Pituitary (2012) 15:110–115
DOI 10.1007/s11102-010-0275-y

Thyroid-stimulating hormone (thyrotropin)-secretion pituitary adenoma in an 8-year-old boy: case report

Yoko Nakayama · Shinya Jinguji · Shin-ichi Kumakura · Keisuke Nagasaki · Manabu Natsumeda · Yuichiro Yoneoka · Takafumi Saito · Yukihiko Fujii

Published online: 27 November 2010

Abstract In this report, an extremely rare case of pediatric thyrotropin-secreting pituitary macroadenoma (TSHoma) is described. An 8-year-old boy, complaining of unsteady gait, was suspected of endocrinopathy because of emaciation and muscle weakness of the legs. Endocrinological work-up established a diagnosis of hyperthyroidism due to syndrome of inappropriate secretion of TSH. Magnetic resonance imaging showed a pituitary macroadenoma with suprasellar and sphenoidal extension without cavernous sinus invasion. He underwent an endoscopic endonasal transsphenoidal adenomectory due to the diagnosis of TSHoma. The adenoma was soft and it was totally removed. Histopathological staining confirmed diagnosis of TSHoma. Postoperative evaluation revealed a subnormal level of TSH (from 13–21 to 0.03 micro U/ml), normalization of alpha-subunit (from 10.0 to 0.09 ng/ml), and as a result, hypothyroidism. The boy left the hospital with oral levothyroxine that continued until 12 months of discharge. The present 8-year-old case is the youngest case to the best of our knowledge based on a bibliographical search. Reasons for endocrinological remission following adenomectomy are (1) correct diagnosis without delay: lack of cavernous sinus invasion, (2) soft and non-fibrous adenoma tissue, and (3) endoscopic technique with wide vision and illumination: safe even for a 8-year-old child. Early recognition/detection and pituitary-conserving adenomectomy can cure TSHoma and avoid long-term medical therapy and/or irradiation, which contribute to the best interests of patients with TSHoma.

Keywords Thyrotropin · Thyroid-stimulating hormone · TSH-secreting pituitary adenoma · Macroadenoma · Pediatric · Endoscopic adenomectomy · Endoscopic surgery

Introduction

Pituitary adenomas in childhood and adolescence constitute 2–6% of all operated pituitary adenomas [1]. Thyroid-stimulating hormone (TSH), also known as thyrotropin, is secreted from cells in the anterior pituitary which is called thyrotrophs and TSH-secreting pituitary adenomas (TSHomas) are rare tumors which classically causing central hyperthyroidism. Hyperthyroidism due to TSHoma is a very rare disorder. It has been estimated that less than 2% of all pituitary tumours are TSHomas, with an incidence of one case per million [2]. A pediatric case of TSHoma is, therefore, extremely rare. In this report, we describe a case of TSHoma in an 8-year-old boy, which has been in remission after endoscopic adenomectomy, and our findings provide useful information for future reference in treating this rare functioning pituitary adenoma in childhood.

Y. Nakayama · S. Jinguji · M. Natsumeda · Y. Yoneoka (✉) · Y. Fujii
Department of Neurosurgery, Brain Research Institute, University of Niigata, 1 Asahimachi-dori Chuo-ku, Niigata 951-8585, Japan
e-mail: yone@bri.niigata-u.ac.jp

S. Kumakura · K. Nagasaki
Department of Pediatrics, Graduate School of Medicine and Dental Sciences, University of Niigata, Niigata, Japan

T. Saito
Department of Neurosurgery, Nagano Red Cross Hospital, Nagano, Japan

Case report

Presentation and examination

This 8-year-old boy presented with mild emaciation and muscle weakness of legs for 2 months before he saw a local orthopedic doctor. The orthopedic doctor was aware of the boy's thin legs and referred him to pediatrics of a general hospital on suspicion of endocrinopathy. He was found to have a syndrome of inappropriate secretion of TSH (SITSH) and the work-up revealed high levels of TSH, free T3, and free T4 (Table 1); low TSH response to TRH stimulation (Table 2); diffuse thyroid goiter without eye signs nor pretibial myxedema. Magnetic resonance (MR) imaging showed a pituitary macroadenoma with suprasellar and sphenoidal extension without cavernous sinus invasion (Fig. 1). His visual fields were intact despite chiasmal compression by the adenoma.

