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Case Report

Double pituitary neuroendocrine tumors in a patient with normal growth hormone level acromegaly: A case report and review of the literature

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ABSTRACT

Background: Acromegaly is a rare disease caused by growth hormone (GH) hypersecretion caused by a pituitary neuroendocrine tumor (PitNET). However, some acromegaly patients show normal GH levels, and they can be a pitfall in clinical diagnosis. Moreover, rarely, synchronous true double or multiple PitNETs are encountered. Moreover, these PitNETs increase the risk of a left lesion during surgical exploration.

Case Description: The patient, who was a 73-year-old female, was referred to our hospital with a chief complaint of headache. Assessment of basal anterior pituitary function revealed a slightly high level of insulin-like growth factor-1 (IGF-1) (standard deviation, 2.4), and her physical findings exhibited mild acromegalic features. The endocrine evaluation confirmed acromegaly and magnetic resonance imaging (MRI) showed a macro PitNET with suprasellar extension. Endoscopic endonasal surgery (EES) was performed to remove the macro PitNET. Although postoperative MRI showed complete removal of the macro PitNET, endocrinological testing indicated no improvement in GH or IGF-1 excess. Pathological examination of the surgical specimen revealed a gonadotropic PitNET. Therefore, we repeated the MRI scan and found a micro PitNET in the thin left normal pituitary gland. A second EES was successfully performed to remove the micro PitNET completely, and both endocrinological and pathological examinations confirmed that the disease was cured.

Conclusion: Diagnosing acromegaly with low GH levels requires close monitoring. Double PitNETs are relatively rare and can cause incomplete remission of functional PitNETs.

Keywords: Acromegaly, Double pituitary neuroendocrine tumor, Endoscopic endonasal surgery, Pituitary, PitNET

INTRODUCTION

Pituitary neuroendocrine tumors (PitNETs) account for 10–15% of all intracranial tumors.[3,10] Synchronous true double or multiple pituitaries are encountered rarely. These multiple-functioning PitNETs increase the risk of overlooking the active hormone-secreting lesions during surgical exploration.[4,6,9,10] Acromegaly is a rare disease caused by hypersecretion

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of growth hormone (GH) by PitNETs[1,2] that causes overproduction of insulin-like growth factor 1 (IGF-1) and many comorbidities, such as hypertension, diabetes, and gastrointestinal and thyroid papillary carcinoma.[1,2,5]

Cases of acromegaly with normal or minimally elevated GH levels but abnormally high IGF-1 levels have been reported, and such "low GH acromegaly" can be a pitfall of clinical diagnosis.[1,2,5] Herein, we describe a case of low GH acromegaly associated with double tumors.

CASE DESCRIPTION

A 73-year-old female was referred to our hospital with a chief complaint of headache. She had a medical history of diabetes mellitus. Computed tomography and magnetic resonance imaging (MRI) scans revealed a macro PitNET (30 × 27 × 25 mm) [Figure 1].

Laboratory findings indicated a normal level of GH: 2.02 ng/mL, normal values: 0.06–5.00 ng/mL, and other anterior pituitary hormones, except a slightly high level of IGF-1: 180 ng/mL, normal values: 54.00–167 ng/mL. Physical findings revealed characteristics of mild acromegaly, including mild facial and acral enlargement. Radiographic findings showed a cauliflower-like enlargement of the distal phalanx of the fingers and a heel pad thickness of 22.28 cm (normal values: <22 cm). Oral glucose tolerance test indicated insufficient suppression of GH (nadir GH: 1.29 ng/mL, normal values: <0.04 ng/mL), and the thyrotropin-releasing hormone stimulation test exhibited a paradoxical rise in serum GH level. These findings confirmed the diagnosis of acromegaly with low GH levels. Endoscopic endonasal surgery (EES) was performed to remove the macro PitNET. Although postoperative MRI showed complete tumor removal [Figure 2], endocrinological examination detected no improvement in GH or IGF-1 levels. Pathological examination of the surgical specimen revealed a gonadotropic PitNET [Figure 3]. Therefore, we re-examined the MRI findings and found a micro PitNET (2.4 × 2 × 1.5 mm) in the left thin, normal pituitary gland [Figure 2]. Accordingly, we diagnosed the patient with double tumors, a combination of micro and macro PitNETs.

The micro PitNET was successfully removed with a second EES [Figure 4], and both endocrinological and pathological examinations confirmed the cure [Figure 5 and Table 1]. Consequently, the patient no longer needs diabetes medication and has been recurrence-free during follow-up.

