doi: 10.4183/aeb.2021.521

CASE REPORT

ECTOPIC TSH-SECRETING PITUITARY ADENOMA IN NASOPHARYNGEAL REGION

F.P. Altay[1,*], M. Kulaksızoğlu[2], S.M. Fenkci[3], N. Yalçın[4], E. Sağtaş[5]

[1]"Baskent" University, Faculty of Medicine - Department of Endocrinology and Metabolism, Bahcelievler, Ankara, [2]"Necmettin Erbakan" University, Faculty of Medicine - Department of Endocrinology and Metabolism, Meram, Konya, "Pamukkale" University, Faculty of Medicine - [3]Department of Endocrinology and Metabolism, [4]Department of Pathology, [5]Department of Radiology, Denizli, Turkey

Abstract

Objective. TSH-secreting pituitary adenomas (TSH-omas) are very rare disorders. This report describes the diagnosis and treatment of a thyroid-stimulating hormone-secreting ectopic pituitary adenoma in the nasopharyngeal region.

Subjects and Methods. We report a 37-year-old male patient with thyroid-stimulating hormone-secreting ectopic pituitary adenoma in nasopharyngeal region.

Results. A patient suffering from sweating, palpitations, dizziness and abnormality in thyroid tests was referred to our clinic. Thyroid function tests showed high basal levels of free thyroxine (FT4), free tri-iodothyronine (FT3), and serum TSH. TRH stimulation test results indicated blunted response. Scintigraphy showed increased radionuclide uptake (iodine-123), and a thyroid ultrasound scan revealed diffuse enlargement of the thyroid gland. A pituitary MRI indicated a normal pituitary. However, MRI showed a mass in the nasopharynx that was confirmed with endoscopy. Endoscopic total endonasal resection was done and the mass was removed. The pathology reported a TSH-secreting pituitary adenoma.

Conclusion. In this report, an identified case of thyroid-stimulating hormone-secreting ectopic pituitary adenoma in nasopharyngeal region is reported and it is the only tenth case in the literature indicated in the nasopharyngeal region. Ectopic TSH-omas should be considered during inappropriate secretion of TSH as a candidate cause to enable correct diagnosis and improve the treatment of patients.

Keywords: TSH-oma, nasopharyngeal region, ectopic pituitary adenoma.

INTRODUCTION

Thyroid-stimulating hormone (TSH)-secreting pituitary adenomas (thyrotropinomas), often referred to as TSH-omas, are rare disorders and it is probable that less than 2% of all kinds of pituitary tumors are TSH-omas, having a rough incidence of one case per million (1,2). In 1960, Jailer and Holub (3) reported a patient with symptoms of hyperthyroidism and expanded sella on X-ray imaging. Between years 1960 and 2013 more than 450 cases of thyrotropin-secreting pituitary adenomas (TSH-omas) were published (4).

Thyrotrophic cells generally comprise 5% of all pituitary cells (5), which may help explain the rarity of TSH-oma. TSH-omas are seen in patients across a wide range of ages but mostly in their 5th and 6th decade of life. Tumor prevalence does not seem to be different between men and women based on the findings of different studies (6). Only a few studies reported that TSH-omas are seen more often in women (7, 8) and in men (9, 10).

Ectopic pituitary adenomas (EPAs) are extremely rare. Since its first description in 1909, there have been around 100 cases reported to date (4). Cases of ectopic TSH-omas are even rarer. The first description of ectopic TSH-oma was provided by Cooper and colleagues in 1996 (11). Since then only 11 cases have been reported, with nine seen in the nasopharynx and two in the suprasellar region.

This paper reports an identified case of Thyroid-Stimulating Hormone-Secreting ectopic pituitary adenoma in the nasopharyngeal region, which is the tenth case in the literature. This case is exceptional, since the literature review reveals that a TSH-secreting ectopic pituitary adenoma is not a common finding, particularly in the nasopharynx. In this context, the clinical and laboratory features of earlier papers are reviewed, as well.

