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CASE REPORT

Doença de Cushing: como conduzir adequadamente esse distúrbio neuroendócrino?

Cushing's disease: how to properly manage this neuroendocrine disorder?

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ABSTRACT

Introduction: The pituitary gland is responsible for hormone synthesis and is located at the base of the brain, inside the sella turcica. Some tumors can affect this gland, among them the adrenocorticotropin (ACTH) secreting tumor, causing Cushing's Disease (CD). In CD, the ACTH-secreting pituitary tumor stimulates cortisol production by the adrenal cortex, leading to characteristic clinical manifestations of this pathology. **Objective:** The present study aims to report a case of CD diagnosed at the Neurology and Neurosurgery Outpatient Clinic of *Santa Casa de Misericórdia de Barbacena* /MG. **Discussion:** CD is a pathology that presents extensive clinical manifestation. Laboratorially, we can use the 24-hour urinary cortisol excretion test and salivary cortisol measurement before sleep for the diagnosis of Cushing's Syndrome (CS). While the ACTH value should be carefully evaluated to discern whether CS is ACTH-dependent or independent. In addition, Magnetic Resonance Imaging of the sella turcica allows visualization of the pituitary gland and enables the establishment of the diagnosis of CD. After diagnosis, transsphenoidal surgery is the basis of treatment for most cases, and is associated with a high-resolution rate when performed by experienced neurosurgeons and in specialized pituitary centers. **Conclusion:** CD presents broad clinical manifestations, requiring a high degree of clinical suspicion together with the analysis of laboratory and imaging tests for correct diagnosis. When the symptoms of CD are approached separately, the diagnosis is not made or is delayed and the patient can develop the complications of this pathology, given that this approach is not curative for the origin of the problem.

Keywords: Pituitary ACTH hypersecretion; Cushing's syndrome; Corticotrophs; Endocrinology; Neurosurgery.

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RESUMO

Introdução: A hipófise é uma glândula responsável pela síntese de hormônios e se localiza na base do cérebro, no interior da sela túrcica. Alguns tumores podem acometer essa glândula, dentre eles o secretor de adrenocorticotrofina (ACTH), provocando a Doença de Cushing (DC). Na DC, o tumor hipofisário secretor de ACTH estimula a produção de cortisol pelo córtex das glândulas suprarrenais, acarretando manifestações clínicas características dessa patologia. **Objetivo:** O presente estudo tem como objetivo relatar um caso de DC diagnosticado no Ambulatório de Neurologia e Neurocirurgia da Santa Casa de Misericórdia de Barbacena/MG. **Discussão:** A DC é uma patologia que apresenta extensa manifestação clínica. Laboratorialmente podemos utilizar o teste de excreção urinária de cortisol em 24 horas e a dosagem de cortisol salivar antes de dormir para o diagnóstico de síndrome de Cushing (SC). Enquanto o valor de ACTH deve ser cuidadosamente avaliado para discernir se a SC é dependente ou independente de ACTH. Em complemento, a Ressonância Magnética da sela túrcica permite a visualização da hipófise e possibilita o estabelecimento do diagnóstico de DC. Após a definição do diagnóstico, a cirurgia transesfenoidal caracteriza-se como a base do tratamento para a maioria dos casos, e está associada a uma alta taxa de resolução, quando realizada por neurocirurgiões experientes e em centros especializados em hipófise. **Conclusão:** A DC apresenta manifestações clínicas amplas, exigindo alto grau de suspeição clínica juntamente com a análise de exames laboratoriais e de imagem para o correto diagnóstico. Quando os sintomas da DC são abordados separadamente, o diagnóstico não é realizado ou adiado e o paciente pode desenvolver as complicações dessa patologia, visto que essa proposta não é curativa para a origem do problema.

Palavras-chave: Hipersecreção hipofisária de ACTH; Síndrome de Cushing; Corticotrofos; Endocrinologia; Neurocirurgia.

Introduction

The pituitary gland is located at the base of the brain, situated within the sella turcica and has two lobes: anterior and posterior. The posterior lobe, also called the neurohypophysis, originates from the floor of the diencephalon and is constituted by axons with neuronal bodies positioned in the hypothalamus, being responsible for the secretion of the hormones oxytocin and vasopressin (ADH). The adenohypophysis, on the other hand, originates from the roof of the primitive mouth, presenting epithelial cells that produce the hormones prolactin (PRL), thyrotropin (TSH), adrenocorticotropin (ACTH), growth hormone (GH), follicle-stimulating hormone (FSH) and luteinizing hormone (LH)[1,2].

