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Case Report

Neurosurgical aspects and clinical outcomes on the treatment of Cushing disease in pediatric patients: Case series and literature review

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ABSTRACT

Background: Cushing disease (CD) is a state of hypercortisolism caused by an adrenocorticotropic hormone-(ACTH) producing pituitary adenoma which rarely occurs in pediatric patients. The outstanding features are weight gain and growth retardation. However, the insidious onset and rarity of the disease in children and adolescents often result in delayed diagnosis.

Case Description: We present five patients <14 years of age who underwent neurosurgical treatment for CD at the Department of Neurosurgery of a public referral hospital in Lima, Peru. Age at diagnosis ranged from 5.5 to 12.5 years with a history of disease from 9 months to 3.5 years of moderate to severe stunting and obesity, among other features of Cushing syndrome (CS). Although biochemical tests and cerebral imaging were crucial for the diagnosis, confirmation was made by bilateral petrosal sinuous sampling. Regarding treatment, three patients underwent transcranial surgery, one patient underwent endoscopic transsphenoidal surgery, and one patient underwent microscopic transsphenoidal surgery. None of the patients underwent radiotherapy or pharmacological treatment. Only one patient had a recurrence and achieved remission until an endoscopic transsphenoidal approach was performed. Short- and long-term endocrinologic follow-up is also described in detail.

Conclusion: CD is a heterogeneous disorder that requires multidisciplinary diagnosis and management. Transsphenoidal selective adenomectomy is the optimal treatment because of its higher remission rates. However, technical and anatomic aspects should be considered in pediatric patients.

Keywords: Pediatric, Pituitary adrenocorticotropic hormone hypersecretion, Transcranial surgery, Transsphenoidal surgery, Treatment outcome

INTRODUCTION

Cushing syndrome is a hormonal disorder due to prolonged cortisol exposure. The most common cause in the pediatric population, as at any age, is exogenous administration of glucocorticoids. On the other hand, endogenous hypercortisolism is a rare condition in children, but when it occurs, an ACTH-secreting pituitary adenoma, known as Cushing disease, is the most common finding.[22] The clinical manifestations are typical of hypercortisolism, but in children and

adolescents, weight gain and growth disturbances are the prominent features.[30] The insidious onset of signs and symptoms, together with the rarity of the disease in pediatric patients often leads to delayed diagnosis.[29] The first-line neurosurgical treatment is removal of the adenoma through a transsphenoidal approach, which may also be accompanied by radiotherapy.[11] Endoscopic transsphenoidal surgery has been shown to be more efficient compared with microscopic transsphenoidal and transcranial surgery.[11,32] After successful treatment, parameters for growth, weight, and sexual development usually improve, but residual defects remain in some children.[38] This study aims to describe the neurosurgical aspects of treatment and endocrinologic parameters during follow-up of five children with CD. A review of the literature on updates in neurosurgical treatment and clinical parameters after surgery in pediatric patients with CD is provided.

RESULTS

Five patients aged <14 years underwent neurosurgery for CD in the Department of Pediatric Neurosurgery at the "Hospital Nacional Edgardo Rebagliati Martins" in Lima, Peru, between 2016 and 2022. Age at diagnosis ranged from 5.5 to 12.5 years with a history of disease from 9 months to 3.5 years of moderate to severe stunting and obesity, among other features associated with CS, such as cushingoid facies, cervical hump, and acanthosis nigricans [Table 1]. A series of biochemical tests and cerebral imaging exams were performed according to an institutional algorithm for the diagnosis of CD in children [Figure 1 and Table 2]. Confirmation was performed in each patient by bilateral petrosal sinus sampling (BPSS). For treatment, three patients underwent transcranial surgery, one patient underwent endoscopic transsphenoidal surgery, and one patient underwent microscopic transsphenoidal surgery [Table 3]. Neither radiotherapy nor medical treatment was applied. Annual follow-up showed improvement in parameters related to growth, weight, sexual development, and other features [Table 4]. Exemplary cases are shown photographically in Figures 2 and 3

CASE 1

A 13-year-old male child presented to the outpatient consultation because he had been ill for 3 years. His mother reported weight gain, darkening of the posterior neck, the appearance of a cervical hump, and episodic headaches that were later accompanied by tinnitus. His clinical presentation consisted of a cushingoid facies, hair proliferation, acanthosis nigricans, a cervical hump, lipomastia, central obesity, headache, tinnitus, abdominal stretch marks, and hypertension. Serologic testing confirmed endogenous hypercortisolism, although magnetic resonance imaging (MRI) was found to be normal. Subsequently, the petrosal sinus sampling revealed a right-sided pituitary adenoma. Two years after diagnosis, a complete resection of a microadenoma through an endoscopic transsphenoidal approach. Apart from an increase in mean arterial blood pressure, which was

Table 1: Clinical aspects at diagnosis.