*Correspondence to: Feride Pınar Altay MD, "Baskent" University, Faculty of Medicine, Department of Endocrinology and Metabolism, Bahcelievler, Ankara, 06490, Turkey, E-mail: fpaltay@gmail.com

CASE REPORT

A 37-year-old man suffering from sweating, palpitations, dizziness and abnormality in thyroid tests was referred to our endocrinology clinic in March 2015. There was no family history of thyroid disease. Physical examination was normal. In laboratory findings thyroid function tests showed high levels of free thyroxine (FT4), free tri-iodothyronine (FT3), and serum TSH. The results obtained from the baseline thyroid function tests and thyroid antibodies were TSH 9.28 μIU/mL (0.32-5.4 μIU/mL), FT4 3.14 ng/dL (0.78-1.81 ng/dL), FT3 10.8 pg/mL (2.2-4.0 pg/mL), Antithyroglobulin (TgAb) <20 IU/mL (0-40 IU/mL), Antithyroid peroxidase (TPOAb) 10.5 IU/mL (0-35 IU/mL) and alpha subunit (α-GSU) 2.20 IU/L (0-0.8).

The other morning hormone levels were as follows: cortisol 9.26 ug/dL (4-22 ug/dL), ACTH 17.5 pg/mL (6-50 pg/mL), FSH 5.82 mIU/mL (0.6-14.7 mIU/mL), LH 5.15 mIU/mL (0.7-7.9 mIU/mL), PRL 5.3 ng/mL (2.1-17.7 ng/mL), Testosterone 4.97 ng/mL (2.4-8.7 ng/mL), IGF-1 136 ug/L (53-331 ug/L). Full blood counts were within the normal range and glucose 106 mg/dL (75-106 mg/dL), creatinine 0.7 mg/dL (0.7-1.3 mg/dL), Na 143 mmol/L (136-146 mmol/L), K 4 mmol/L (3.5-4.5 mmol/L), ALT 37 U/L (0-45 U/L).

The results of thyroid scintigraphy of 4th hr image shown in Figure 1 indicate increased radionuclide uptake (iodine-123) in the area of the thyroid gland, and an ultrasound scan revealed diffuse enlargement of the gland.

A TRH stimulation test was conducted intravenously in order to assess response of TSH levels. Before the subject was submitted to TRH test, a blood sample was obtained to note baseline TSH. Following 200 μg TRH (TRH Ferring 0.2 mg/mL) intravenous injection, TSH levels were measured at 15, 30, 60 and 120 minutes after the injection. Results obtained during TRH stimulation test are given in Figure 2. Given that there was less than two times increase in TSH level, the TRH stimulation test results indicated a blunted response (normal response leads to between a 2-8 times increase) (12). This result supported differential diagnosis of TSH-oma, but in order to support this finding further with another test a T3 suppression test was planned.

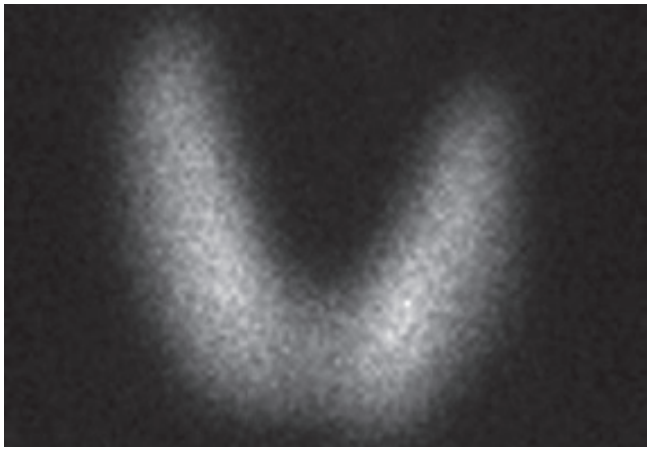

Figure 1. Thyroid scintigraphy 4th hr image with increased radionuclide uptake (iodine-123) in the area of the thyroid gland.

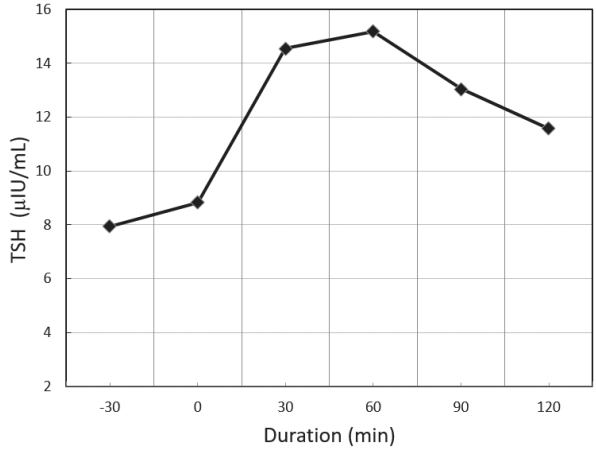

Figure 2. Result obtained during TRH stimulation test. Test results indicated a blunted response (normal response leads to between a 2-8 times increase).