Cushing's Disease (CD) is caused by ACTH-secreting pituitary tumors, which stimulate cortisol secretion by the adrenal cortex. This condition is the most common etiology (70% to 80% of cases) of endogenous Cushing's Syndrome (CS), which is the set of signs and symptoms generated by supraphysiological levels of circulating cortisol[3].

The description of this report demonstrates that complaints can be erroneously addressed when a precise diagnosis and treatment of the underlying cause that justifies the repertoire of signs and symptoms presented by a patient are not carried out in a complete manner. If not effectively managed, CD is associated with arterial hypertension, diabetes, obesity, osteoporosis, vascular diseases and reduced life expectancy[4]. Therefore, the present study aims to report a case of classic CD and its correct therapy.

Case Report

A 30-year-old male patient,rural worker, was referred by an endocrinologist to the Neurosurgery service of Santa Casa de Misericórdia de Barbacena/MG, presenting with

insomnia, adynamia and systemic arterial hypertension for three years. He reported that, over this period, he evolved with progressive weight gain of approximately 30kg. He was using Losartan 50mg (1-0-1), Atenolol 25mg (1-0-1), Spironolactone 25mg (0-1-0), Simvastatin 20mg (0-0-1) and Alprazolam 2mg (0-0-1). He denied the use of glucocorticoids by any route of administration.

During ectoscopy, the presence of "moon face" / cushingoid facies was observed (Figure 1A). On inspection of the thoracoabdominal region, rude violaceous cutaneous striae were identified in the lateral thoracic and bilateral abdominal regions, as well as centripetal obesity (Figure 1B). Neurological examination revealed a normal level of consciousness, mental state, cranial nerves, coordination and balance, gait, motility, reflexes and sensitivity. In addition, no visual field compromises or papilledema were detected.

Laboratory tests analyzed during the consultation showed elevated salivary cortisol before sleep and 24h urinary cortisol (Table 1).

Based on clinical and laboratory data, the diagnostic hypothesis of a functioning adenoma was raised. Due to the onset of the condition in a young adult, for differential diagnosis, it was necessary to investigate the possibility of Multiple Endocrine Neoplasia type-1 (MEN-1). The absence of a family history compatible with MEN-1, together with unaltered laboratory tests, allowed the exclusion of this genetic entity. The investigation proceeded with the request for a pituitary magnetic resonance imaging (MRI), revealing enlargement of the sella turcica and an expansive lesion in the central sellar region, right paramedian, with heterogeneous enhancement, measuring 1.3 x 1.0 cm, suggestive of macroadenoma (Figures 2A and 2B). Despite its location and macroadenoma characteristic, the patient did not present complaints related to visual field loss, such as the typical bilateral hemianopsia, caused by compression of the optic chiasm.

Thus, the finding of a sellar tumor > 0.6cm confirmed the possibility of CD, as opposed to pituitary incidentalomas, which are commonly smaller lesions. Next, we referred the patient for transsphenoidal surgery as initial treatment[5]. When successful, the patient can achieve a cure for CD, and eventually, remain without alterations in hypothalamus-pituitary-adrenal function[6]. However, recurrences are not uncommon, presenting up to 10 years after successful treatment, justifying the need for clinical follow-up thereafter[7].

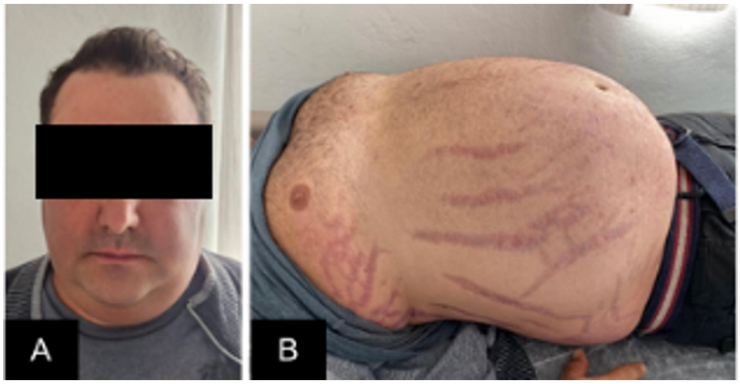

Figure 1. Ectoscopy and physical examination data. **A.** Typical facies: "moon face" or cushingoid; **B**. Violaceous striae in the lateral thoracic and abdominal regions.