Aspect	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Sex	M	F	M	F	M
Presentation	Cushingoid facies, cervical hump, headache, acanthosis nigricans lipomastia, central obesity, stretch marks, hair increase, emotional lability, hypertension	Cushingoid facies, cervical hump, axillary odor, gynecomastia, pubic hair, central obesity, hypertension	Cushingoid facies, cervical hump, acne, facial flushing, acanthosis nigricans, central obesity, stretch marks, hirsutism, hypertension	Cushingoid facies, tendency to sleep, central obesity	Cushingoid facies, cervical hump, acne, headache, acanthosis nigricans, hirsutism, central obesity
Age at diagnosis (years)	12.2	5.5	8.4	12	12.5
Time until diagnosis (years)	3	3	0.75	2.5	3.5
Height (SDS)	−1.72	−3.43	−2.15	−2.66	−2.42
Weight (SDS)	1.92	1.81	1.95	1.52	1.15
BMI (SDS)	2.82	3.82	2.98	0.06	2.50
Tanner stage	G2 PH 1	B1 PH 3	G1 PH 1	B1 PH 3	G1 PH 1
Bone age (months*)	NA	9	16	14	11

BMI: Body mass index, B: Breast, F: Female, G: Genitalia, M: Male, NA: Not available, PH: Pubic hair, SDS: Standard deviation score. *Delta of true bone age and reported bone age by Greulich and Pyle.

Table 2: Confirmation of diagnosis.

Aspect	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Urine free cortisol (μg/24 h)	464.3	299.7	1754.3	536	262.3
Serum cortisol 8 am–4 pm–11 pm (μg/dL)	18.10–12.90–12.10	27.9–16.9–17.8	24.80–29.10–22.40	19.7–6.6–4.3	16.4–16–14.10
DST 1 mg (cortisol μg/dL)	NA	10.1	28.3	NA	NA
Serum ACTH (pg/mL)	42.8	37.28	37.8	30.7	136
DST 8 mg					
Basal cortisol (μg/dL)	17.40	27.9	28.4	17.7	16.2
Cortisol after suppression (μg/dL)	1.39	2.34	2.46	1.1	0.3.08
Basal ACTH (pg/mL)	29.80	37.28	57.8	NA	NA
ACTH after suppression (pg/mL)	7.45	8.96	13.1	NA	NA
TSH (Uui/mL)	2.46	0.962	0.987	1.04	1.62
Free T4 (ng/dL)	1.19	1.2	1.08	1.1	1.21
Size	**Microadenoma**	**Microadenoma**	**Microadenoma**	**Microadenoma**	**Microadenoma**
Location					
MRI	N	N	R	R	L, ML
BPSS	L	L	R	R, ML	L, ML
Histology	No	Yes	Yes	No	No

ACTH: Adrenocorticotropic hormone, BPSS: Bilateral petrosal sinuous sampling, DST: Dexamethasone supression text, L: Left, ML: Midline, MRI: Magnetic resonance imaging, NA: Not available, N: Normal, R: Right, T4: Thyroxine, TSH: Thyroid-stimulating hormone.