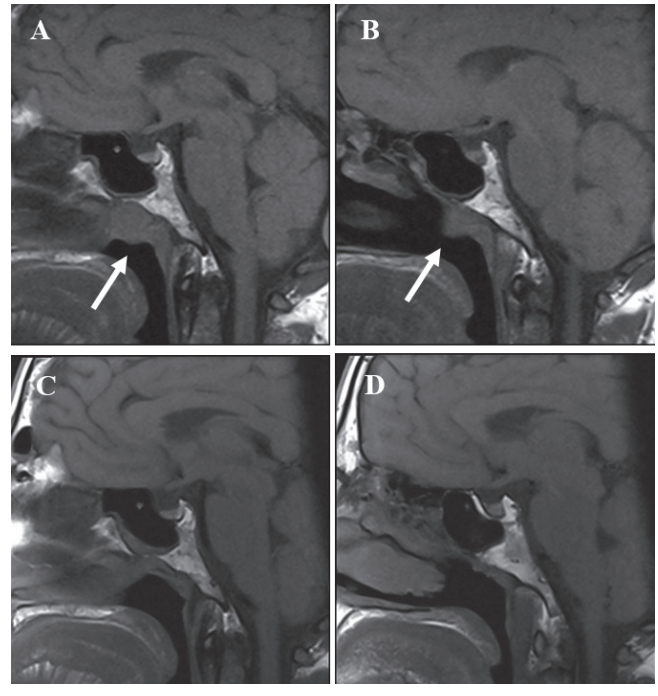

Figure 3. Pituitary MRI images. (A) and (B) pre-operative views indicate a mass lesion (22 x 20 mm) projected by an arrow, which is located in the nasopharyngeal ceiling. Post-operative views (C) and (D) confirm the removal of the mass lesion.

A T3 suppression test was then conducted by oral administration of T3 to assess TSH response. T3 was administered orally in sequential and graded doses of L-T3 (50, 100, and 200 µg/day), each given over 3 days, similar to the administration reported in a previous study (13). Each dose was divided to be administered as two equal doses. Before the test and also during the sequential increases of the doses, thyroid function tests were measured. TSH levels are not suppressed totally in TSH-omas by utilizing the T3 suppression test. Following T3 administration obtaining a TSH level of 10% of baseline or less is a normal response. Results of the T3 suppression tests are given in Table 1 below which is shown that TSH level was not suppressed in our patient.

Since a TSH-secreting pituitary adenoma was suspected, a pituitary magnetic resonance imaging (MRI) was performed, but there were no pituitary abnormalities. However, MRI showed a 22x20 mm mass in the nasopharynx as shown in Figure 3. In this figure, (A) and (B) pre-operative views indicate a mass lesion projected by an arrow, which is located in the nasopharyngeal ceiling. Post-operative views (C) and (D) confirm the removal of the mass lesion.