Source: Personal archive.

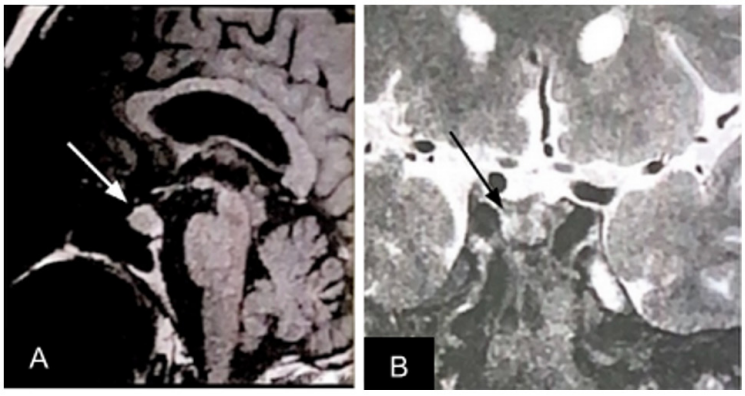

Figure 2. Pituitary MRI. **A.** Expansive sellar lesion highlighted in the sagittal view (white arrow). **B.** Expansive sellar lesion highlighted in the coronal view (black arrow).

Source: Personal archive.

Four months after the surgical treatment was indicated, the operation was performed. The serum cortisol concentration was 48 nmol/L (1.74 µg/dL) after the procedure. As the remission criterion was met (< 55 nmol/L), glucocorticoid replacement was initiated, which should continue until recovery of the axis. In the immediate and intermediate postoperative period, there were no clinically relevant complications, and the patient was discharged on the seventh day, with vital signs within normal limits, except for mild hypertension. However, in the late postoperative period, during his home recovery, the patient began complaining of pain in his right lower limb and dyspnea, progressing to lethargy. After seeking medical attention, the diagnostic hypothesis of sepsis of pulmonary origin was raised, evolving to death on the twelfth postoperative day in the intensive care unit. Nevertheless, the diagnostic probability of a venous thromboembolism should prevail and be managed as such. Furthermore, thromboprophylaxis with low molecular weight heparin should be considered, lasting from the diagnosis until 3 months after biochemical remission, given that there were no evident contraindications[8].

Table 1. Admission laboratory tests.

Complete Blood Count	
Hemoglobin (NR = 14-18 g/dl)	13,8 g/dl
Hematocrit (NR = 41-54%)	41%
Leukocytes (NR= 4.000-10.000 /mm^3)	11.500 /mm^3
Segmented (NR = 1.800-7.500 /mm^3)	9.200 /mm^3
Typical Lymphocytes (NR = 1.200-5.200 /mm^3)	2.185 /mm^3
Monocytes (NR = 80-800 /mm^3)	115 /mm^3
Eosinophils (NR = 40-450 /mm^3)	0 /mm^3
Platelets (NR = 150.000-450.000 /mm^3)	299.000 /mm^3
Lipid and Glycemic Profile	
Total Cholesterol (NR ≤ 200)	211,0 mg/dl
HDL Cholesterol (NR ≥ 35)	61,0 mg/dl
LDL Cholesterol (NR ≤ 100)	131,4 mg/dl
VLDL Cholesterol (NR ≤ 34)	18,6 mg/dl
Triglycerides (NR ≤ 200)	93 mg/dl
Glucose (NR = 65-99 mg/dl)	79 mg/dl
Glycated Hemoglobin (NR ≤ 5,7%)	5,4%
Liver Profile	
Aspartate Aminotransferase - AST (NR = Up to 40 U/L)	13 U/L
Alanine Aminotransferase - ALT (VN = Up to 40 U/L)	24 U/L
Electrolyte and Renal Profile	
Sodium (NR = 130-150 mEq/L)	131,0 mEq/L
Potassium (NR = 3,5-5,0 mEq/L)	4,6 mEq/L
Calcium (NR = 8,8-10,2 mg/dl)	9,2 mg/dl
Creatinine (NR = Up to 1,4 mg/dl)	0,91 mg/dl
Urinary creatinine (NR = 1.300-2.050 mg/24h)	1.876 mg/24h
Endocrine Profile	
Free Thyroxine- T4 (NR = 0,70-1,80 ng/dl)	0,91 ng/dl
Parathyroid Hormone (NR = 10-65 pg/mL)	46 pg/mL
Vitamin D - 25 hydroxy (NR ≥ 20 ng/ml)	28,4 ng/ml
Thyroid Stimulating Hormone - TSH (NR = 0,400-4,300 uUI/ml)	0,610 uUI/ml
Prolactin (NR = 4,04-15,2 ng/ml)	26,9 ng/ml
Macroprolactin (NR ≥ 65%)	96% - Negative
Night Salivary Cortisol (NR ≤ 0,274 ug/dl)	0,848 ug/dl
Urinary Cortisol (NR = 21-111 ug/24h)	811 ug/24h
Serum Cortisol at Midnight (NR ≤ 7,5 ug/dl)	16,1 ug/dl
Adrenocorticotropic Hormone - ACTH (NR = Up to 46 pg/ml)	40,8 pg/ml

