



LEFT OUT - PERSISTENT PEDIATRIC DEPRESSION IN PANHYPOPITUITARISM: A CASE REPORT

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ABSTRACT

This is a case of a 15-year-old Filipino male with a history of craniopharyngioma who underwent trans-sphenoidal surgery with panhypopituitarism as its sequelae. The biological factors of the patient's disease contributed to his persistent depression and were perpetuated by psychosocial and cognitive factors. A biopsychosocial approach was used in understanding this case to arrive at individualized treatment and management.

KEYWORDS: Craniopharyngioma, Depression, Biopsychosocial approach

INTRODUCTION

Craniopharyngiomas (CP) are rare intracranial tumors of low histological malignancy, derived from malformation of embryonal tissue and most frequently located in the sellar and parasellar region of the brain. Due to their proximity to the pituitary gland and the hypothalamus, CPs often cause hypothalamic dysfunction, including endocrine deficiencies and obesity, resulting in neurocognitive impairments and behavioral changes as well as impairments in social-emotional functions. (1)

Its incidence is 1.5 per million per year. The age distribution is bimodal, with the first peak in childhood at the age of 5 to 14 years and the second peak at 65 to 74 years. The most common symptoms of craniopharyngioma are: headaches, temporal visual field defects, decreased growth rate, polydipsia/polyuria, and excessive weight loss or weight gain. After tumor removal as in our case, patients often suffer from chronic disease due to hypothalamic injury or hypopituitarism, which may have a severe impact on daily life. Patients with early-onset craniopharyngioma have increased rates of

depression and anxiety, and they feel impaired in their social and professional integration as an effect of the disease. (2)

In children with depression due to a medical condition, there are some atypical presentations of depression. In DSM - V TR, atypical manifestation includes mood reactivity and two of the following four symptoms or features also must be present: 1) hyperphagia or weight gain, 2) hypersomnia, 3) leaden paralysis, and 4) interpersonal rejection sensitivity. Although this is mostly best understood in adults, it has been found out to have a different pathophysiology, presentation, prognosis, and response to pharmacologic treatments. (3)

Another contributing factor in the case was the absent parent particularly the father is seen in this case. It has been found out that there was evidence for a main effect of father absence in early childhood on depressive symptoms at age 14 years old. The interaction between gender and father absence in early childhood, indicating that the association between father absence and depressive symptoms was stronger

in girls than in boys. The mechanisms linking early father absence to an increased risk of depressive symptoms in girls remain unclear. It has been previously suggested that biological and psychosocial effects of advancing puberty may be implicated which complicates that this patient had problems in his hormones that affected his puberty. (4)

In this case report, it has been shown that not only the biological factors of sequelae of craniopharyngioma contributed to the depression of the patient. It is a complex interaction between the biological, psychosocial, and cognitive factors that contribute to the patient's persistent depression.

CLINICAL HISTORY

The patient is a 15-year-old male, single, right-handed, Roman Catholic, junior high school student, an only child, from a city in Rizal. This is his first psychiatric consult. He was brought to our institution due to suicidality, sadness, and withdrawal as an outpatient pediatric neurology referral. The patient is known to be jolly, obedient, extrovert, frank pre-morbid but became irritable, easily angered, and suicidal.

In 2008, when the patient was three years of age, he started to complain of episodic headaches, around 1-2x/week, uncharacterized. He was brought to a pediatrician and was advised to lessen gadget use. In the interim, there was the persistence of headaches with increasing frequency but no vomiting. He was brought for follow-up but advised to consult with a pediatric neurologist. There was no note of behavioral changes such as depressed mood or irritability.

In October 2011 (aged 5, Grade 1), his headaches became more frequent and intense accompanied with vomiting. He subsequently had loss of consciousness and was brought to a nearby hospital. Cranial CT scan showed acute hemorrhage, suprasellar cistern with intraventricular extension, and mild obstructive hydrocephalus; cranial MRI was then done, which showed vertically oriented peripherally enhancing suprasellar mass (2.1x 1.8 x 4.1cm), which was consistent with craniopharyngioma. The patient underwent trans-sphenoidal surgery for resection of the tumor. Post-operatively, there were endocrinologic complications—hypothyroidism and central diabetes insipidus;

hence he was given hormonal supplementation. He was then discharged after a month with residual bi-temporal hemianopsia, but he recovered functionally. The mother became protective of her son due to his condition and prevented him from doing strenuous physical activities. The mother would even say that he "special" and "not normal" unlike other kids because of his illness. When he returned to school, the patient had difficulty adjusting to the school work due to the one-month delay. He was noted to become more extrovert and frank in expressing his feelings.

