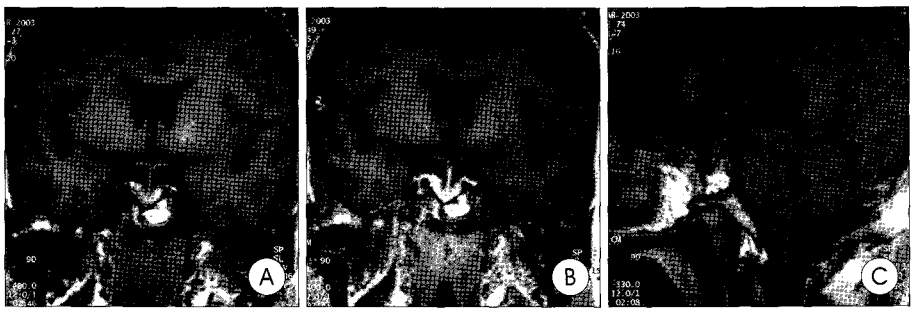

Fig. 3. Postoperative T1-weighted coronal magnetic resonance(MR) imaging (A), gadolinium-enhanced coronal MR imaging (B) and T1-weighted sagittal MR imaging (C) show fat signal in the tumor bed, which is separated from normal pituitary gland.

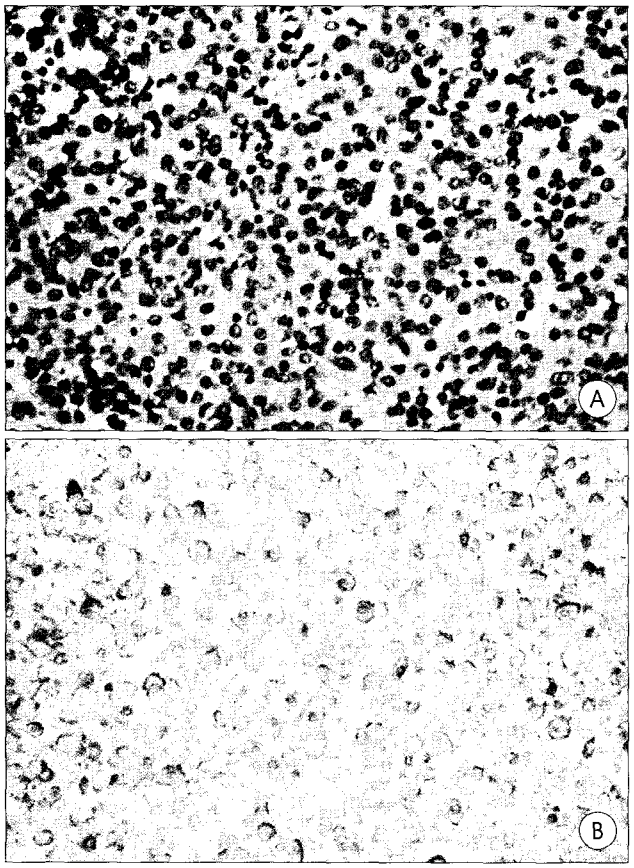

Fig. 4. A : The tumor is composed of diffusely arranged round to polygonal cells with eosinophilic cytoplasm (H&E, x100). B : Immunohistochemical staining of tumor cells for growth hormone shows diffuse strong positivity with pancytoplasmic pattern (x100).

cations of the pituitary adenomas, the suprasellar cistern and sphenoid sinus were the most frequent locations for ectopic adenomas (31 cases), followed by the clivus (8 cases) and the cavernous sinus (8 cases). Other anatomical locations were only sporadically reported. In regard to hormonal activities of ectopic pituitary adenomas, ACTH-secreting adenomas were the most frequently reported (30 cases), followed by prolactinomas (23 cases), and nonfunctioning adenomas (20 cases). Among the 11 cases of GH-secreting pituitary adenomas, no one was reported to be located in the clivus.