Legend: NR = Normal reference.
Source: Prepared by the authors based on the tests presented by the patient.

Discussion

CD was first described by Harvey Cushing in 1932[8] and currently has a prevalence of 40 cases per million inhabitants and an incidence of 1-3 newly diagnosed cases per 1 million people per year. The average age of diagnosis for adults is between 40 and 50 years of age[3].

The tumors responsible for triggering CD are almost always benign and are usually microadenomas (< 10mm in diameter), and, for this reason, are often only identified upon microscopic examination. Only in 10 to 25 percent of cases does the lesion grow to cause changes in imaging exams of the sella turcica, demarcating a macroadenoma[9].

Clinically, they manifest through CS, with a wide range of systems affected by excess cortisol (table 2)[10].

The aforementioned symptoms present in CD, when managed separately and not analyzed as a syndrome, with glucocorticoid levels remaining above the normal limit, are responsible for generating complications such as cardiac and cerebrovascular events, immunosuppression, osteoporosis, psychiatric disorders, obesity and diabetes. In addition, the prolonged elevation of cortisol in patients with CD stimulates hepatic cholesterol synthesis, inducing changes in eating habits, such as the preference for foods rich in lipids and carbohydrates, which directly contributes to the increase in LDL-c[2], and consequently contributes to cardiovascular complications[5].

Together, these complications in an untreated individual generate an estimated standardized mortality rate (ratio between observed CD-related deaths and expected deaths in the general population) of 1.9-4.8[4].

Due to the onset of the condition in a young adult, there is a need to investigate Multiple Endocrine Neoplasia type-1 (MEN-1), a rare hereditary genetic disease that requires a high index of suspicion. In clinical practice, it can be ruled out by the association of a negative family history, especially for tumors arising from the parathyroid glands (hyperplasia or adenoma), the anterior pituitary and the pancreatic islets, together with the request for serum calcium analysis accompanied by parathyroid hormone (PTH), which consequently should be within normal limits, excluding hyperparathyroidism. As both criteria were met in this clinical case, it was possible to rule out this important differential diagnosis. Ideally, genetic testing for the pathogenic MEN1 variant is advisable[1].

Furthermore, due to exogenous corticosteroids being the main cause of hypercortisolism, their use should be actively questioned during the consultation and excluded according to the detailed anamnesis of the patient[5].

The interpretation of the elevated PRL value also deserves caution. The slightly increased value is likely justified by the enlargement of the sella turcica, compromising the inhibitory dopaminergic pathways. Thus, the test should be repeated on a fasting sample before considering the patient to have hyperprolactinemia1[2]. Furthermore, we must remember pharmacological etiologies, with emphasis on psychotropics. In this case, the daily use of benzodiazepine medication

Table 2. Main signs and symptoms in Cushing's syndrome.

