Clinical and Anatomic Features of Supraglandular Pituitary Adenomas

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■ OBJECTIVE: **Supraglandular pituitary adenoma (SGPA) is one of the extraordinary pituitary adenomas and shows different clinical and radiologic features. We retrospectively reviewed our cases of SGPAs to elucidate the radiologic, anatomic, and clinical features.**

■ METHODS: **We identified 9 patients with pathologically proven SGPA and classified them into 2 groups radiologically: either glandular or stalk types. Magnetic resonance images were correlated with intraoperative anatomic differences between the groups. Clinical and endocrinologic characteristics and surgical outcomes were reviewed.**

■ RESULTS: **The proportion of SGPAs was 1.2% of all pituitary adenomas surgically treated in our patient cohort. The glandular-type tumors ($n = 7$) had a thinned or defective diaphragma sellae. There was a clear plane between the tumor and pituitary stalk. For the stalk-type tumors ($n = 2$), the diaphragma sellae was intact and no clear border between the mass and stalk was found. Endocrinologic and immunohistochemical evaluation showed that 5 of 7 glandular-type tumors (71%) were functioning pituitary adenomas, whereas 2 stalk-type tumors were nonfunctioning. Eight of 9 patients underwent an endoscopic endonasal approach and tumor was totally removed in 7 (78%).**

■ CONCLUSIONS: **SGPAs are rare and preoperative diagnosis is possible based on their distinct radiologic, clinical, and anatomic features. SGPAs can be divided into 2 groups according to the anatomic features. The origin of tumor, whether the superior surface of the gland or the pituitary stalk, determined the location, extent, and relationship with the diaphragma sellae. The surgical outcome via an endoscopic endonasal approach was favorable.**

INTRODUCTION

Pituitary adenomas (PAs) usually arise from the anterior lobe of the hypophysis, which is located in the sella turcica. PAs are sometimes found in ectopic sites out of the sella turcica, such as sphenoid sinus, cavernous sinus, third ventricle, or interpeduncular cistern.[7,11,14-16] In the literature, the suprasellar area emerges as one of the frequent locations of ectopic PAs. However, PAs arising from the suprasellar area are a confusing entity because many of the lesions are not truly ectopic: some suprasellar PAs are located above the diaphragma sellae without any connection to the normal pituitary gland,[4,9] but the others may originate from the upward extension of the pituitary gland through the defect of diaphragma sellae. Nonetheless, PAs situated both in the suprasellar and in the supraglandular locations have distinct results on magnetic resonance imaging (MRI), in which there is a boundary distinguishing the tumor from the underlying pituitary gland. The unusual imaging features, which are different from ordinary PAs, and the rarity of this entity make appropriate diagnosis of these supraglandular PAs (SGPAs) a demanding task.

The optimal surgical approach to SGPA is also controversial. Many clinicians advocate a transcranial approach,[3,12] but an extended transsphenoidal approach through the tuberculum sellae became more feasible with the advent of endoscopic endonasal

Key words
- Endonasal
- Endoscopy
- Pituitary adenoma
- Supraglandular

Abbreviations and Acronyms
ACTH: Adrenocorticotropic hormone
CV: Coefficient of variation
DI: Diabetes insipidus
GH: Growth hormone
IGF-1: Insulinlike growth factor 1
MRI: Magnetic resonance image
PA: Pituitary adenoma
SFT: Solitary fibrous tumor
SGPA: Supraglandular pituitary adenoma
TSH: Thyroid-stimulating hormone

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surgical techniques.[6] The transtuberculum approach with an endoscope may be advantageous because the surgeon can easily identify and preserve the normal pituitary gland and surrounding neurovascular structures above the diaphragma sellae.

Reports of SGPAs have been increasing in the literature. However, the definition and description of SGPAs have been inconsistent, making comprehensive understanding of the disease discouraged. We analyzed 9 consecutive patients with SGPAs treated in our institution to calculate the hospital-based incidence, to identify common clinical and radiologic features, and to suggest an alternative surgical approach using endoscopy for the disease.

METHODS

The institutional review board of the Seoul National University Hospital approved this study. We searched for patients who were pathologically diagnosed with PA in Seoul National University Children's Hospital and Seoul National University Hospital between January 2007 and May 2015. A total of 735 cases were retrieved from the database during this period. We reviewed preoperative images and operative records to identify patients with SGPAs. The tumor should be located above the sella turcica (suprasellar) and pituitary gland (supraglandular) with a distinguishable border between the tumor mass and underlying pituitary gland on MRI. A small inferior portion of the tumor can be situated in the sella turcica if the underlying pituitary gland was compressed by the tumor. The operative records of all suspicious candidates were reviewed to confirm the relative location of tumor to pituitary gland and diaphragma sellae. We identified 9 patients with SGPAs. The medical records of these patients were evaluated to define the clinical characteristics of SGPAs. Preoperative clinical and imaging features, intraoperative findings, and postoperative visual and endocrinologic outcomes were assessed.