The mother disclosed to all of her son's teachers and classmates that he needed special help in all activities due to the deficits that he had after the surgery (bi-temporal hemianopsia). His classmates treated him as & "special"; because they were afraid that they would get in trouble should the patient get hurt. They excluded him from group activities (academic group work and play), which made him feel isolated and sad. Due to his deficits and the inculcation that he was different, the patient began to feel incompetent, thus would always ask for clarifications from his classmates and teachers about assignments and group projects they had in school. When the patient told his mother, she perceived that her son was considered a burden to other students—making the group slower and the dynamics of their group complicated. But instead of consoling the patient, patient's mother would often tell him that maybe he makes his classmates angry by irritating them; which led to more frustrations and worsening of patient's sadness. Nevertheless, the patient was able to finish Grade 1 without failing grades but was below average.

In 2012 (aged 6, Grade 2), the patient continued to be excluded by his classmates in some activities but was less problematic as there were less group activities at this time. Although he was able to develop a couple of friends that he frequently played with, he still felt sad and unwanted about not being included in group work.

This pattern of behavior towards the patient continued up to 2015 when he was 9 years old, (Grade 4) that teachers would have to be the ones to assign him to a group. Much as he wanted to be a leader, he was never chosen as such.

Although he had some friends, they still didn't invite him to their outings (e.g., swimming) and would sometimes eat lunch alone in school. He was noted to cry more often and was no longer interested in doing his hobbies such as basketball. He also over ate when he was stressed. He told his mother that his classmates would say that they didn't want to play with him because they might get into trouble when he got hurt. The mother consoled him yet would often say he did something wrong to his classmates thus they don't want to be with him; this just intensified his frustration and began to blame himself and his disease. Despite this, the patient was able to perform in school with no academic performance problems and obtain average grades.

In late 2015, the patient became a picky eater—preferring to eat certain foods such as pasta and instant noodles. He was also noted to drink 20 glasses of water per day. He gained more weight (compared to his pre-medical condition). Due to his health condition, his mother frequently reminded him to have a healthy diet and to lose weight. He felt unwanted because of his weight. His mother often compared him to his cousins, telling him that his cousins were obedient with their mothers and he wasn't (e.g., regarding food intake and diet), which would often lead to arguments between the two. The patient would often feel unwanted and sad, and at times would hit his head using his fist out of frustration. Whenever he would hurt himself, he was often physically restrained and verbally reprimanded, thus increasing his agitation. He would only stop whenever he was tired, and subsequently, would get what he wanted. They followed up with his pediatrician, and he was advised to consult with a psychiatrist but could not comply due to the mother's schedule. These symptoms persisted until 2016.

In June 2016 (aged 10, Grade 5), the patient and his mother transferred to their new house in Antipolo, Rizal, where his aunt and two cousins (11-year-old boy and 12-year-old girl) stayed with him for several months. His symptoms were noted to have declined initially—no crying episodes were reported, and he was seen enjoying the company of his cousins. However, when he attended his new school, his expectations of a different environment were not met. At school, his classmates would often

exclude him once again in their group activities, and often his schoolmates would ask him if he was a boy or a girl because he looked and sounded like a girl. He also had difficulty gaining friends.

This, on top of repeated arguments with his mother, led to worsening feelings of sadness. He was easily irritated and seemed to be wallowing in self-pity. His behavior of hitting his head with his fist recurred. He would often verbalize that he wanted to die. Again, they consulted with his pediatrician, and he was advised to seek consultation with a psychiatrist but did not comply. The symptoms persisted until the following year.

In 2017 (aged 11, Grade 6), the patient was seen crying during their recognition day because his mother could not attend the awarding due to her work. He was angry with his mother because he expected her to be there for him when he would receive his first academic award for being an achiever. He felt sad that he was not that important to his mother. Upon arriving home after his mother fetched him, he went straight to his room and locked the door. His mother heard loud noises, so she forced her way into the room and saw her son strangling himself with a belt. Due to this incident, he was brought to his pediatrician, who again advised consultation with a child psychiatrist. Instead of consulting with a psychiatrist, his mother resigned from her work and set up a home business selling jewelry and clothing so she could spend more time with her son. After knowing what their son did, the father scolded him, saying that he did this to himself without thinking of his parents' feelings, which further convinced him that he was insignificant to his parents. Much as patient wanted to die, there were no other suicidal attempts.