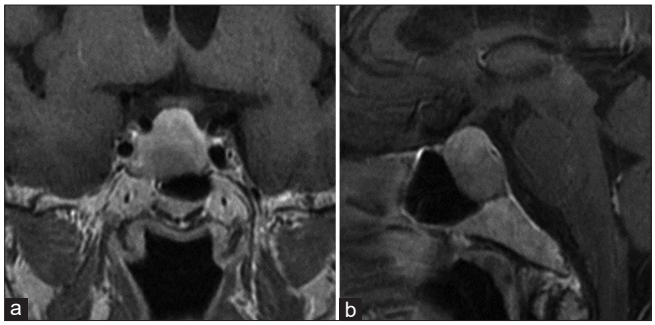

Figure 1: (a) Magnetic resonance imaging (MRI) coronal section preoperative brain MRI reveals a macro pituitary neuroendocrine tumor (PitNET) (30 × 27 × 25 mm). (b) MRI sagittal section preoperative brain MRI reveals a macro PitNET (30 × 27 × 25 mm).

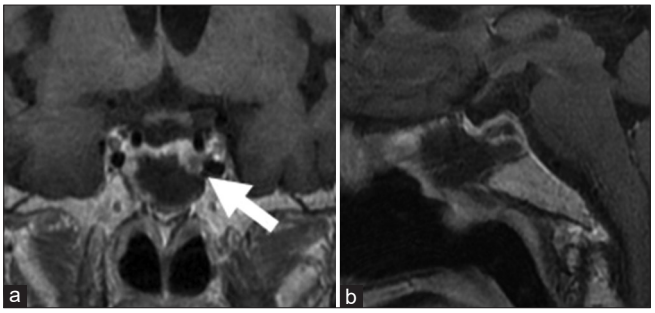

Figure 2: (a) Magnetic resonance imaging (MRI) coronal section postoperative MRI reveals a complete removal of the macro pituitary neuroendocrine tumor (PitNET) and the residual micro PitNET (arrow) in the left thin, normal pituitary gland. (b) MRI sagittal section postoperative MRI reveals a complete removal of the macro PitNET.

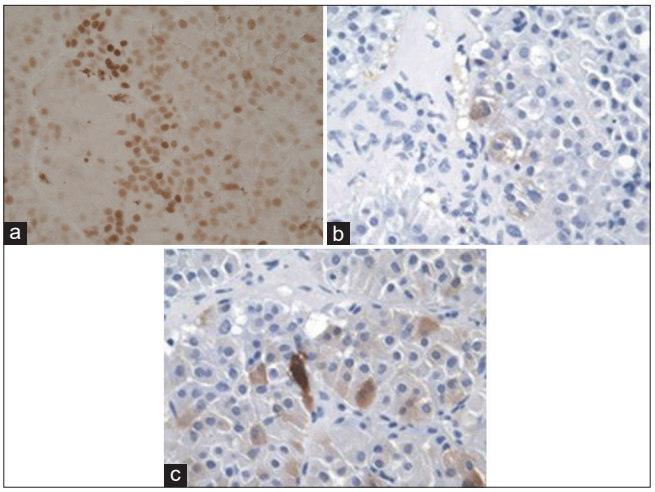

Figure 3: (a) Steroidogenic factor-1 (SF-1)-positive image immunohistochemical staining of the first surgical specimen shows positive staining for SF-1, follicle-stimulating hormone (FSH), and α-subunit, indicating that the resected tumor is a gonadotroph pituitary neuroendocrine tumor (PitNET), (b) FSH-positive image immunohistochemical staining of the first surgical specimen shows positive staining for SF-1, FSH, and α-subunit, indicating that the resected tumor is a gonadotroph PitNET, (c) α-subunit-positive image immunohistochemical staining of the first surgical specimen shows positive staining for SF-1, FSH, and α-subunit, indicating that the resected tumor is a gonadotroph PitNET.

Table 1: Summary of pre and postoperative endocrinological findings.

	Standard values	Preoperative values	Post-1st operative values	Post-2nd operative values
GH (ng/mL)	0.06–5.00	2.02	1.85	0.21
IGF-l (ng/mL)	56–172	180	166	70
Nadir GH during OGTT	<0.04	1.29	1.78	0.17

IGF-1: Insulin-like growth factor-1, GH: Growth hormone, OGTT: Oral glucose tolerance test. A preoperative endocrinological examination revealed normal serum GH levels and slightly elevated serum IGF-1 levels. After the 1st operation, an endocrinological examination showed no improvement in GH or IGF-1 excess. After the 2nd operation, serum IGF-1 levels were within normal limits, and OGTT confirmed the cure of the disease.

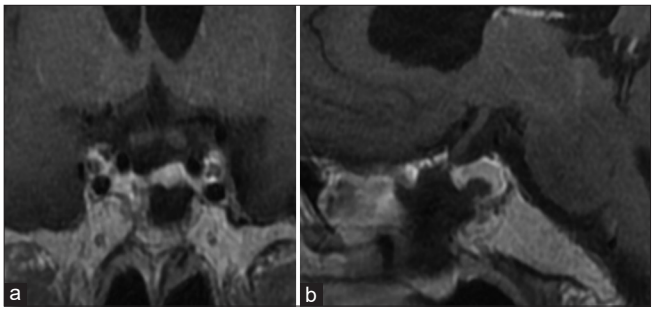

Figure 4: (a) Magnetic resonance imaging (MRI) coronal section MRI after the second operation shows the complete removal of the residual micro pituitary neuroendocrine tumor (PitNET) in the left thin, normal pituitary gland, (b) MRI sagittal section MRI after second operation shows the complete removal of the residual micro PitNET in the left thin, normal pituitary gland.