Operation

As hyperthyroidism due to SITSH caused by TSHoma was diagnosed in the boy, he underwent an endoscopic endonasal transsphenoidal adenomectory (EETS-adenomectomy). When the sphenoidal extension of the adenoma was removed, we encountered profuse epidural/dural bleeding. The sphenoidal and intrasellar adenoma tissues were hemorrhagic (Fig. 2, upper left and right), however, they were sucked out and removed with a 3-mm-across suction tube and curettage. On the other hand, suprasellar adenoma bulk was much softer, whitish, and non-hemorrhagic (Fig. 2, lower left), and the adenoma was thus totally removed (Fig. 2, lower right). Estimated blood loss was 100 ml in this surgery.

Postoperative course

His postoperative course was uneventful except for diabetes insipidus that resolved spontaneously within 1 week. Postoperative evaluation revealed a subnormal level of TSH (from 13–21 to 0.03 μU/ml), normalization of alpha-subunit (from 10.0 to 0.09 ng/ml), and as a result, hypothyroidism (Table 1, Fig. 3). Histopathological diagnosis was chromophobe pituitary adenoma with positivity for TSH-beta moderately and for growth hormone and prolactin slightly (Fig. 4). Postoperative MR imaging showed no residual adenoma (Fig. 5). The boy left hospital with oral administration of levothyroxine that continued 12 months after discharge. His serum TSH level rose up to 0.57 and 0.89 micro U/ml (normal range: 0.54–4.26) one and 11 months after the operation, respectively (Fig. 3).

Table 1 Perioperative blood examination of thyroid function

	Preoperative	Postoperative	Normal range
Free T3 (ng/dl)	11.3	1.3	(2.29–4.17)
Free T4 (ng/dl)	3.8	0.4	(0.72–1.52)
TSH (μU/ml)	13.17	0.12	(0.54–4.26)
Alpha-subunit (IU/L)	10.0	0.09	(< 0.5)

Table 2 Results of insulin-TRH-LHRH-loading test

	Baseline	15 min	30 min	60 min	90 min	120 min
BG (mg/dl)	93	30	37	86	90	92
TSH (μIU)	**13.17**	**14.55**	**16.97**	**18.00**	**15.47**	**14.26**
PRL (ng/ml)	8.8	22.0	20.5	14.5	10.9	11.3
LH (mIU)	<0.6	0.7	1.1	1.3	1.1	0.9
FSH (mIU)	1.8	2.5	3.0	3.6	4.0	3.9
GH (ng/ml)	1.7	1.0	1.3	1.3	2.2	2.2
COR (μg)	11.0	13.0	12.5	20.3	10.3	7.0
ACTH (pg/m)	39.5	45.7	69.3	61.0	24.9	21.4

Bold values mean that the continuous excessive secretion of TSH indicates hypersecretion from tumor

BG blood glucose, *TSH* thyroid-stimulating hormone, *PRL* prolactin, *LH* lutenizing hormone, *FSH* follicle-stimulating hormone, *GH* growth hormone, *COR* cortisol, *ACTH* adrenocorticotropic hormone

Discussion

Six cases of TSHoma aged 15 and under have been described previously (Table 3) [3–8]. The present 8-year-old case is the youngest case at present to the best of our knowledge based on our bibliographical search. Among these pediatric cases of TSHoma, including our case, two cases out of six cases were in remission following adenomectomy.

This case manifested hyperthyroidism associated with mild emaciation and muscle weakness as the initial symptoms and reached a diagnosis without undue delay. This is because clinicians are more familiar with the concept of inappropriate secretion of TSH [9]. Misdiagnosis leads to inappropriate thyroid ablation (surgery of radioiodine) and/or delayed diagnose, and these tumors often exhibit progressive growth and invasiveness [2, 10].