In 2018 (aged 12, Grade 7), the patient had frequent arguments with his cousins who were supposed to keep him company but preferred to focus on their gadgets than on him. He was heard questioning himself, "Why doesn't anybody like me?". This just made his cousins avoid him even more. The patient would have crying episodes, became more irritable, and frequently quarreled with his mother, especially regarding household chores. In 2019 (aged 13, Grade 8), the patient's feelings of sadness, self-

pity, and being unwanted persisted, and his self-harming behavior became more alarming. In one instance, his mother stopped him from stabbing himself in the kitchen after they argued about his food choices.

He was again reprimanded for this behavior, and his father once more told him why he should not do it again. In an attempt to help her son recover, the mother asked some of his classmates to befriend him. Some of his classmates invited the patient to join them when they went to malls, played online games, and joined their group chats. However, the patient was told that there was a limit to how he would be involved in their conversations, and they will exclude the patient in some activities such as swimming and outings. He labeled his classmates as "fake friends" because he assumed they only liked him when he treated them out to eat. His relationship with his "fake friends" faltered, and he thought he was just being used. This resulted in him having no friends at all.

In March 2020, at the start of the pandemic (aged 14, Grade 9), because of the shift to online classes, the patient and his mother were able to spend more time together, they would often watch movies on Netflix together, and they considered each other's best friend because they shared their problems and supported each other. However, they still argued about his food preferences and his excessive water intake of 6 liters per day. He became more irritable argumentative and verbalized that he was unwanted, useless, and burdened by his parents. He thought that his parents were better off without him. He was more often seen by his mother hitting his head with his fists and repeatedly saying that he was a burden to this family. This time, due to the limitations set by the pandemic, they were again unable to seek psychiatric consult.

In June 2020 (aged 14, Grade 9), the patient started having difficulty with school projects because his classmates refused to help him, so he had to do them all by himself. The crying episodes and increased irritability recurred. He also complained of generalized headaches, 7/10 in intensity, squeezing in character, aggravated by stresses and emotions, and was relieved by rest. This prompted a consult with his pediatrician, and he was advised to undergo repeat cranial neuroimaging.

In the interim, there was the persistence of the previous symptoms and behavior. In July 2021, the patient's follow-up cranial neuroimaging showed a nodule in the suprasellar-sellar region measuring 1.5x1.7x1.7cm, indents the optic chiasm and adhered to the pituitary stalk, but with intact pituitary gland.

The patient's parents decided to postpone his education, and just focus on his medical condition, which patient initially accepted even if deep down he wanted to continue with his education. In September 2021, his headache worsened, becoming more frequent. Hence, he consulted with his pediatrician, who attributed the symptom to the craniopharyngioma. Repeat cranial neuroimaging was requested, and advised that patient undergo repeat excision of the mass or radiation therapy. But due to financial constraints, their family could not proceed with the management and instead followed through on the psychiatric tele-consultation.

The patient's past medical history revealed primary hypothyroidism, central diabetes insipidus, and primary hypogonadism due to his craniopharyngioma. Family and personal social history were non-contributory. Developmental history was at par with age but delayed sexual maturity Tanner Stage I.

The patient lived with his parents until he was 3 years old when his father went to work in Dubai and was the primary disciplinarian. He would return to the Philippines yearly for about 2 weeks. The patient considered his interactions with his father insufficient, and he wanted to be with his father most of the time. He had thoughts of being inadequate and a burden to his family, believing that his illness was the reason why his dad had to work abroad. Because of this, the patient would always cry whenever his father would leave the country.

The patient grew up with his mother who usually gave in to all of patient's requests since she was afraid that if he was stressed his headaches would worsen. The mother described her son as easy to take care of when he was a baby. Whenever the mother had to go to work, her sister (a maternal aunt) would take care of patient. The patient was breastfed for six months, then later shifted to bottle feeding for

another six months. Whenever the patient would cry, his mother would immediately attend to him. He was weaned off from bottle feeding at the age of 2 years old. There was no note of thumb-sucking or further use of soothers. His developmental milestones were at par with age. At the age of two, toilet training was initiated. The training was strict, guided primarily by her mother, and was completed at three years of age.

PHYSICAL & MENTAL STATUS EXAM

The patient was overweight with a BMI of 30.3 (z-score= +2) and a height of 160cm (z score = -1). Physical exam revealed Tanner Stage I, and in the neurological exam, the patient had bilateral temporal hemianopsia.