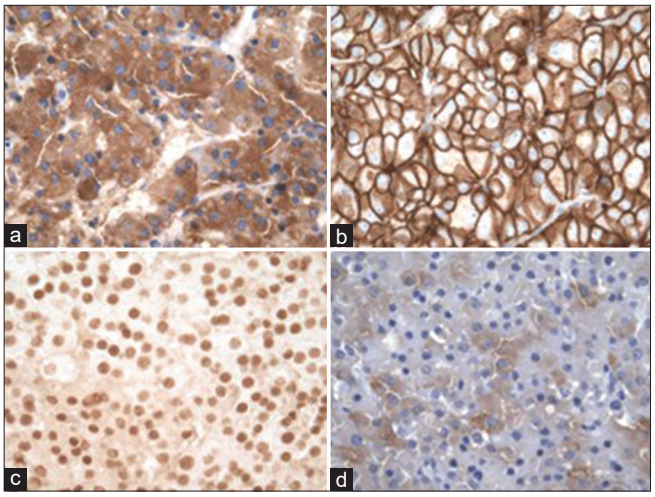

Figure 5: (a) Growth hormone (GH)-Positive Image Immunohistochemical staining of the 2nd surgical specimen exhibits positive staining for GH, somatostatin receptor type 2 (SSTR-2), POU1F1/GHF-1(Pit-1), and α-subunit, which mean that the resected tumor is a somatotroph pituitary neuroendocrine tumor (PitNET), (b) SSTR2-positive image immunohistochemical staining of the 2nd surgical specimen exhibits positive staining for GH, SSTR-2, Pit-1, and α-subunit, which mean that the resected tumor is a somatotroph PitNET, (c) Pit-1-positive Image Immunohistochemical staining of the 2nd surgical specimen exhibits positive staining for GH, SSTR-2, Pit-1, and α-subunit, which mean that the resected tumor is a somatotroph PitNET, (d) α-subunit-Positive Image Immunohistochemical staining of the 2nd surgical specimen exhibits positive staining for GH, SSTR-2, Pit-1, and α-subunit, which mean that the resected tumor is a somatotroph PitNET.

DISCUSSION

The overall prevalence of "normal GH acromegaly," whose serum GH level is within normal limits, is reported to be about 25–30% in all acromegaly.[1,2] The normal GH acromegaly shows an elevated age-adjusted IGF-1 concentration.[1,2] Some cases are a lack of suppression of GH levels <1 ng/mL after administration of an oral glucose load.[1,2]

Some research has shown that the tumor size of normal-GH acromegaly is smaller than that of high-GH acromegaly.[1,3,7] Average age of patients with normal-GH acromegaly is higher than that of typical acromegaly.[10] Elevated IGF-1 has been associated with acromegaly activity, and these patients with normal GH acromegaly have the same frequency and severity of clinical signs and comorbidities as patients with classic acromegaly. Therefore, it is conceivable that these acromegaly are not simply acromegaly in their early stages.[1,2,8]

Sometimes, patients have double or multiple pituitary neuroendocrine tumors in the pituitary fossa.[1,4,6] The incidence of multiple PitNETs is reported to be 0.2–2.6% in surgically treated cases. The most frequent clinical syndrome is acromegaly; histologically, most reported multiple PitNETs are immunopositive for GH.[1,6] Multiple PitNETs are sometimes difficult to identify on preoperative MRI and could be a clinical pitfall, especially in cases of endocrinopathies.[1,4,6]

In this case, the patient had double PitNETs; one was a macro gonadotroph PitNET located in the center of the sella turcica, and the other was a micro somatotroph PitNET located in the thin, normal pituitary gland; therefore, we could not find the micro PitNET in the preoperative MRI before the 1st operation and failed to remove the responsible GH-producing tumor. The diagnosis of acromegaly was made based on elevated IGF-1 and clinical symptoms. Both histological findings and endocrinological examination allowed us to determine the failure of the 1st surgery, and we could then identify the residual responsible tumor using MRI.

CONCLUSION

Here, we report a case of double pituitary neuroendocrine tumors (PitNETs) in a patient with normal GH-level acromegaly. Double PitNETs may be a clinical pitfall, particularly in patients with endocrinopathy. If postoperative pituitary hormone excess does not improve after the complete removal of the tumor, we need to recheck pre and postoperative radiographic and pathological findings to explore the cause of surgical failure.

Ethical approval

Not applicable.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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