Metabolic	
Weight gain Central Obesity "Moon face"	Dorsal fat pad "Buffalo Hump" Glucose intolerance
Cardiovascular	
Arterial hypertension Atherosclerosis Propensity for venous thromboembolism	ECG Abnormalities: Sinus Tachycardia; Repolarization abnormalities; QT Interval prolongation
Hyperandrogenism (women) and Hypogonadism	
Decreased libido Hirsutism	Menstrual changes Female Baldness
Neuropsychiatric	
Depression Lethargy	Headache Cognitive impairment
Dermatological and musculoskeletal	
Violaceous striae Acne Plethoric facies Ecchymosis	Low back pain Abdominal Pain Proximal muscle weakness Osteopenia Fragility Fracture
Immunological	
Recurrent infections	

Source: Elaborated by the authors.

can also be a cofactor for transient PRL elevations[13]. PRL is capable of reducing gonadotropins, generating in men a drop in testosterone, with oligospermia or azoospermia, loss of libido and impotence, in addition to the classic clinical picture (although rare in men) of galactorrhea, which were not present in this case[14].

Regarding diagnostic laboratory tests, the 24-hour urinary cortisol excretion test provides a practical and reliable index of cortisol secretion, being validated for screening[15,16]. To validate urine collection, it must be accompanied by 24-hour creatinine in the same sample[5]. As seen in this report, it can be presumed that the patient has SC if the basal urinary cortisol excretion is abnormal and accompanied by another altered test. This other test can be salivary cortisol measurement before sleep, performed concomitantly with the previous one, enhancing the total sensitivity to establish the diagnosis of CS[17]. Its performance is routinely feasible as it is non-invasive, and cortisol is stable in saliva even at room temperature for several days. However, to reduce false results, the patient should be instructed to avoid some practices before collection, such as oral hygiene, smoking, ingestion of food or drinks, physical exercise, among others[18].

To confirm the diagnosis of CD, as opposed to CS alone, we requested serum cortisol at midnight. In addition, the dexamethasone or desmopressin tests can also be performed. Another fundamental laboratory point for clinical reasoning refers to the ACTH value. What becomes clinically relevant are ACTH values > 10 pg/ml, which in fact correlate with ACTH-dependent CS[5]. The next step is to find out if the source of excess ACTH comes from the pituitary or is ectopic. Among the possible strategies for this definition, we opted for pituitary MRI for two reasons: to exclude the possibility of a tumor larger than 6 mm, and consequently avoid the need for petrosal sampling[19], and preoperatively to document the anatomy of the sella turcica and enable better transsphenoidal exploration.

Once the clinical-laboratory diagnosis of CS and the diagnosis of CD through MRI with visualization of the pituitary tumor are concluded, transsphenoidal surgery is the pillar of treatment for most types of pituitary macroadenomas and other sellar masses. It presents a cure rate of 75% to 90%, if under the care of experienced neurosurgeons, and is relatively non-invasive, as access for tumor resection is made through the posterior nasopharynx, with an incision in the sphenoidal ostia or in the posterior septum[5] (Figure 3)[20]. The main risks of surgery include hormonal deficiencies and damage to parasellar structures; however, these are less frequent if performed by more experienced surgeons and institutions[21]. If surgery is successful, serum cortisol commonly drops drastically on the first or second postoperative day. Still, even effectively treated, some patients may have a higher frequency of diabetes, obesity and dyslipidemia compared to controls[4]. Furthermore, as recurrence is not uncommon, reoperation is an option, with approximately 40% to 60% success[22], or instead, clinical treatment with medication therapy or radiotherapy can be offered[5]. Recurrence is believed to be due to invasion of neoplastic cells into the dura mater, a