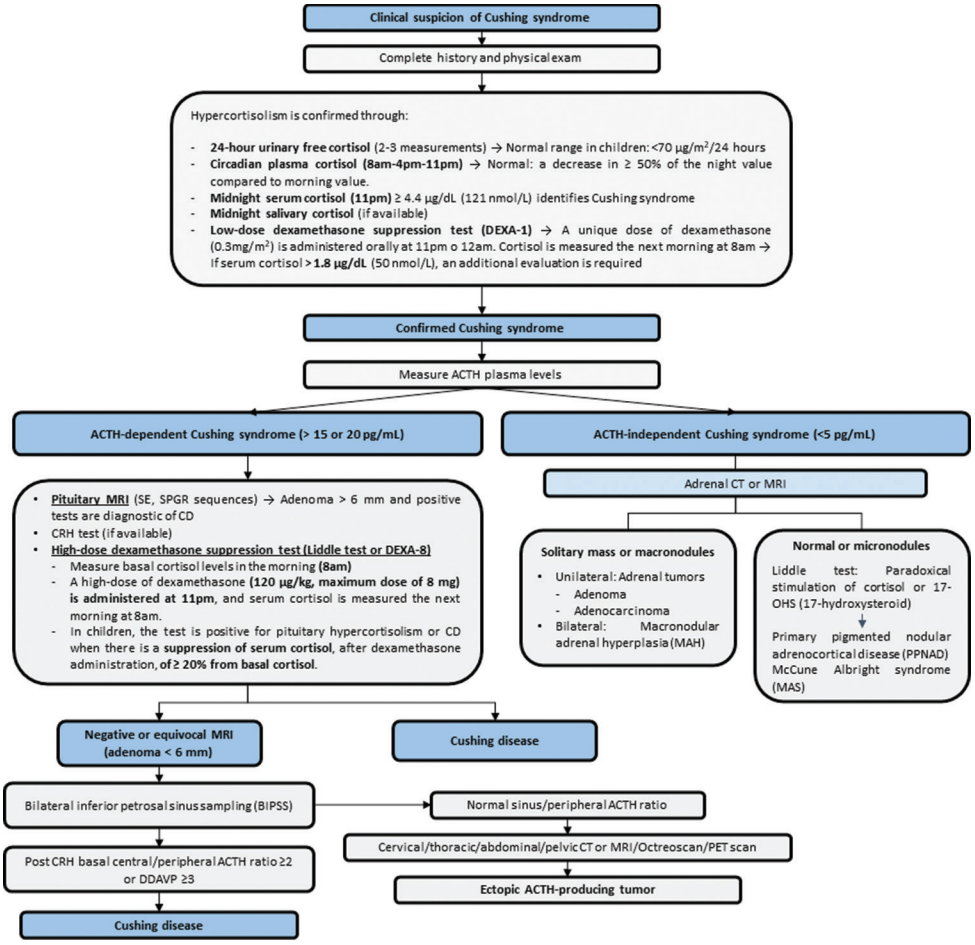

Figure 1: Diagnostic algorithm for Cushing disease in pediatric patients. ACTH: Adrenocorticotropic hormone, CD: Cushing disease, CRH: Corticotropin-releasing hormone, CT: Computed tomography, DDAVP: desmopressin, MRI: Magnetic resonance imaging, PET: Positron emission tomography, SE: Spin echo, SPGR: Spoiled gradient-recalled acquisition.

Table 3: Neurosurgical aspects.

Aspect	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Number of surgeries	1	1	1	3	1
Surgery					
Type	ETS@#	TC	TC	1° TC 2° MTS 3° ETS	MTS
Complications	Increased MAP after placement of adrenaline in nostrils	No	No	2° Massive bleeding	No
Recurrence (months)	No	No	No	3	No
Cortisol 8 am (µg/dL)					
Immediate	NA	35.8	84.7	5.48	<1.00
Week	NA	4.75	<1.00	19.1	<1.00
ACTH 8 am (µg/dL)					
Immediate	NA	<5	15.4	17.9	12.8
Week	NA	<5	6.72	48.4	8.37

ACTH: Adrenocorticotropic hormone, ETS: Endoscopic Transsphenoidal surgery, MAP: Mean arterial pressure, MTS: Microscopic transsphenoidal surgery, NA: Not available, TC: Transcranial surgery

Figure 2: Patient before surgery (a), after transcranial surgery through mini-pterional approach (b), and at 1-year follow-up. No intraoperative or postoperative complications occurred.

satisfactorily treated, no complications occurred. The patient progressed favorably and is currently under endocrinological monitoring. Since surgery was recently performed, follow-up after 1 month is offered [Table 4].