The present case of TSHoma was a macroadenoma with suprasellar and sphenoidal extension albeit without cavernous sinus invasion. And this adenoma was not fibrous but soft enough to remove with suction and gentle curettage unlike a report by Sanno et al. [11]. On the other hand, intrasphenoidal adenomectomy caused profuse epidural/dural hemorrhaging, which is compatible with previous suggestions: The majority of TSHomas are macroadenomas and invasive [1, 12]. Our speculation is that

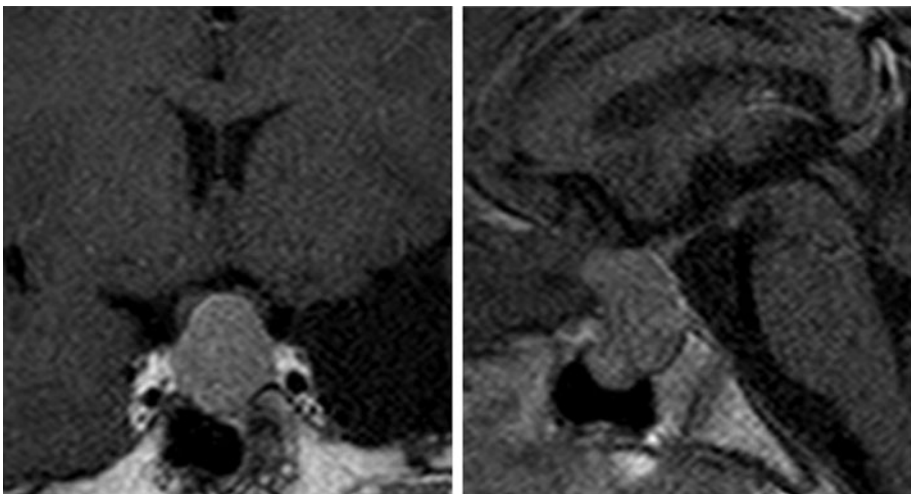

Fig. 1 Post-contrast MR images show a macroadenoma extending into the sphenoid sinus and suprasellar region without cavernous sinus invasion. The adenoma displaces the optic pathway upward. Arachnoid cyst is shown in the *left middle* cranial fossa