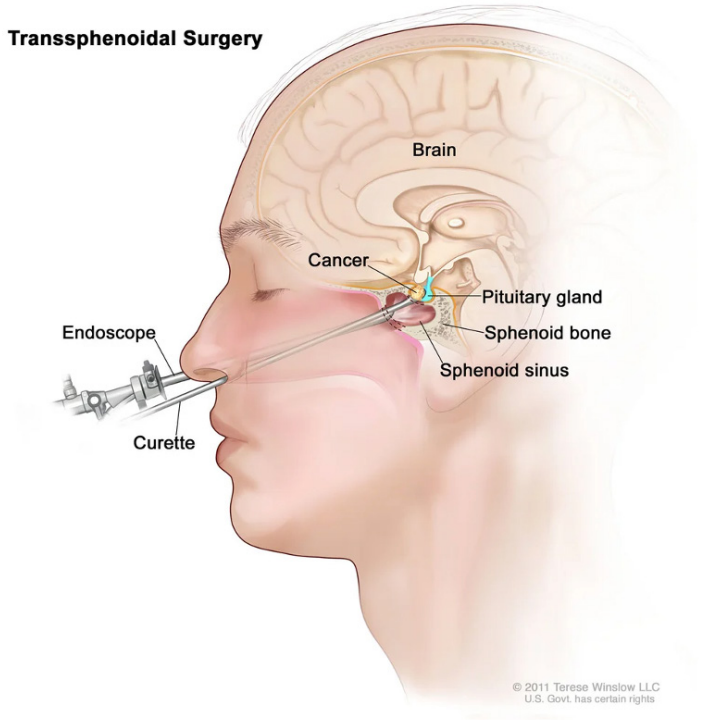

Figure 3. Transsphenoidal approach for access to the sella turcica.

Source: Transsphenoidal Surgery, 2011. Terese Winslow LLC.

technically difficult site to resect, estimated at approximately 34% of cases based on dural biopsies[23].

The material extracted from the procedure, in this case, was characterized by several soft, light brown fragments, measuring together 2.1x0.8x0.4cm. The anatomopathological report highlighted the presence of polygonal cells with rounded nuclei and ample eosinophilic cytoplasm arranged in solid arrays or in rows along thin connective-vascular trabeculae, in addition to the absence of evident signs of malignancy. Immunohistochemistry showed positivity for TPIT, ACTH, and CAM 5.2. These findings are compatible with an ACTH-secreting pituitary adenoma, confirming the diagnosis.

Conclusion

Given the above, a general and integrated clinical view of the complaints of a young adult patient, as presented in this report, is essential, and the need to investigate differential diagnoses that can justify the syndrome is required. Hence, we cannot merely be content with treating signs and symptoms individually.

Furthermore, it is observed that when the symptoms of CD are treated separately, the diagnosis is delayed and the patient can develop complications of this pathology, since the cause of the problem is not being addressed.

Such complications, combined with intrinsic intercurrences of surgical treatment or even concerning the hospital stay itself, are potential causes of unfavorable outcomes, as occurred in this case.

Author Contributions

The authors' contributions are structured according to the (CRediT) taxonomy described below:

Conceptualization, Data Curation, Formal Analysis, Investigation, Methodology, and Writing – Original Draft: IS de L Castro; CC Carvalho; RGF Ramos. *Supervision, Validation, and Writing – Review & Editing*: TA de Oliveira.