The patient was seen sitting on a chair in front of a laptop during the online interview examination. He had short hair, was well-kempt, wearing a white shirt and shorts. He had good eye contact. He spoke in a low and soft tone of voice with an average rate of speech. He claimed to be depressed and affect was appropriate. He would repeatedly say, "Am I evil? Did I do something wrong to them? Why doesn't anybody love me?" He claimed he frequently thought it was better if he were gone. He verbalized that he did not know why he felt this way. There was no tangentiality and circumstantiality. He denied hallucinations or delusions. No impairments in abstract thinking and planning were observed by asking similarities of two words and using the Montreal Cognitive Assessment - Philippines. The patient was successful in identifying train and bicycle as "transportation" and weighing scale and ruler as "sukatan". He had partial insight as he did not understand his illness or why he feels this way but is willing to be helped and cooperate in therapy. The patient was considered to have only fair judgment as he was not remorseful of his suicidal attempts. When asked, why he attempted suicide; he would just ignore the questions and remained silent.

TREATMENT AND MANAGEMENT

The patient was started on low-dose Escitalopram 10mg ½ tab at night. He was advised to have a neuropsychological examination to assess cognitive capacity and explore personality traits, but was not done due to financial constraints.

The patient's differential diagnosis was persistent depressive disorder, as the patient fulfilled the criteria of depression for more than one year. Still, due to the multifactorial consideration of the robust findings of panhypopituitarism, depression secondary to a general medical condition was considered. Overeating, could be attributable to the medical condition while low self-esteem and hopelessness, were considered an effect of psychosocial and socio-cognitive factors.

The patient also responded well with cognitive behavioral therapy for three sessions that identified his thoughts, emotions, and actions. Later his sessions were focused on identifying his cognitive distortions such as negative mental filtering and polarized thinking that resulted in decreased irritability, euthymic mood, and reduced arguments at home. In the last follow-up, the mother reported improvement in the patient's mood, which was not euthymic, and he did not argue as much with his mother. He often could control his urges to drink and eat more than his usual serving.

Cognitive behavioral therapy was used in this case because of the common change and mechanisms specifically targeted for pediatric depression. Particularly behavioral activation and cognitive restructuring have been most consistently correlated with improvements in depression among adolescents. Behavioral activation includes bringing positive reinforcements, specifically physical and social activities, leads to increased engagement in activities. Cognitive restructuring includes generation of realistic and positive perspective in patients thru challenging negative thoughts. (5) Family therapy was conducted to teach his parents proper behavior modification, such as being consistent on how they would discipline and improve family dynamics thru better communication. The patient was referred back to pediatric neurology and endocrinology for close follow-up. Repeat hormonal assay, such as testosterone, follicle-stimulating hormone, luteinizing hormone, thyroid function tests, and metabolic workup were scheduled.

DISCUSSION

The predominant symptoms in this case were sadness, self-harming behavior, self-blame, and worthlessness, which are constitutional signs of

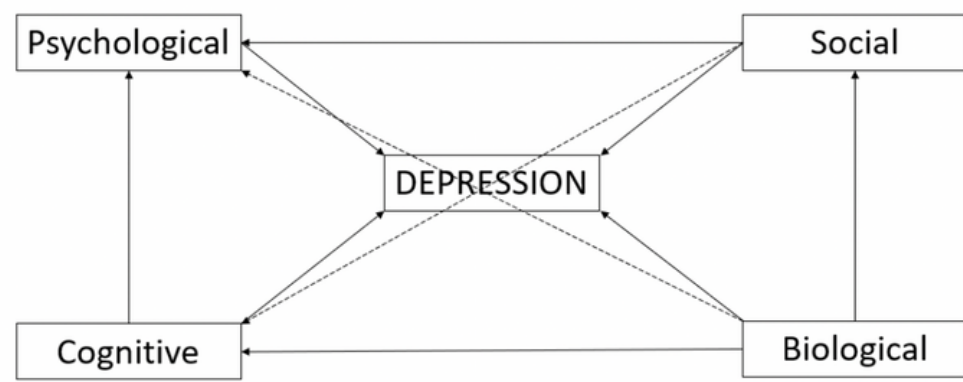


Figure 1. Biopsychosocial Formulation

depression. There are four main pillars that significantly contribute to the development of depression in this case: psychological, cognitive, social, and biological. Both social and cognitive factors greatly influence the psychological factor. The social factor also affects cognition. (Figure 1). Additional dwelling on the biological origins of depression is the psychoendocrinology of behavior. A discussion of the hypothalamus-pituitary-gonadal axis is warranted to correlate the symptoms of the patient's case with biological underpinnings.