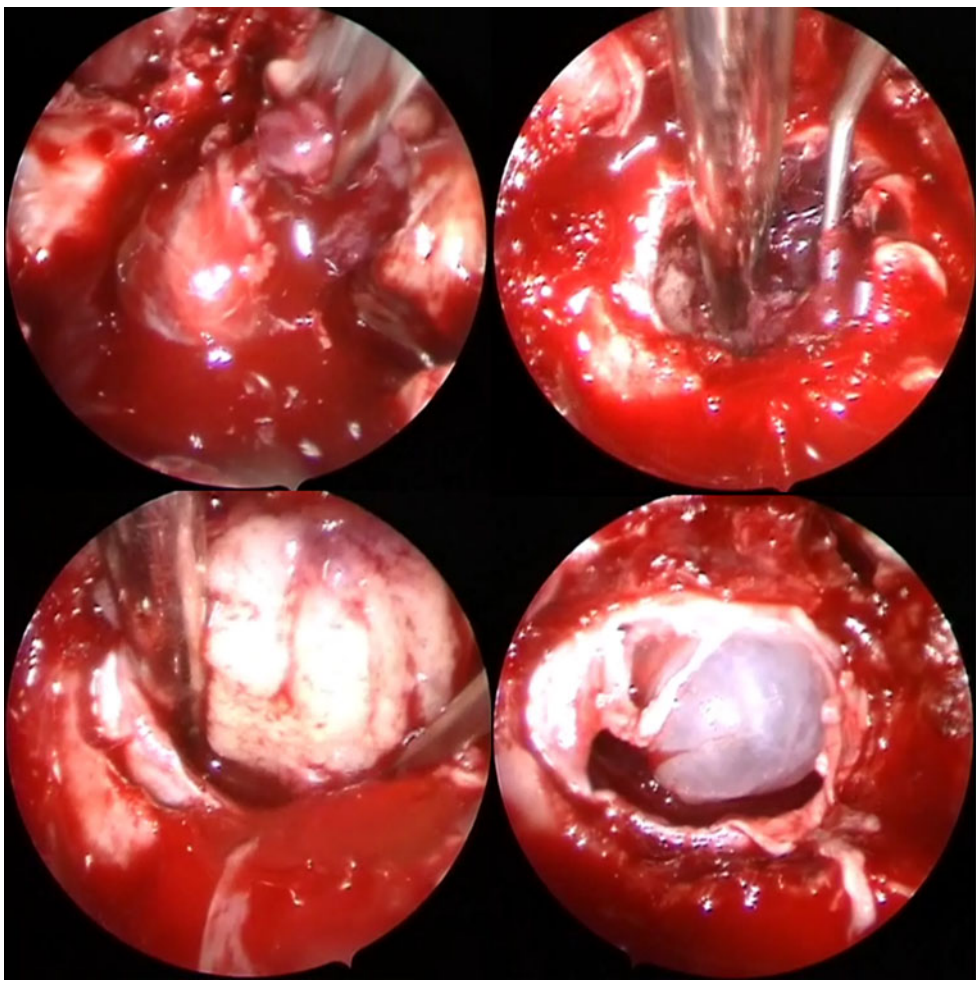

Fig. 2 Intraoperative findings. The intrasphenoidal-intrasellar part was hemorrhagic and *reddish* (*upper left and right*) but the suprasellar part was non-hemorrhagic, whitish and soft enough to remove with suction and gentle curettage (*lower left*), which were totally removed (*lower right*)

aggressive/invasive functioning adenomas require more blood flow than normal, and the aggressiveness/invasiveness of this TSHoma has shares features with cases of growth hormone-secreting pituitary adenoma in childhood as reported by Abe et al. [13]. Thus, surgeons need to prepare properly for hemostasis in resection of pediatric functioning adenomas. This careful preparation requires appropriate hemostatic materials such as oxidized

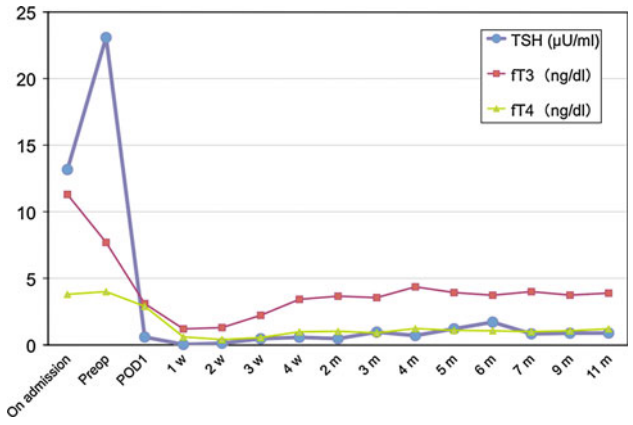

Fig. 3 A *line graph* shows perioperative values of TSH, free-T3, and free-T4. Alpha-subunit is also reduced drastically as well as TSH

cellulose, microfibrillar collagen hemostat, and so on to control bleeding during adenomectomy.

The primary goal of treatment of TSHomas is to remove the pituitary tumor and to restore euthyroidism. Some authors state, however, that this may be particularly difficult because of the marked fibrosis of these tumors, possibly related to high expression of basic fibroblast growth factor [14]. In the recent reports, 50–62.5% of TSHomas are in remission following surgery [11, 15].

Our case achieved remission after endoscopic adenomectomy. The causes of surgical remission were (1) mainly soft tumor and (2) without cavernous sinus invasion. For the last 15 years, among 915 cases of pituitary adenoma in our institute, seven cases (0.77%) of TSHomas were histopathologically confirmed. In particular, among the 915 cases of ours, a pediatric TSHoma is this case only (0.11%). Five out of the seven attained remission with adenomectomy: 71.4% were in remission following surgery. The five case lacked apparent cavernous sinus invasion. Four out of the five (80% of remission cases following surgery) underwent endoscopic adenomectomy.

The patient boy left our hospital without sequelae under oral levothyroxine that continued until 12 months of discharge. His TSH, free-T3, and free-T4 value was 0.68 μU/ml, 3.70 ng/dl, and 1.07 ng/dl respectively. Attention of pediatric endocrinologists is vital to manage a special case like this appropriately.

His TSH value rose slightly 1 month after operation. He has regained and enjoyed his fruitful school life through hypophysis-sparing adenomectomy under endoscopic vision. The clinical course of our case supports that the endoscopic method is a safe, hardly invasive, and efficient surgical technique in the treatment of pediatric functioning pituitary adenomas [16] as well as in TSHomas. Although