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References

1. Moore KL, Persaud TVN, Torchia MG. Embriologia Clínica. 10th ed. Rio de Janeiro: Elsevier; 2016.
2. Hall JE, Hall ME. Guyton & Hall - Tratado de Fisiologia Médica. 14th ed. Rio de Janeiro: Grupo GEN; 2021.
3. Castinetti F, Morange I, Conte-Devolx B, Brue T. Cushing's disease. Orphanet J Rare Dis. 2012 Jun 18;7:41. DOI: https://doi.org/10.1186/1750-1172-7-41.
4. Lonser RR, Nieman L, Oldfield EH. Cushing's disease: pathobiology, diagnosis, and management. J Neurosurg. 2017 Feb;126(2):404-17. DOI: https://doi.org/10.3171/2016.1.JNS152119.
5. Fleseriu M, Auchus R, Bancos I, Ben-Shlomo A, Bertherat J, Biermasz NR, et al. Consensus on diagnosis and management of Cushing's disease: a guideline update. Lancet Diabetes Endocrinol. 2021 Dec;9(12):847-75. DOI: https://doi.org/10.1016/S2213-8587(21)00235-7.
6. Khan DZ, Hanrahan JG, Baldeweg SE, Dorward NL, Stoyanov D, Marcus HJ. Current and Future Advances in Surgical Therapy for Pituitary Adenoma. Endocr Rev. 2023;44(5):947-59.
7. Stroud A, Dhaliwal P, Alvarado R, Winder MJ, Jonker BP, Grayson JW, et al. Outcomes of pituitary surgery for Cushing's disease: a systematic review and meta-analysis. Pituitary. 2020 Oct;23(5):595-609. DOI: https://doi.org/10.1007/s11102-020-01066-8.
8. Isand K, Arima H, Bertherat J, Dekkers OM, Feelders RA, Fleseriu M, et al. Delphi panel consensus on recommendations for thromboprophylaxis of venous thromboembolism in endogenous Cushing's syndrome: a position statement. Eur J Endocrinol. 2025 Mar 3;192(3):R17-R27. DOI: https://doi.org/10.1093/ejendo/lvaf017.
9. Brasileiro Filho G. Bogliolo - Patologia. 10. ed. Rio de Janeiro: Editora Guanabara Koogan; 2021.
10. Nieman LK. Cushing's syndrome: update on signs, symptoms and biochemical screening. Eur J Endocrinol. 2015 Oct;173(4):M33-8. DOI: https://doi.org/10.1530/EJE-15-0464.
11. Thakker RV, Newey PJ, Walls GV, Bilezikian J, Dralle H; Endocrine Society, et al. Clinical practice guidelines for multiple endocrine neoplasia type 1 (MEN1). J Clin Endocrinol Metab. 2012 Sep;97(9):2990-3011. DOI: https://doi.org/10.1210/jc.2012-1230.
12. Casanueva FF, Molitch ME, Schlechte JA, Abs R, Bonert V, Bronstein MD, et al. Guidelines of the Pituitary Society for the diagnosis and management of prolactinomas. Clin Endocrinol (Oxf). 2006 Aug;65(2):265-73. DOI: https://doi.org/10.1111/j.1365-2265.2006.02562.x.
13. Ajmal A, Joffe H, Nachtigall LB. Psychotropic-induced hyperprolactinemia: a clinical review. Psychosomatics. 2014 Jan/Feb;55(1):29-36. DOI: https://doi.org/10.1016/j.psym.2013.08.008..
14. Segal S, Yaffe H, Laufer N, Ben-David M. Male hyperprolactinemia:effects on fertility. Fertil Steril. 1979 Nov;32(5):556-61. DOI: https://doi.org/10.1016/s0015-0282(16)44359-1.
15. Crapo L. Cushing's syndrome: a review of diagnostic tests. Metabolism. 1979 Sep;28(9):955-77. DOI: https://doi.org/10.1016/0026-0495(79)90097-0.
16. Elamin MB, Murad MH, Mullan R, Erickson D, Harris K, Nadeem S, et al. Accuracy of diagnostic tests for Cushing's syndrome: a systematic review and metaanalyses. J Clin Endocrinol Metab. 2008 May;93(5):1553-62. DOI: https://doi.org/10.1210/jc.2008-0139.

17. Papanicolaou DA, Mullen N, Kyrou I, Nieman LK. Nighttime salivary cortisol: a useful test for the diagnosis of Cushing's syndrome. J Clin Endocrinol Metab. 2002 Oct;87(10):4515-21. DOI: https://doi.org/10.1210/jc.2002-020534.

18. Chen YM, Cintrón NM, Whitson PA. Long-term storage of salivary cortisol samples at room temperature. Clin Chem. 1992 Feb;38(2):304.

19. Hall WA, Luciano MG, Doppman JL, Patronas NJ, Oldfield EH. Pituitary magnetic resonance imaging in normal human volunteers: occult adenomas in the general population. Ann Intern Med. 1994 May 15;120(10):817-20. DOI: https://doi.org/10.7326/0003-4819-120-10-199405150-00001.

20. Winslow T. Cirurgia Transesfenoidal [Internet]. 2011; [cited 25 oct 2025]. Available from: https://www.teresewinslow.com/#/head/.

21. Barker FG 2nd, Klibanski A, Swearingen B. Transsphenoidal surgery for pituitary tumors in the United States, 1996-2000: mortality, morbidity, and the effects of hospital and surgeon volume. J Clin Endocrinol Metab 2003;88(10):4709-19.

22. Hofmann BM, Hlavac M, Kreutzer J, Grabenbauer G, Fahlbusch R. Surgical treatment of recurrent Cushing's disease. Neurosurgery. 2006 Jun;58(6):1108-18. DOI: https://doi.org/10.1227/01.NEU.0000215945.26764.92.

23. Lonser RR, Ksendzovsky A, Wind JJ, Vortmeyer AO, Oldfield EH. Prospective evaluation of the characteristics and incidence of adenoma-associated dural invasion in Cushing disease. J Neurosurg. 2012 Feb;116(2):272-9. DOI: https://doi.org/10.3171/2011.8.JNS11456.

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