CASE 2

A 5-year-old female child presented to the outpatient clinic because she had been ill for 3 years. The mother reported having noticing body and facial changes, and axillary odor. On physical examination, the child presented cushingoid facies, facial flushing, a cervical hump, gynecomastia, pubic hair, central obesity, short stature, and hypertension. In suspicion of hypercortisolism, the complete blood test algorithm was held and CD was diagnosed. The MRI was interpreted as normal. The diagnosis was definitively confirmed through the petrosal sinus sampling, which demonstrated a left-sided pituitary corticotroph adenoma. One month after diagnosis, a complete excision of the pituitary gland was performed via a transcranial approach (mini-pterional craniotomy). The patient did not have a recurrence, and she continues her follow-up visitis with the pediatric endocrinologist for postsurgical hypopituitarism. After 2 years, due to the patient's persistent short stature, growth hormone therapy was initiated.

Figure 3: Patient before transcranial surgery through mini-pterional approach (a) and at 1-year follow-up (b). Another patient in position for microscope-guided endonasal transsphenoidal surgery (c).

CASE 3

An 8-year-old male child presented to the outpatient consultation with a 2-year history of illness. The mother reported weight gain, hair growth, facial acne, and axillary odor. On physical examination, the child showed central obesity, cushingoid facies, a cervical hump, facial flushing, acne, acanthosis nigricans, hirsutism, abdominal stretch marks, and hypertension. Laboratory tests confirmed endogenous hypercortisolism. The MRI revealed a right-sided pituitary microadenoma. The petrosal sinus sampling confirmed the location of the adenoma, and a diagnosis of CD was established. The patient underwent transcranial surgery (mini-pterional craniotomy) with total exeresis of the pituitary gland. The child did not present recurrence.

CASE 4

A 12-year-old female adolescent presented to the outpatient consultation with an illness history of 2.5 years. The father stated that he noticed a short stature for her age, increased body and facial hair, and a round face. He also reported her child was forgetful and tired. On physical examination, the child had cushingoid facies, short stature, hirsutism, and central obesity. Laboratory tests confirmed endogenous hypercortisolism. The MRI showed a microadenoma on the right side and midline, which was later confirmed by petrosal sinus sampling test. Initially, a selective adenomectomy through a transcranial approach was performed. However, due to persistent hypercortisolism, a hypophysectomy through a microscopic transsphenoidal approach was then intended after 6 months. Unfortunately, a neoformation of the intercavernous sinus in the sellar diaphragm provoked abundant bleeding when opening it, and the operation was aborted. A third and definitive procedure was performed through an endoscopic transsphenoidal approach. The patient continues her control queries with the pediatric endocrinologist for postsurgical hypopituitarism.

CASE 5

A 12-year-old male adolescent presented to the outpatient consultation with an illness history of 4 years. The mother stated that she noticed weight gain and short stature. She also reported hyperpigmentation of the skin and acne. Two years earlier, hair began to appear on her face and body. An MRI showed an intrasellar pituitary expansion process, located inferomedially in the adenohypophysis. The patient denied impaired vision and nausea but reported joint pain in the knees, and lumbar region. Laboratory tests revealed endogenous hypercortisolism. Physical examination, confirmed the presence of facial acne, acanthosis nigricans, dry skin, hypertrichosis, and cushingoid facies. At other consultations, the patient reported occasional headache and mild fatigue. He was referred to the Department of Pediatric Neurosurgery for microscopic transsphenoidal surgery. The patient has been following her control queries with the pediatric endocrinologist for 2 years.

DISCUSSION

Clinical presentation

CD has an insidious onset in most children and is usually manifested by gain, lack of height gain, and changes in facial

Table 4: Postoperative outcomes.