Like the other hormones governed by the hypothalamus and pituitary, the cascade of hormonal reactions in the HPG axis starts with the release of hypothalamus and pituitary, the cascade of hormonal reactions in the HPG axis starts with the release of the GnRH or gonadotropin-releasing hormone by the hypothalamus, leading to the activation of the pituitary gland leading to the release of the luteinizing hormone and follicular stimulating hormone. The LH and FSH activate the conversion of precursor substance to testosterone. Essential to take note in this is that testosterone is the sole precursor of estradiol in males. HPA controls secretion of corticotropin-releasing hormone (CRH), which in turn controls glucocorticoid secretion and may affect depressed mood. (Figure 2) (6)(7)

A neurobiological reason for the reduced psychological status of individuals with craniopharyngioma is the lack of hormones due to an impaired HPA axis. Involvement of the hypothalamus is neurobiological explanation of impaired quality of life. In this patient, his condition led to reduced self-confidence and coping skills thru his feelings of being inferior due to his physical illness.

There are two ways of involvement of testosterone in behavior and, most importantly, depression. The addictive effect of testosterone

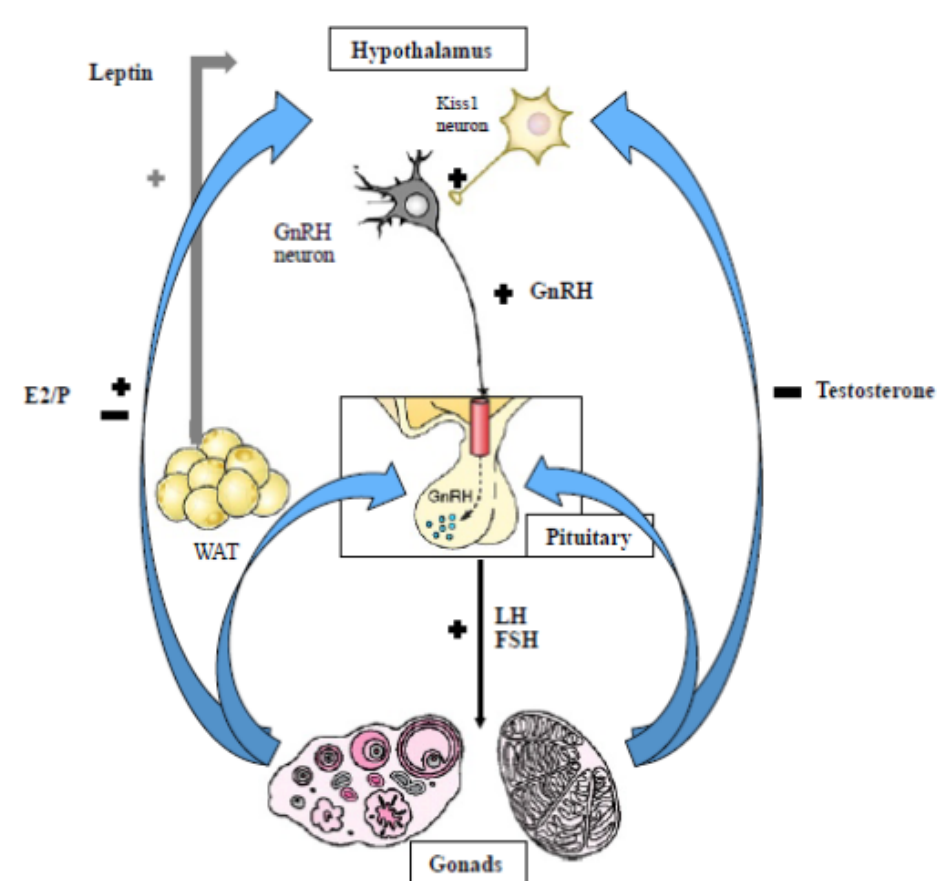
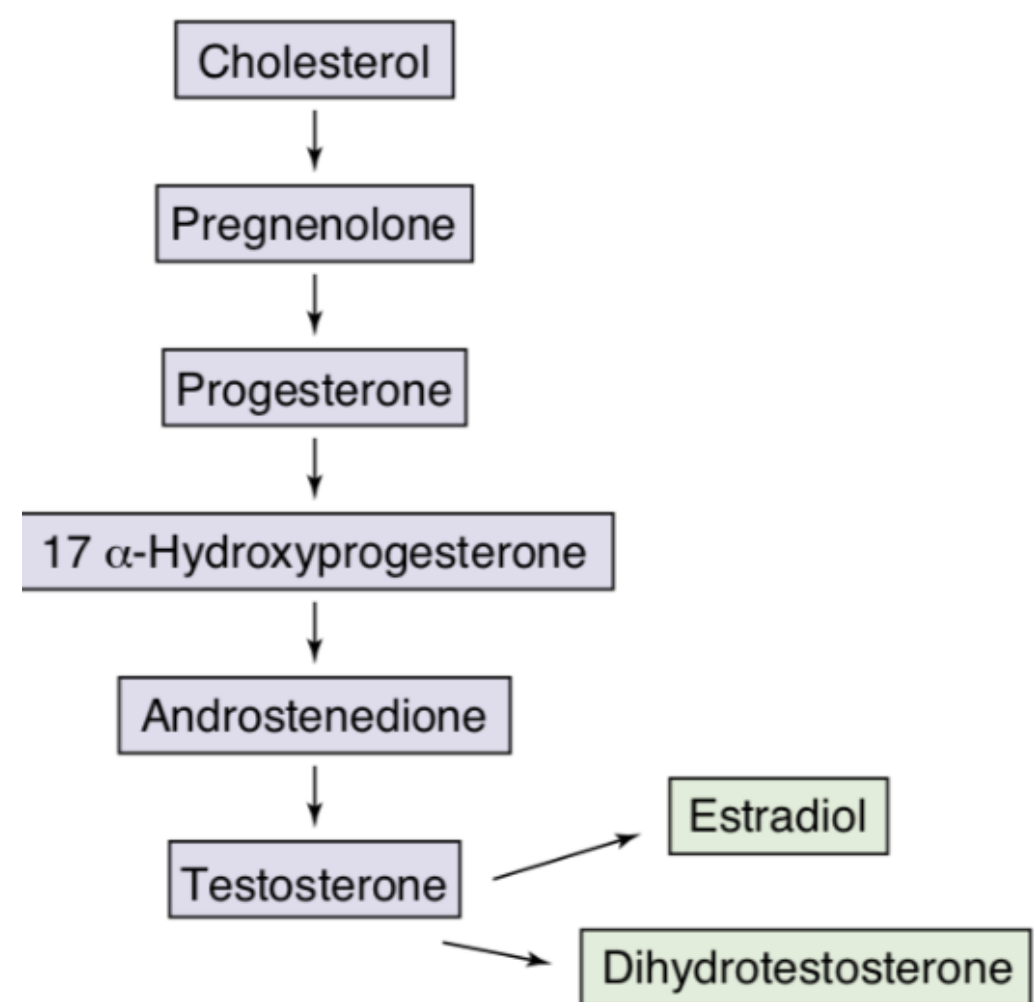