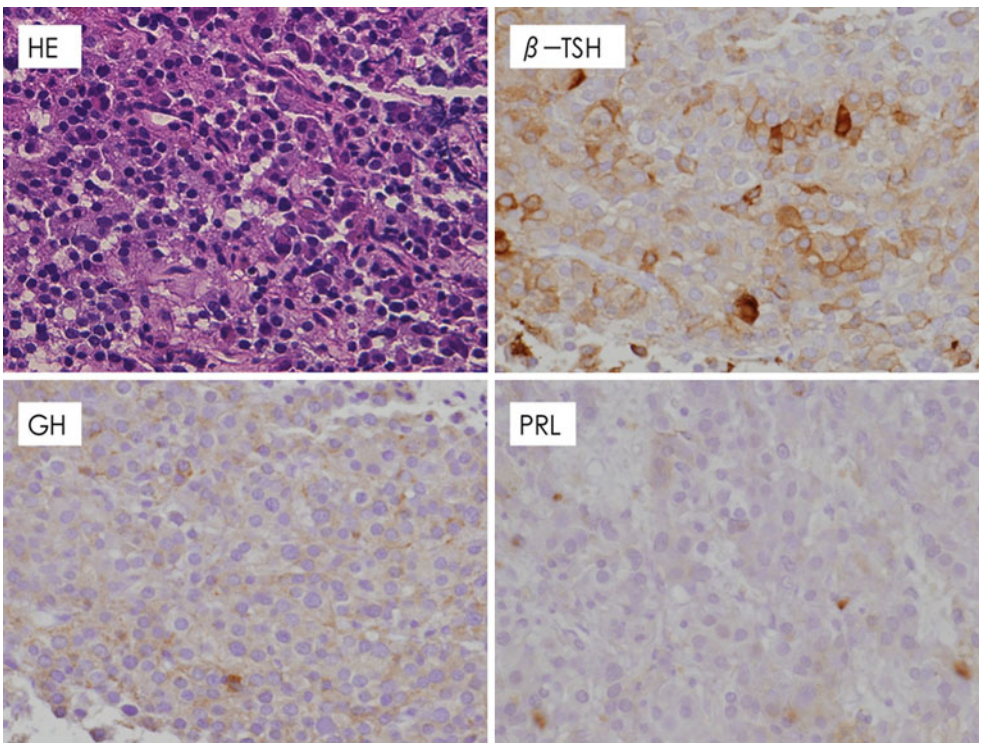

Fig. 4 Photomicrographs of the surgical specimen revealing positivity for TSH-beta (*upper right*), and co-expression of growth hormone (*lower left*) and prolactin (*lower right*). The tumor is composed of uniform small cells with only a small amount of cytoplasm (*upper left*, hematoxylin and eosin staining)

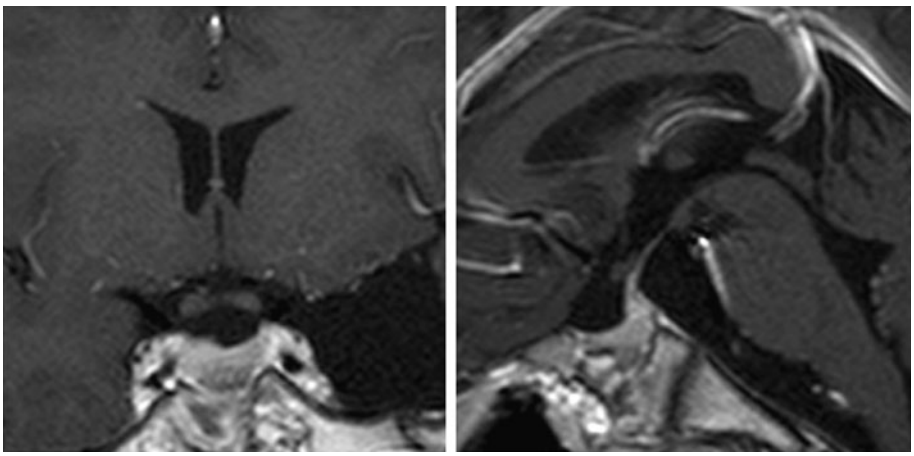

Fig. 5 Postoperative contrasted MR imaging demonstrated no residual adenoma

Table 3 Summary of the 6 cases reported in the literature of pediatric TSH-secreting pituitary adenomas and the present case, aged 15 and under

Authors and year	Patient age (year), sex	Macro- or microadenoma	Surgery, removal level	Remission through surgery
The present case	8, M	Macro	TSS, total removal	Yes
Suntornlohanakul et al. [8]	11, M	Macro	N/A, partial removal	No
Avamides et al. [3]	11, F	Macro	TCS, partial removal	No
Korn et al. [5]	13. F	Micro	TSS, total removal	Yes
Phillip et al. [6]	13, M	Macro	TSS, total removal	No
Stanley et al. [7]	15, M	Macro	TSS, total removal	No
Gannage et al. [4]	15, F	N/A	N/A, N/A	N/A

TSS transsphenoidal surgery, *TCS* transcranial surgery, *N/A* not available

effectiveness of somatostain therapy for TSHoma has been reported [13], early recognition/detection [2] and pituitary-conserving adenomectomy can avoid long-term medical therapy and/or irradiation.