Aspect	Patient 1	Patient 2				Patient 3					Patient 4	Patient 5	
	1 month	1 year	2 year	3 year	5 year	6 year	1 year	2 year	3 year	4 year	5 year	6 year	1 year	1 year	2 year
Height (SDS)	−2.63	−3.85	−4.87	−3.56	−2.85	−2.35	NA	−2.57	−2.59	NA	−1.8	−2.04	−3.49	−2.31	−2.1
Weight (SDS)	1.02	−0.01	−0.18	−0.24	0.17	−0.35	NA	−1.07	−1	NA	−0.35	−0.84	−0.46	0.95	0.34
Tanner stage	G3 PH 3	B1 PH 3	B1 PH	B1 PH	B1 PH	B2 PH	G1 PH	G1 PH	G1 PH	G1 PH	G1 PH	NA	B4 PH 4	G1 PH 1	G2 PH 2
BMI (SDS)	2.62	2.30	2.71	2.27	2.95	2.34	NA	0.80	0.81	NA	1.02	NA	1.74	2.07	1.32
Pituitary function profile															
Cortisol (µg/dL)	<1[♦]	14.3[♦]	<1	13.7[♦]	29.2[♦]	12.5[♦]	<1	<1	5.92	<1	2.91	<1	<1	<1	<1
ACTH (pg/mL)	NA	<5	<5	<5	<5	<5	21.4	13.4	12.5	<5	NA	<5	13.3	8.37	20.70
Free T4 (ng/dL)	0.75	1.54	1.4	1.06	1.15	1.04	0.721	0.95	1.14	1.19	0.478	0.407	1.39	1.280	0.804
TSH (uUI/mL)	5.38	<0.004	0.007	0.005	<0.004	<0.004	0.07	NA	0.013	NA	NA	0.936	0.005	3.640	5.880
FSH (mUI/mL)	NA	<0.1	<0.1	NA	NA	NA	NA	0.7	1.22	NA	1.17	1.71	4.99	4.45	NA
LH (mUI/mL)	NA	0.11	<0.1	NA	NA	NA	NA	NA	0.7	NA	NA	0.57	5.39	2.19	NA
Estradiol (pg/mL)	NA	25	41.1	NA	<20	NA	NA	NA	NA	NA	NA	NA	35.1	NA	NA
Prolactina (ng/mL)	NA	<0.5	<0.5	NA	NA	NA	NA	<0.5	<0.5	<0.5	NA	<0.5	0.62	NA	11.40
IGF-1 (ng/mL)	243	34.3	41	255	343	362	41.4	27.6	44.8	198	383	117	96.1	255	189

ACTH: Adrenocorticotropic hormone, B: Breast, BMI: Body mass index, FSH: Follicle-stimulating hormone, G: Genitalia, IGF-1: Insulin-like growth factor 1, LH: Luteinizing hormone, NA: Not available, PH: Pubic hair, SDS: Standard deviation score, T4: Thyroxine.. [♦]Post-hidrocortisone administration

appearance.[30] Other common symptoms and signs are headache, emotional lability, hypertension, and hirsutism.[30] It is also mildly common to see acne and striae on the skin. Striae are almost never present in children between the ages of 5 and 7, but they are more frequent in older patients.[30,33] Furthermore, pubescent children may present with virilization, evidenced by an advanced in Tanner pubic hair stage compared with testicular volume or breast development.[33]

It is important to add that subtle or subclinical presentation is uncommon. Nevertheless, parents and general practitioners fail to identify the pathological changes in the child's appearance. For this reason, the duration of symptoms until a diagnosis ranges from 0.5 to 3.5 years.[38] Compared to adults with this disease, in children, symptoms such as sleep disturbances, memory problems, easy bruising, and muscle weakness are less common.[30,33]

Regarding a gender-dependent analysis in the context of pediatric CD, contrary to the situation in adults, the distribution between males and females is equal, but male patients have higher body mass index, shorter stature, and higher elevated plasma ACTH levels.[20] This suggests a possibly more aggressive presentation in boys.

Diagnosis

The diagnosis of CD is based on clinical suspicion, laboratory tests, and medical imaging. After excluding prolonged exogenous glucocorticoid intake, the first step is to measure cortisol levels by the following tests: 24-hour urinary free cortisol (UFC), dexamethasone suppression test (DST), or late-night salivary/serum cortisol. Two abnormal results are required to confirm hypercortisolism.[10]

A 24 hour-UFC with a cut-off value of >193 nmoL/day has a sensitivity of 88% in the pediatric population and serial measurements are recommended to increase its accuracy.[3] The DST is another screening test that can be evaluated by two techniques: Overnight DST and low-dose DST.[10]