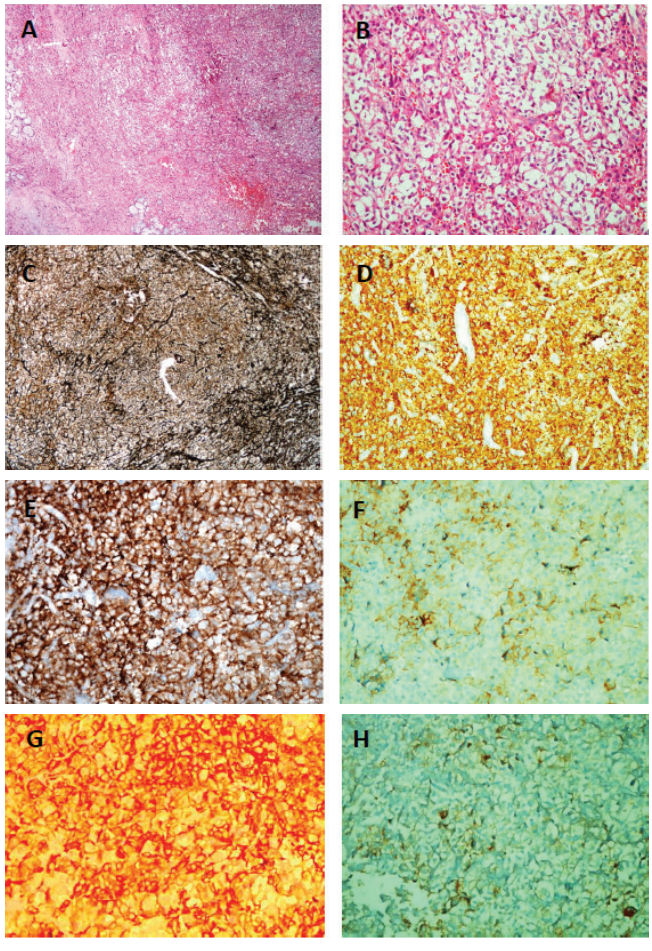

Figure 4. (A) Adenoma area surrounded by salivary glands (H&E;X40), (B) Nest formation in adenoma area (H&E;X400), (C) Spread of reticular roof in adenoma area (Reticulin stain; X200), (D) Brown cytoplasmic staining of Positive synaptophysin (IHC; X200), (E) Positive CD56 appears as brown cytoplasmic staining (IHC; X200), (F) TSH brown cytoplasmic staining positive in adenoma area (IHC; X400), (G) Prolactin positive areas appear as dark brown cytoplasmic staining (IHC; X400), (H) GH positive areas appear as dark brown cytoplasmic staining (IHC; X400).

Octreotide treatment was utilized in pre-operative period to obtain euthyroidism. An operation was planned once normal thyroid function was obtained following octreotide treatment. In June 2015, a mass in the nasopharynx was detected with endoscopy. The patient was admitted for otolaryngology and an endoscopic total endonasal resection was done and the mass was removed. FT4 levels were normalized by antithyroid therapy. The pathology reported a TSH-secreting pituitary adenoma.

Immunohistochemical staining was fixed in formalin, 3 µm thick sections were taken from paraffin-embedded tissues onto electrostatically charged slides and dried in the oven at 60 °C for at least two hours. The entire staining process, including deparaffinization and antigen revealing, was performed on the Ventana, BenchMark LT fully automated immunohistochemistry stainer. Positive and negative controls were used. Normal pituitary tissue was used as positive control. Cytoplasmic staining of the pharyngeal mass was positive.

All pathological views indicates an adenoma area surrounded by salivary glands (Fig. 4A) with nest formation in adenoma area (Fig. 4B). In the tissue with salivary glands in the prepared sections of the excision material, tumoral proliferation formed by cells with uniform, round nuclei, large clear, eosinophilic cytoplasm is observed. This tumoral proliferation creates a nest pattern and a trabecular pattern and shows spread of reticular roof in adenoma area (Fig. 4A). There was no necrosis in the tumor tissue. It was separated from the surrounding tissue with a partial good margin. Breakdown of acinar architecture was observed in the histochemical stain of reticulin. This appearance was compatible with the adenoma. Loss of acinar pattern in reticulin dye is reported as an appearance compatible with an adenoma (14). In our case, it was observed that the reticular roof was disintegrated. Brown cytoplasmic staining of positive synaptophysin is given in Figure 4 (D). Positive CD56 appears as brown cytoplasmic staining in Figure 4 (E). TSH brown cytoplasmic staining (focal) was positive in adenoma area (Fig. 4F), while prolactin positive areas

Table 1. Results of the T3 suppression tests

	TSH (uIU/mL)	FT3 (pg/mL)	FT4 (ng/dL)
Before T3 suppression test	12.76	12.23	3.09
3th day of the test	11.08	15.26	3.8
6th day of the test	7.57	12.93	3.09
9th day of the test	5.25	15.17	2.96

Table 2. Reported cases of Thyroid-Stimulating Hormone-Secreting Ectopic Pituitary Adenoma in Nasopharynx

Case Number	Author, Year	Diagnosis Age	Test Results			Size of adenoma (mm)
1	Cooper and Wenig, 1996	66	T_3 ↑	FT_4 ↑	TSH ↑	8
2	Pasquini *et al.*, 2003	52	FT_3 ↑	FT_4 ↑	TSH ↑	25
3	Collie and Collie,2005	50	FT_3 ↑	FT_4 ↑	TSH ↑	20
4	Tong *et al.*, 2013	49	FT_3 ↑	FT_4 ↑	TSH ↑	20
5	Nishiike *et al.*, 2014	46	FT_3↑	FT_4 ↑	TSH (n)	15
6	Song *et al.*, 2014	41	FT_3 ↑	FT_4 ↑	TSH ↑	19
7	Yang *et al.*, 2017	37	FT_3 ↑	FT_4 ↑	TSH ↑	N/A
8	Kim *et al.*, 2019	48	FT_3 ↑	FT_4 ↑	TSH (n)	11
9	Trummer *et al.*, 2020	48	FT_3 ↑	FT_4 ↑	TSH ↑	20
10	Current case	37	FT_3 ↑	FT_4 ↑	TSH ↑	22

↑ : High level, n : Normal level , N/A : Not applicable.

appear as dark brown cytoplasmic staining (diffuse) in (Fig. 4G). Growth hormone (GH) positive areas appear as dark brown cytoplasmic staining (focal) in Figure 4 (H).