The theory of ectopic pituitary adenoma is that adenomatous change occurs in aberrant pituitary tissues deposited along the route of fetal pituitary development[6,8,9]. The anterior pituitary gland develops from Rathke's pouch while the posterior pituitary gland originate from the infundibulum. When Rathke's pouch migrates upward, it may leave ectopic pituitary tissue behind in its path. Infrasellar and suprasellar aberrant adenohypophyseal cells develop at different embryonal stages. The adenohypophysis develops from Rathke's pouch, and is seen as early as the 6.5mm embryonal stage. It loses its attachment to the pharyngeal roof by rupture of its stalk during the 12 to 20mm stage. In the infrasellar region, ectopia of the adenohypophysis due to partial persistence of the pouch in the wall of the buccal cavity. The remnant can be identified as a pharyngeal pituitary gland in the wall of the nasal cavity and sphenoid sinus. In contrast, suprasellar aberrant adenohypophysis may originate later when the pars tuberalis develops from the pars anterior of the pituitary at the 41 to 55mm stage. In support of this aberrant pituitary tissue theory, Hori reported he could identify suprasellar ectopic grandular cells in 15 adult brains out of 20 examined specimens[4]. Adenomatous change of these ectopic pituitary tissues would lead to the formation of ectopic pituitary adenomas.

Ectopic pituitary adenoma have multiple clinical manifestations but are primarily related to local mass effect and the destructive behavior of the tumor or associated hormonal activity. With the use of modern imaging techniques such as CT and MRI scans, small ectopic pituitary may be diagnosed accurately at an early stage, but still the diagnosis of ectopic pituitary adenoma requires confirmation by intraoperative observation of the relationship among the adenoma, the diaphragma sellae, pituitary stalk and normal pituitary gland. Histochemical staining is important in ascertaining the functional nature of these neoplasms. Because their location and radiologic appearance can mimic a variety of skull base lesions, the diagnosis of an ectopic pituitary adenoma can be made only on the basis of accurate histopathologic and radiologic assessment. In our patient, a clival mass located outside sella turcica without continuity with intrasellar normal pituitary gland and immunohistochemical staining showed GH-immunopositive pituitary adenoma.

Treatment modalities of ectopic pituitary adenomas include surgery, pharmacotherapy and radiotherapy as usual pituitary gland tumor. Like other pituitary tumors, surgical excision is the most important treatment modality. As in our case of upper

clival location, wider opening than usual TSA and directed more downward angle is recommended. Furthermore, more careful resection of the tumor is required not to injure the posterior lobe of the pituitary gland, which is located directly anterior to the ectopic pituitary tumor.

Conclusion

Ectopic pituitary adenomas may have variable anatomic locations. Radiologically, ectopic pituitary adenomas resemble many different tumors of the sphenoid sinus and skull base. For diagnostic confirmation of ectopic pituitary adenomas, preoperative endocrine study and postoperative histopathological study are needed.

The authors present a rare case of GH-secreting ectopic pituitary adenoma arising from the clivus with literature review.

References

1. Chan MR, Ziebert M, Maas DL, Chan PS : "My rings won't fit anymore." Ectopic growth hormone-secreting tumor. **Am Fam Physician 71 :** 1766-1767, 2005
2. Erdheim J : Uber einen Hypophysen tumor van ungewohnlichem Sitz. **Beitr Pathol Anat 46 :** 223-249, 1909
3. Gondim JA, Schops M, Ferreira E, Bulcao T, Mota JI, Silveira C : Acromegaly due to an ectopic pituitary adenoma in the sphenoid sinus. **Acta Radiol 45 :** 689-691, 2004
4. Hori A : Suprasellar peri-infundibular ectopic adenohypophysis in fetal and adult brains. **J Neurosurg 63 :** 113-115, 1985
5. Horiuchi T, Tanaka Y, Kobayashi S, Unoki T, Yokoh A : Rapidly-growing ectopic pituitary adenoma within the sphenoid sinus. Case report. **Neurol Med Chir (Tokyo) 37 :** 399-402, 1997
6. Kohno M, Sasaki T, Narita Y, Teramoto A, Takakura K : Suprasellar ectopic pituitary adenoma. Case report. **Neurol Med Chir (Tokyo) 34 :** 538-542, 1994
7. Lee SY, Heo SH, Chung JG, Jang YG, Gill SB : Ectopic piuitary adenoma within the sphenoid sinus. Case report. **J Korean Neurosurg Soc 30 :** 227-230, 2001
8. Luk KH, Lam KS, Kung AW, Fung CF, Leung SY : Suprasellar ectopic pituitary adenoma presenting as cranial diabetes insipidus. **Postgrad Med J 68 :** 467-469, 1992
9. Mitsuya K, Nakasu Y, Nioka H, Nakasu S : Ectopic growth hormone-releasing adenoma in the cavernous sinus. case report. **Neurol Med Chir (Tokyo) 44 :** 380-385, 2004
10. Peker S, Sun I, Kurtkaya-Yapicier O, Elmaci I, Pamir MN : Ectopic pituitary adenoma located at the pituitary stalk. case report. **J Neurosurg Sci 49 :** 25-29, 2005