Figure 2. Hypothalamus-Pituitary-Gonadal Axis (6) (8)



is due to its activation of the dopaminergic system leading to reward regulation and positive affectivity. Testosterone also influences the prefrontal cortex via the dopaminergic system leading to motivational regulation. (Figure 3) (9)

The patient's levels of testosterone as correlated in the year April 2019 (35.6 ng/dL) and August 2019 (26.9ng/dL) as normal values should be 208.08-496.58 ng/dL. This low testosterone level concurrently coincides with the patient's depressed mood and suicidality. The testosterone level of the patient was consistently low.

The diagram below notes that testosterone is the sole origin of estradiol in males, which increases the conversion of tryptophan to serotonin in the CNS serotonin system.

Estradiol also inhibits the monoamine oxidase A, which decreases the degradation of serotonin. Cumulatively the effect of estradiol increases the CNS serotonin levels, which is essential for cognition and mood regulation. (Figure 3) (6)

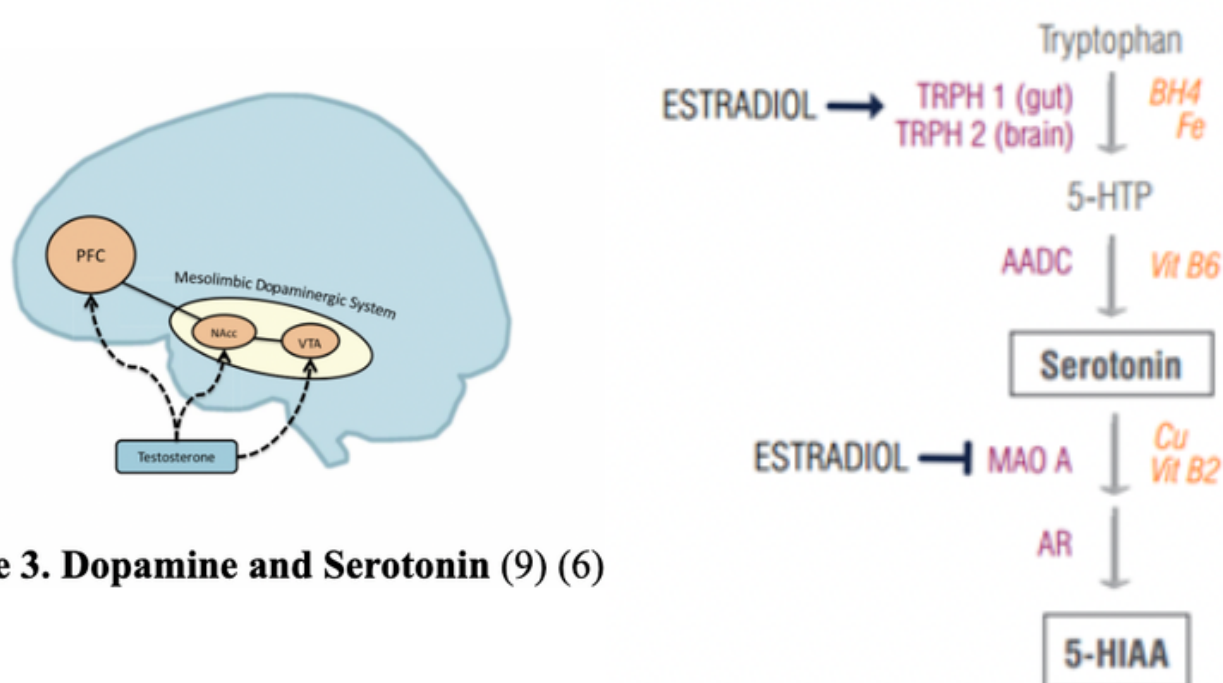


Figure 3. Dopamine and Serotonin (9) (6)

For the Hypothalamus-Pituitary-Thyroid axis, the hypothalamus releases thyrotropin-releasing hormone, activating the release of the thyroid-stimulating hormone by the pituitary. The thyroid-stimulating hormone then stimulates multiple reactions and cascades, leading to the production and release of thyroid hormones -T4 and T3. Far more critical is its effect on mood regulation, as deficits of thyroid hormone leads to depression. (Figure 4)

The patient was hypothyroid with TSH levels of 0.49mU/L (normal value: 0.7 - 6.6 mU/L) last October 2011 at age 5. This coincided with the start of the depressed mood after patient's transphenoidal surgery.

The thyroid hormone has direct effects on the synthesis and release of serotonin as well as increasing receptor sensitivity of the hippocampus and cortex leading to mood regulation. On the other hand, hypothyroid states result in an increase in 5-HT turnover in the brainstem. Increased 5-HT turnover in hypothyroid states may lead to an increase in raphe 5-HT1A autoreceptor activity and a decrease in cortical 5-HT concentrations leading to depression. The inverse effect of the thyroid hormone at the 5HT1A receptor, a presynaptic inhibitory at the raphe nucleus, leads to decreased serotonin reuptake.

Thyroid hormone application may desensitize presynaptic 5-HT1A raphe autoreceptors, and thus increase cortical serotonin release. In addition, thyroid hormone-induced increases in 5-HT2 receptor sensitivity might potentiate the effects of antidepressant drugs on the 5-HT2 receptors (Figure 4) (10)