In immunohistochemical examination, synaptophysin (+), CD56 (+), ChromograninA (+), TSH (+), Prolactin (+), GH (+), cytoplasmic staining was detected (Fig. 4), FSH (-), LH (-), ACTH (-). Ki-67 proliferation index was 1-2% (not shown). Ventana polyclonal antibodies were used for TSH, GH, ACTH, LH, FSH. On the other hand, Dako Ab was used for Prolactin.

Other immunohistochemical stainings were PANCK (-), CK7 (-), CK20 (-), CK19 (-), LMWCK (-), EMA (-), S100 (-), Vimentin (-), tyrosine hydroxylase (-), TTF- 1 (-), p53 (-), Neurofilament (-), GFAP (-), PR (-), Actin (-), Galectin-3 (-). With these immunohistochemical stainings, the differentiation of adenoma from metastatic carcinoma, other malignant tumors and paraganglioma was made.

DISCUSSION

Ectopic pituitary adenoma is a pituitary adenoma occurring outside of the sella turcica, without any direct connection to either the intrasellar gland or the pituitary stalk (15). Although extracranial pituitary adenomas comprise the majority of the reported ectopic adenomas, it is most commonly seen in the sphenoid sinus and suprasellar region (16). They are usually located in extra-cranial sites, especially in the sphenoid sinus (17-21). Other extra-cranial sites include the nasal cavity, nasopharynx, mid-nasal duct, clivus, petrous, temporal bone, cavernous sinus, and third ventricle.

From the time of Cooper and colleagues' report in 1996 (11), only 11 cases have been reported, in which just two of them were the pituitary adenoma located in the suprasellar region while the remainder were in the nasopharynx (22, 11, 23-29). In this paper, an identified case of TSH-secreting ectopic pituitary adenoma in the nasopharyngeal region is reported as the tenth case. This case is exceptional, since the literature review reveals that a TSH-secreting ectopic pituitary adenoma is not a common finding, particularly in the nasopharynx.

Regarding the phylogenetics of ectopic pituitary adenoma, it is thought that the origin of the tumor is in embryonic residues of pituitary cells along with the path of migration of Rathke's pouch (24). The anterior pituitary primordium appears at the fourth week of embryogenesis. The pituitary then divides into the sellar and pharyngeal part in the eighth week. The craniopharyngeal canal allows for migration of the pituitary tissue into the sphenoid sinus or nasopharynx (24).

TSH-omas are generally considered in cases where TSH level is inappropriately elevated or normal in patients with increased serum T4 levels whether the tumor is seen on imaging or not. Modern imaging techniques, including computed tomography (CT scan) and MRI have enabled the detection of pituitary tumors more accurately (30,31).

There has been remarkable progress in separating TSH-oma with a proper laboratory procedure. The ideal diagnostic approach would be to receive simultaneously both hormonal and morphologic information, as with functional imaging. Future progress within the imaging field will play an important role in providing methods for a more efficient diagnosis of this rare condition (32).

Sometimes, TSH-oma patients are falsely treated as Graves' disease and as a consequence, patients have long-term thyroid dysfunction (33-34). However, the treatment of TSH-oma differs from primary hyperthyroidism. If the case is treated as a primary hyperthyroidism, progression of TSH-oma can be seen, causing significant complications. Therefore, accurate diagnosis has remarkable importance for the treatment of TSH-oma. Failure to recognize the presence of a TSH-oma may result in critical consequences such as thyroid ablation that may cause further growth in pituitary tumor (35).

In the differential diagnosis, TSH-omas and resistance to thyroid hormone action (RTH) are the two main diseases in thyroid hormone excess. The main difference between these two syndromes consists in the presence of signs and symptoms of hyperthyroidism in patients with TSH-oma, while RTH patients are in general in an euthyroid state (36). In terms of baseline TSH levels and free thyroid hormones basically there is no difference between RTH and TSH-secreting adenoma (1,37). One of the distinguishing methods might be TRH stimulation and octreotide inhibitions tests. A study indicated that 96% of TSH secreting tumors revealed a blunted TSH response to the TRH test and 97% of RTH were excited by TRH (1). The other important method to differentiate TSH-omas from RTH is alpha subunit (α-GSU) /TSH molar ratio. A high α-GSU/TSH molar ratio {[α-GSU (μg/l)/TSH (mU/l)] x 10} is present in about 80% of TSH-omas (6). It is meaningful to consider TSH-omas when the ratio is greater than one and our case indicates high molar ratio (>2).