Once the diagnosis of hypercortisolism is established, morning plasma ACTH levels are assessed to determine the etiology. Levels higher than 29 pg/mL suggest ACTH-dependent CS with a sensitivity of 70% and a specificity of 100%, while values <5 pg/mL indicate ACTH-independent CS.[3] To differentiate between ectopic ACTH secretion and CD, children must undergo a corticotropin-releasing hormone (CRH) stimulation test. Pituitary tumors respond to intravenous administration of CRH, resulting in an increase in ACTH and cortisol levels, with a sensitivity of 74% when cortisol levels increase by >20% from baseline, and a sensitivity of 81% when ACTH levels increase by >35% from basal values.[24]

To localize the pituitary tumor, the standard medical imaging technique is MRI with contrast.[22] However, a special sequence called Spoiled Gradient Recalled (SPGR) is the optimal modality for detecting pituitary microadenomas due to its higher sensitivity compared with conventional and dynamic contrast-enhanced MRI.[13,27] In post-contrast SPGR scans, the adenoma shows up as a hypointense lesion, which can have a small hyperintense focus in the center.[27] The diagnosis of CD is confirmed by the presence of an adenoma >6 mm and concordant positive laboratory tests.[6] If the tumor's size is <6 mm, BPSS must be performed.[6]

BPSS is a confirmatory procedure used when MRI does not show a pituitary adenoma, its size is <6 mm or tests are inconclusive.[6] It distinguishes CD from ectopic ACTH production and allows accurate localization and lateralization of the pituitary adenoma. An ACTH ratio between the inferior petrosal sinus and the periphery (IPS/P) of >2 before desmopressin or CRH stimulation and >3 after stimulation confirms CD.[7,37] CRH stimulation was found to have a sensitivity of 87.5%, whereas desmopressin stimulation reported 83.33%.[7,37] In our case series, two patients had a MRI reported as normal, and BPSS established the definitive diagnosis.

Management

CD is a heterogeneous disorder that requires multidisciplinary management by pediatric neurosurgeons, pediatric endocrinologists, and radiologists. Therapeutic options include medical treatment, pituitary surgery, and radiotherapy. As it is a localized tumor, the ideal procedure is surgical resection by selective adenomectomy. Surgical approaches include transcranial surgery, and endoscopic or microscopic transsphenoidal surgery.[23] In the 2015 Endocrine Society Clinical Practice Guidelines on the treatment of CD, initial resection through transsphenoidal selective adenomectomy by an experienced pituitary surgeon is considered the optimal treatment for CD in children.[23,32] In recent years, endoscopic transsphenoidal surgery has been preferred over microscopic transsphenoidal surgery due to its higher remission rates after the procedure, ranging from 65% to 90% in patients with microadenomas.[5,17] Second-line treatments for patients who have undergone an initial noncurative surgery or for whom surgery is not feasible include a second transsphenoidal surgery, radiotherapy, medical therapy, and bilateral adrenalectomy.[23]

Regarding transsphenoidal surgery, some technical and anatomical aspects, such as pneumatization of the sphenoid sinus and intercarotid distance, should be considered in pediatric patients. First, the surgical corridor is smaller in children due to their smaller nostrils, which makes maneuvering in the posterior fossa more difficult.[34] In addition, pneumatization of the sphenoid sinus is a process that begins at 2 years of age, so low pneumatization in children makes it difficult to identify bony landmarks and access the pituitary gland compared with adults.[21] Likewise, the intercarotid distance and the piriform aperture width are both smaller before the age of 7 years of age.[34] On the other hand, transcranial surgery is an alternative to the transsphenoidal approach that is indicated for dumbbell tumors with large suprasellar extension, multicompartmental tumors, and non-pneumatized sphenoid sinus.[25]

Pituitary radiotherapy is a second-line treatment option following an unsuccessful surgery for pediatric CD and requires combination with pharmacological agents such as ketoconazole.[18,28] To achieve remission, radiotherapy must be performed over several months; 87.5% of pediatric patients recover after 12 months of treatment.[10] There are reports of long-term efficacy, which is more successful in children than in adults.[1] Despite this, an important postoperative complication is growth hormone deficiency, which occurs in approximately more than 86% of patients, as well as permanent hypopituitarism.[16,31]