More practical experience must be acquired for further study of this rare functioning pituitary adenoma in pediatric populations.

References

1. De Menis E, Visentin A, Billeci D, Tramontin P, Agostini S, Marton E, Conte N (2001) Pituitary adenomas in childhood and adolescence. Clinical analysis of 10 cases. J Endocrinol Invest 24:92–97
2. Beck-Peccoz P, Brucker-Davis F, Persani L, Smallridge RC, Weintraub BD (1996) Thyrotropin-secreting pituitary tumors. Endocr Rev 17:610–638
3. Avramides A, Karapiperis A, Triantafyllidou E, Vayas S, Moshidou A, Vyzantiadis A (1992) TSH-secreting pituitary macroadenoma in an 11-year-old girl. Acta Paediatr 81:1058–1060
4. Gannage MH, Maacaron C, Okais N, Halaby G (1997) Thyroid-stimulating hormone hypophyseal adenoma. A case report. J Med Liban 45:97–101 (Article in French)
5. Korn EA, Gaich G, Brines M, Carpenter TO (1994) Thyrotropin-secreting adenoma in an adolescent girl without increased serum thyrotropin-alpha. Horm Res 42:120–123
6. Phillip M, Hershkovitz E, Kornmehl P, Cohen A, Leiberman E (1995) Thyrotropin secreting pituitary adenoma associated with hypopituitarism and diabetes insipidus in an adolescent boy. J Pediatr Endocrinol Metab 8:47–50
7. Stanley JM, Najjar SS (1991) Hyperthyroidism secondary to a TSH-secreting pituitary adenoma in a 15-year-old male. Clin Pediatr (Phila) 30:109–111
8. Suntornlohanakul S, Vasiknanont P, Mo-Suwan L, Phuenpathom N, Chongchitnant N (1990) TSH secreting pituitary adenoma in children: a case report. J Med Assoc Thai 73:175–178
9. Socin HV, Chanson P, Delemer B, Tabarin A, Rohmer V, Mockel J, Stevenaert A, Beckers A (2003) The changing spectrum of TSH-secreting pituitary adenomas: diagnosis and management in 43 patients. Eur J Endocrinol 148:433–442
10. Brucker-Davis F, Oldfield EH, Skarulis MC, Doppman JL, Weintraub BD (1999) Thyrotropin-secreting pituitary tumors: diagnostic criteria, thyroid hormone sensitivity, and treatment outcome in 25 patients followed at the National Institutes of Health. The Journal of Clinical Endocrinology and Metabolism 84:476–486
11. Sanno N, Teramoto A, Osamura RY (2000) Long-term surgical outcome in 16 patients with thyrotropin pituitary adenoma. J Neurosurg 93:194–200
12. Ness-Abramof R, Ishay A, Harel G, Sylvetzky N, Baron E, Greenman Y, Shimon I (2007) TSH-secreting pituitary adenomas: follow-up of 11 cases and review of the literature. Pituitary 10:307–310
13. Abe T, Tara LA, Ludecke DK (1999) Growth hormone-secreting pituitary adenomas in childhood and adolescence: features and results of transnasal surgery. Neurosurgery 45:1–10

14. Ezzat S, Horvath E, Kovacs K, Smyth HS, Singer W, Asa SL (1995) Basic fibroblast growth factor expression by two prolactin and thyrotropin-producing pituitary adenomas. Endocr Pathol 6:125–134
15. Clarke MJ, Erickson D, Castro MR, Atkinson JL (2008) Thyroid-stimulating hormone pituitary adenomas. J Neurosurg 109:17–22
16. De Divitiis E, Cappabianca P, Gangemi M, Cavallo LM (2000) The role of the endoscopic transsphenoidal approach in pediatric neurosurgery. Childs Nerv Syst 16:692–696