Literature assessment related to TSH-omas in nasopharyngeal region is given in following statements. In Case 1 (11), the tumor located in the nasopharynx caused hyperthyroidism for many years and the patient had been treated for Graves' disease, receiving antithyroid drugs for an extended period before radioiodine thyroid ablation. Case 2 (22) indicated no evidence of a pituitary tumor by MRI, but a large space-occupying lesion involving the nasal cavity and nasopharynx was incidentally discovered. Case 3 (23) reported an ectopic nasopharygeal TSH-secreting extracranial pituitary adenoma. Case 4 (26) shared an ectopic TSH-secreting tumor, which had plurihormonal secretion *in vitro*, including TSH, GH, and PRL, octreotide was useful in the diagnosis and treatment of this ectopic TSH-secreting tumor. Case 5 of a TSH-secreting ectopic pituitary adenoma of the nasopharynx described the clinical presentation and radiologic findings in one patient with those lesions (25). Case 6 (24) indicated both TSH-oma and resistance to thyroid hormone syndrome. TRH stimulating test was negative, whereas octreotide inhibition test showed a reduction in TSH by 30.8%. Computed tomography and MRI revealed a large space-occupying lesion located at the nasopharynx. Case 7 (27) shared that first radioiodine therapy was carried out followed by levothyroxine replacement therapy. Consequently, the symptoms were relieved, whereas serum TSH remained at high levels even with adequate levothyroxine. Unexpectedly, a thyroid papillary carcinoma and a neoplasm in her nasopharynx were successively detected later, which were then removed by surgery. Case 8 (28) reported a case of an ectopic TSH-secreting pituitary adenoma located in the nasopharynx. This was the first reported use of 68Ga-DOTATATE PET-CT (positron emission tomography-computed tomography) to help in localizing an ectopic TSH secreting tumor. The last case, which is Case 9, (29) indicated a rare case of an ectopic TSH-PitNET (Thyrotropin-secreting neuroendocrine pituitary tumor) with surgical removal following preoperative treatment with octreotide and positive imaging in a Ga68- DOTATATE PET-CT. The patient had an inconspicuous pituitary MRI, however the F19-F-DOPA PET-CT showed a tumor mass located at the pharyngeal roof. Table 2 given below summarizes important parameters of the reported cases of Thyroid-Stimulating Hormone-Secreting Ectopic Pituitary Adenoma in the Nasopharynx.

In our case, age of diagnosis is less than that of eight of the nine previously reported cases. When tumor sizes are considered, only the first case was less than 10 mm as indicated in Table 1. Hormone test results in all cases including our case had high FT3, FT4, TSH levels except for cases 5 and 8, where the TSH level was normal. The first four cases had symptoms of airway obstruction that originated from space-occupying effects, but in our case there was no airway abnormality. Only cases 8 and 9 utilized the Gallium 68 DOTATATE PET-CT method for imaging.

Immunohistochemical staining showed that

this ectopic TSH-secreting tumor secretes TSH, GH and PRL. When all cases of TSH-secreting ectopic pituitary adenoma in nasopharyngeal region (Cases 1-9) are considered, six cases secreted more than one hormone (Cases 1, 3-4, 6 and 8-9). Case 5 and Case 7 did not share any data related to hormone secretion apart from TSH. Immunohistochemical staining of our case indicated TSH (+), GH (+), PRL (+), ACTH (-), FSH (-), LH (-). When all reported cases are assessed, it was realized that Case 4 (26) showed the same immunohistochemical findings; TSH (+), GH (+), PRL (+), ACTH (-), FSH (-), LH (-). Although immunohistochemical staining revealed GH (+) and PRL (+), the results of clinical and laboratory assessment of the patient were not consistent with those findings. IGF-1 and PRL levels were within normal range.

In conclusion, in this report, an identified case of a TSH-secreting ectopic pituitary adenoma in nasopharyngeal region is reported and to the best of our knowledge, it is the tenth case in the literature located in the nasopharyngeal region. In this context, the clinical and laboratory features of earlier papers were reviewed, as well. Although ectopic TSH-omas are rare, they should be considered during inappropriate secretion of TSH as a candidate cause to enable correct diagnosis and treatment.