The degree of tumor removal was determined by postoperative MRI taken within 48 hours after surgery. In all patients, growth hormone (GH), insulinlike growth factor 1 (IGF-I), luteinizing hormone, follicle-stimulating hormone, estradiol (E2) or total testosterone, prolactin, free T4, thyroid-stimulating hormone (TSH), adrenocorticotropic hormone (ACTH), and serum cortisol levels were measured. Serum GH level was measured using an immunoradiometric assay (IRMA [DiaSorin Inc., Stillwater, Minnesota, USA]) with an analytic sensitivity of 0.04 ng/mL, intraassay coefficient of variation (CV) of 1.9%–3.9%, and interassay CV of 2.5%–4.1% until April 2014. Since then, serum GH has been measured using a human chorionic gonadotropin [^{125}I] IRMA RK-5CT kit (IZOTOP, Budapest, Hungary). Intra- and interassay CVs were 1.5% and 2.5%, respectively. Serum IGF-1 level was measured using high-sensitivity enzymatic assay (Active Non Extraction IGF-I IRMA, DSL-2800 [Diagnostic Systems Laboratories Inc., Webster, USA]) before 2012 and using an Immunotech IRMA kit (Beckman Coulter, Gladesville, New South Wales, Australia) after 2012. Intra- and interassay CVs were 6.3% and 6.8%, respectively, with the detection limit of 2 ng/mL. Serum prolactin was measured using the RAIKEY prolactin IRMA technique. Acromegaly was diagnosed according to high GH/IGF-1 levels and typical acromegalic features such as frontal bossing, prognathism, and acral growth. Prolactinoma was diagnosed in patients who presented with amenorrhea with hyperprolactinemia and showed the positive immunohistochemical staining of prolactin. Clinically silent ACTH-producing adenoma was diagnosed in 1 patient with a high ACTH level but normal cortisol level without typical cushingoid features and positive immunohistochemical staining of ACTH.

Endocrinologic remission of hormone-secreting tumors was assessed according to the current consensus criteria: a nadir serum GH level of <0.4 ng/mL after an oral glucose load, and subsequent normal sex- and age-adjusted IGF-1 levels for acromegaly; normal plasma prolactin levels (<25 ng/mL) at 3 months after surgery for hyperprolactinemia; normal plasma ACTH levels and 24-hour urinary cortisol within the contemporary reference range for clinically silent ACTH-producing adenoma; normalized TSH, free T4, and T3 for TSH-secreting PA.

RESULTS

We identified 9 patients with SGPA of the 735 patients with pathologically proven PA. Therefore, the hospital-based incidence of SGPAs was 1.2% in our cohort. Eight patients were female and 1 was male. The median age of the patients was 37 years (range, 14–54 years). The tumors were removed using an endoscopic transtuberculum approach in 8 patients and pterional approach in 1 patient.

Clinical and Radiologic Features

Eight patients had macroadenomas (largest diameter >10 mm), and the median largest diameter of tumors in the midsagittal plane was 36.6 mm (range, 19.7–48.4 mm). One patient had a microadenoma above the pituitary gland (largest diameter, 6.6 mm).

The pituitary stalk was clearly demarcated from the tumor on MRI in 7 patients. The stalk was not clearly distinguished from the tumor in the other 2 patients. Therefore, we classified the former 7 cases as a glandular type and the latter 2 cases as a stalk type (Figure 1). In 7 glandular-type tumors, there were tumors anterior to the pituitary stalk in 3 patients, mainly anterior with posterior extension in 2 patients and posterior to the stalk in 2 patients. Although the pituitary gland was slightly displaced inferiorly by the tumor, the overall shape of the gland was preserved in 7 glandular types.

Two stalk types were superior to the pituitary gland and extended into the third ventricle. There was a cerebrospinal fluid space between the pituitary gland and inferior surface of tumor. The pituitary stalk was displaced by the tumor and it was not delineated on MRI. The location and relationship with the pituitary stalk of the stalk-type tumors were similar to those in retrochiasmatic craniopharyngiomas.

The pituitary gland itself showed higher attenuation than tumors and its shape was well preserved on gadolinium-enhanced T1 sagittal images in all cases. The tumors were enhanced moderately and homogeneously with gadolinium and the overall contour of tumors was not as round as in meningioma or craniopharyngioma. The signal attenuation and intratumoral component were similar to those of the usual pituitary macroadenomas. Two tumors showed intratumoral cysts with the similar attenuation that was usually found in PAs (Figure 1D, H); however, there were not multiple