Postoperative complications

Between transsphenoidal and transcranial approaches, the latter is associated with more postoperative complications.[14] Although infrequent, complications of transsphenoidal procedures are more common in male patients under 10 years of age.[14] These include diabetes insipidus (30.4%), panhypopituitarism (10.2%), visual disturbances (6.4%), brain bleeding, and CSF leakage (<5%).[14] Other complications include persistence of high body mass index, growth hormone deficiency, and altered mental status (anxiety, depression, suicidal ideation, and mood disorders).[10] Because of the higher incidence of visual deterioration and morbidity with transcranial surgery, transsphenoidal surgery is the preferred approach in children.[25] In our case series, no patient experienced postoperative complications related to the transcranial or transsphenoidal approach, such as CSF leakage, infection, or optic nerve damage. On the other hand, radiotherapy remains a controversial treatment due to adverse consequences in children, such as impaired cognitive development.[10]

Remission and recurrence

The goal of adenomectomy is remission or cure, although the term "remission" is more appropriate due to the high recurrence rate of CD. At present, there is no consensus on the definition of remission, but the main objectives are reversal of clinical features, normalization of biochemical changes with minimal morbidity, and long-term control

without recurrence.[4] Remission is generally defined as morning serum cortisol values <5 μg/dL (<138 nmoL/L) or UFC <28–56 nmoL/d (<10–20 μg/day) within 7 days of adenomectomy.[23] Preoperative biochemical and imaging parameters are associated with remission rate. Predictive factors for remission include low cortisol levels immediately after surgery, identification of a microadenoma on preoperative imaging, and histologic confirmation of an ACTH-secreting adenoma.[2,15] By contrast, higher preoperative ACTH levels and non-visualization of the tumor on MRI are predictive factors for recurrence.[26,35] In our case series, one patient had clinical recurrence after 3 months after transcranial surgery for tumor exeresis; she achieved remission with a third definitive endoscopic transsphenoidal surgery.

Post-transsphenoidal surgery remission rate ranges from 70% to 100% over a median time of 7.2 years.[9,10,19] Having negative MRI (non-visible tumor) has been associated with a lower probability of post-surgical remission.[35] Likewise, remission rates after the first transsphenoidal surgery are poor in patients with macroadenomas and in patients undergoing a second transsphenoidal surgery.[29] After surgery, a variable period of adrenal insufficiency (AI) can be expected, requiring several months of corticosteroid replacement with hydrocortisone 8–12 mg/m^2/day, which is completed at a median time of 12.7 months.[10,36] However, there is an association between early recovery of AI and a higher risk of recurrence, with the risk of recovery decreasing by 14% with each month.[36] Finally, the contribution of race to disease prognosis has been reported. At a median follow-up of 2.3 years after surgery, the relative risk of persistent CD combined with recurrence is 2.8 times higher in Hispanic/Latino or African-American children compared with white children.[10,12]

Long-term outcomes

Each patient's catch-up growth depends on early identification of growth hormone deficiency and subsequent treatment after surgery or radiotherapy completion. Overall, patients treated with growth hormone therapy and those without the deficiency complication show improvement in standard deviation of height and attainment of target height in adulthood.[10,18,28] Reported outcomes of height improvement have been established in previous studies; for example, pediatric patients cured from CD achieve a mean standard deviation of final height of −1.6, with a mean difference between the final deviation of final height and the target height of −1.2.[8] In addition, patients may have vertebral fractures due to compression and/or scoliosis as a result of hypercortisolism, which may affect final height.[8] On the other hand, in many patients, total body fat remains abnormally high, representing an increased body mass index.[28] In our case series, there was an improvement in height and weight at annual follow-up, although they continued with short stature and tendance to be overweight [Table 4].

CONCLUSION

CD in children is a heterogeneous disorder that requires multidisciplinary diagnosis and management by pediatric neurosurgeons, pediatric endocrinologists, and radiologists. It should be considered in the differential diagnosis of a child or adolescent who presents mainly with growth failure and obesity. Serial laboratory tests are crucial for diagnosis. Although the preferred imaging to localize the tumor is MRI with contrast, in some cases, no pituitary adenoma could be detected. Then, BPSS gives an accurate localization and lateralization of the adenoma. Regarding treatment, transsphenoidal selective adenomectomy is the optimal treatment due to its higher remission rates. However, technical and anatomical aspects, such as smaller operative corridors, little pneumatization of the sphenoid sinus, and smaller intercarotid distance and piriform distance, should be considered in pediatric patients. A close follow-up of growth, weight, sexual development, and pituitary function parameters is strictly necessary after surgery.

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.

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