Conflict of interest

The authors declare that they have no conflict of interest.

References

1. Beck-Peccoz P, Persani L, Mannavola D, Campi I. Pituitary tumours: TSH-secreting adenomas. Best Pract Res Clin Endocrinol Metab. 2009;23:597–606.
2. Sanno N, Teramoto A, Osamura RY. Long-term surgical outcome in 16 patients with thyrotropin pituitary adenoma. J Neurosurg. 2000;93:194-200.
3. Jailer JW, Holub DA. Remission of Graves' disease following radiotherapy of a pituitary neoplasm. American Journal of Medicine 1960 28 497–500.
4. Beck-Peccoz P, Lania A, Beckers A, Chatterjee K , Wemeau JL. 2013 European thyroid association guidelines for the diagnosis and treatment of thyrotropin-secreting pituitary tumors. Eur Thyroid J. 2013;2:76–82.
5. Scheithauer BW, Horvath E, Lloyd RV, Kovacs K. Pathology of pituitary adenomas and pituitary hyperplasia. In Diagnosis and Management of Pituitary Tumors, pp 91–154. Eds K Thapar, K Kovacs, BW Scheithauer & RV Lloyd. Totowa, NJ: Humana Press, 2001.
6. Amlashi FG, Tritos NA. Thyrotropin-secreting pituitary adenomas: epidemiology, diagnosis, and management. Endocrine. 2016; 52(3):427-440.
7. Onnestam L, Berinder K, Burman P, Dahlqvist P, Engström BE, Wahlberg J, Nyström HF: National incidence and prevalence of TSHsecreting pituitary adenomas in Sweden. J Clin Endocrinol Metab 2013;98:626–635.
8. Mindermann T, Wilson CB. Age-related and gender-related occurrence of pituitary adenomas. Clin Endocrinol (Oxf). 1994; 41:359 –364.
9. Polanco Santos C, Sandouk Z, Yogi-Morren D, Prayson R, Recinos P, Kennedy L, Hamrahian AH, Pantalone KM. TSH-staining pituitary adenomas: rare, silent, and plurihormonal. Endocr Pract 2018;24:580-588.
10. Azzalin A, Appin CL, Schniederjan MJ, Constantin T, Ritchie JC, Veledar E, Oyesiku NM, Ioachimescu AG. Comprehensive evaluation of thyrotropinomas: single-center 20-year experience. Pituitary. 2016;19(2):183-193.
11. Cooper DS, Wenig BM. Hyperthyroidism caused by an ectopic TSH-secreting pituitary tumor. Thyroid 1996, 6:337–343.
12. Deniz F, Başaran Y. Endokrinoloji ve Metabolizma Hastalıklarında Kullanılan Dinamik Testler (in Turkish). 2013.
13. Dare GL, de Castro M, Maciel LM. Hypothalamic-pituitary axis and peripheral tissue responses to TRH stimulation and liothyronine suppression tests in normal subjects evaluated by current methods. Thyroid. 2008; 18: 401–409.
14. Al-Brahim NY, Asa SL. My approach to pathology of the pituitary gland. J Clin Pathol. 2006;59(12):1245-1253.
15. Seltzer J, Lucas J, Commins D, Lerner O, Lerner A, Carmichael JD, Zada G. Ectopic ACTH secreting pituitary adenoma of the sphenoid sinus: case report of endoscopic endonasal resection and systematic review of the literature. Neurosurg Focus. 2015;38:E10.
16. Langford L, Baksakis J. Pathology consultation pituitary gland involvement of the sinonasal tract. Ann Otol Rhinol Laryngol 1995;104:167–169.
17. Heitzmann A, Jan M, Lecomte P, Ruchoux MM, Lhuintre Y, Tillet Y. Ectopic prolactinoma within the sphenoid sinus. Neurosurgery. 1989; 24: 279–282.
18. Lloyd RV, Chandler WF, Kovacs K, Ryan N. Ectopic pituitary adenomas with normal anterior pituitary glands. American Journal of Surgical Pathology. 1986; 10: 546–552.
19. Madonna D, Kendler A, Soliman AM. Ectopic growth hormonesecreting pituitary adenoma in the sphenoid sinus. Annals of Otology, Rhinology and Laryngology. 2001; 110: 99–101.
20. Siegert B, vz Muhlen A, Brabant G, Saeger W, Vogt-Hohenlinde C. Ectopic nonfunctioning pituitary adenoma in the sphenoid sinus. Journal of Clinical Endocrinology and Metabolism. 1996; 81: 430–431.
21. Tovi F, Hirsch M, Sacks M, Leiberman A. Ectopic pituitary adenoma of the sphenoid sinus: report of a case and review of the literature. Head and Neck 1990; 12: 264–268.
22. Pasquini E, Faustini-Fustini M, Sciarretta V, Saggese D, Roncaroli F, Serra D, Frank G. Ectopic TSH-secreting pituitary adenoma of the vomerosphenoidal junction. Eur J Endocrinol. 2003; 148:253-257.
23. Collie RB, Collie MJ. Extracranial thyroidstimulating hormone-secreting ectopic pituitary adenoma of the nasopharynx. Otolaryngol Head Neck Surg. 2005;133:453-454.
24. Song M, Wang H, Song L, Tian H, Ge Q, Li J, Zhu Y, Li J, Zhao R, Ji H. Ectopic TSH-secreting pituitary tumor: a case report and review of prior cases. BMC Cancer. 2014;14:544.
25. Nishiike S, Tatsumi KI, Shikina T, Masumura C, Inohara H. Thyroid stimulating hormonesecreting ectopic pituitary adenoma of the nasopharynx. Auris Nasus Larynx. 2014;41:586-588.
26. Tong A, Xia W, Qi F, Jin Z, Yang D, Zhang Z, Li F, Xing X, Lian X. Hyperthyroidism caused by an ectopic thyrotropin-secreting tumor of the nasopharynx: a case report and review of the literature. Thyroid. 2013;23:1172-1177.
27. Yang J, Liu S, Yang Z, Shi YB. Ectopic thyrotropin secreting pituitary adenoma concomitant with papillary thyroid carcinoma: case report. Medicine. 2017;96:e8912.

28. Kim S, Dillon WP, Hope TA, El-Sayed IH, van Zante A, Wu K, Masharani U. Ectopic Thyroid-Stimulating Hormone-Secreting Pituitary Adenoma of the Nasopharynx Diagnosed by Gallium 68 DOTATATE Positron Emission Tomography/Computed Tomography. World Neurosurg. 2019;125:400-404.
29. Trummer C, Reiher H, Theiler-Schwetz V, Pandis M, Gstettner C, Potzinger P, Keck T, Pieber TR, Lax S, Haybaeck J, Stepan V, Pilz S. Secondary Hyperthyroidism due to an Ectopic Thyrotropin-Secreting Neuroendocrine Pituitary Tumor: A Case Report. Eur Thyroid J. 2020;9(2):106-112.
30. Davis PC, Hoffman JC Jr, Tindall GT, Braun IF. CT-surgical correlation in pituitary adenomas: evaluation in 113 patients. AJNR Am J Neuroradiol. 1985;6(5):711-716.
31. Kucharczyk W, Davis DO, Kelly WM, Sze G, Norman D, Newton TH. Pituitary adenomas: high-resolution MR imaging at 1.5 T. Radiology. 1986; 161(3): 761–765.
32. Tjornstrand A, Nystrom HF. Diagnosis of endocrine disease: Diagnostic approach to TSH producing pituitary adenoma. Eur J Endocrinol. 2017, 177:183–197.
33. Zhao W, Ye H, Li Y, Zhou L, Lu B, Zhang S, Wen J, Li S, Yang Y, Hu R. Thyrotropin-secreting pituitary adenomas: diagnosis and management of patients from one Chinese center. Wien Klin Wochenschr. 2012;124(19-20):678-684.
34. Beck-Peccoz P, Persani L. TSH-producing adenomas. DeGroot LJ, Jameson JL editors. Endocrinology, 5th ed. Philadelphia: Elsevier Saundres; 2006: 475–484.
35. Kienitz T, Quinkler M, Strasburger CJ, Ventz M. Long-term management in five cases of TSH-secreting pituitary adenomas: a single center study and review of the literature. Eur J Endocrinol. 2007;157:39–46.
36. Beck-Paccoz P, Brucker-Davis F, Persani L, Smallridge RC & Weintraub BD. Thyrotropin-secreting pituitary tumors. Endocrine Reviews. 1996; 17: 610–638.
37. Brucker-Davis F, Oldfield EH, Skarulis MC, Doppman JL, Weintraub BD: Thyrotropin-secreting pituitary tumors: diagnostic criteria, thyroid hormone sensitivity, and treatment outcome in 25 patients followed at the National Institutes of Health. J Clin Endocrinol Metab. 1999; 84(2):476–486.