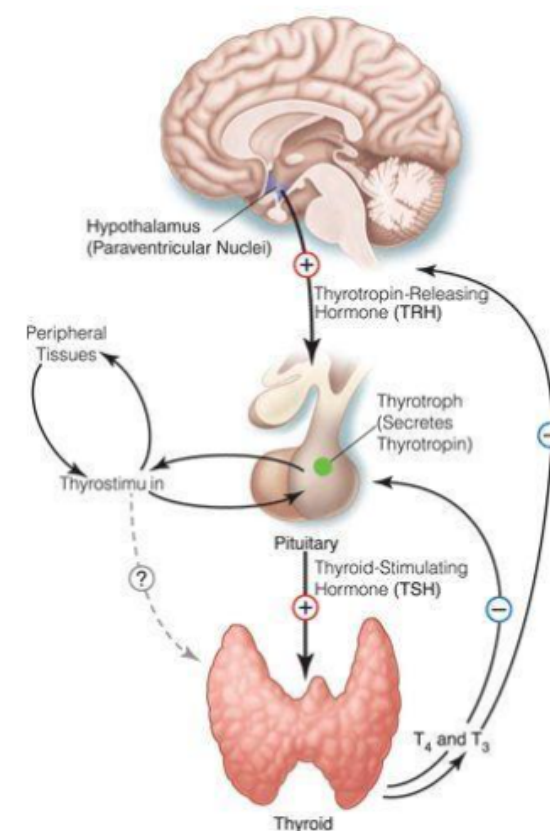
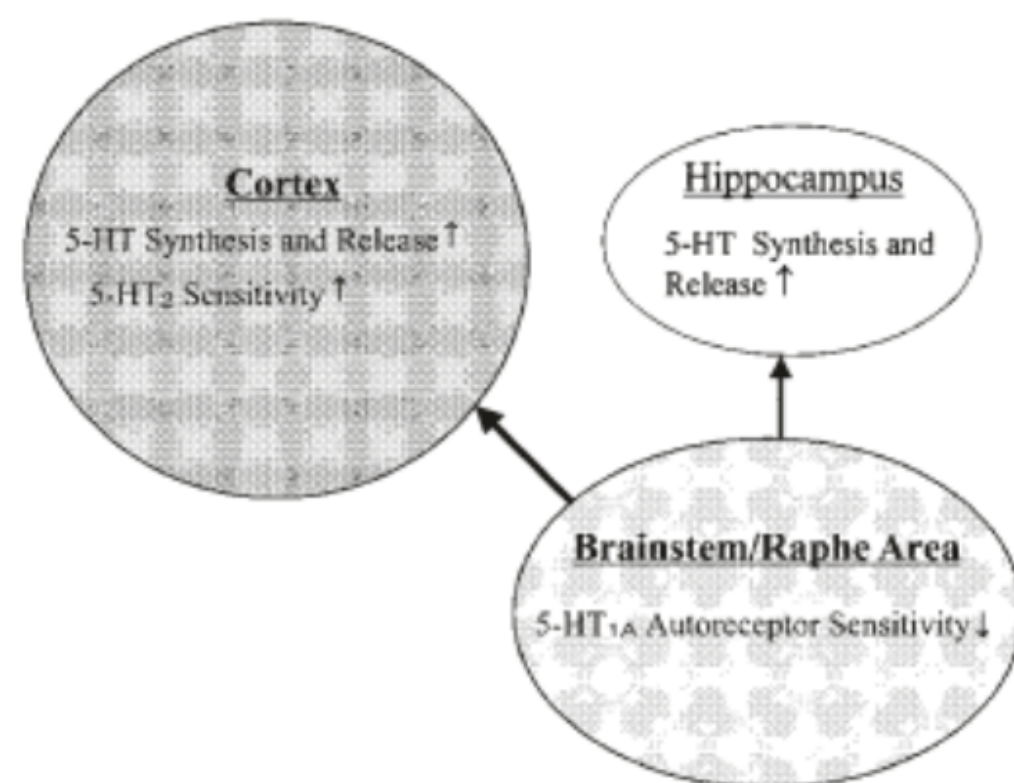


Figure 4 Hypothalamus-Pituitary- Thyroid Axis (10,11)



For the Hypothalamus-Pituitary-Adrenal (HPA) axis, elevation in glucocorticoids, either primary or secondary, can cause depression or psychosis when stressed. The hypothalamus releases the corticotropin-releasing hormone, which activates the release of the pro-opiomelanocortin (POMC) precursor peptide

prior to its cleavage to form adrenocorticotropin releasing hormone. Part of the POMC peptide is the endogenous opioid B-endorphin that is vital in the modulation of stress and pain. In conditions that decrease the functionality of the pituitary hormone, the production of endogenous B-endorphin peptides is reduced. (8)

The patient was also worked up with cortisol assay last December 2011 with normal results of 8.32 ug/dL with normal values of 6.2-19.4 ug/dL.

The neuropeptides, oxytocin, and vasopressin, may also be involved in hypopituitarism when the posterior pituitary is involved since our patient was worked up for Diabetes Insipidus last 2011. Both oxytocin and vasopressin promote social cognition; males have androgen-dependent vasopressin receptors in the lateral septal nucleus. The hippocampus is involved in mechanisms of learning and memory consolidation whereas the lateral septal nucleus is important for social recognition and related social behaviors. Vasopressin and oxytocin activate both pyramidal neurons and GABAergic interneurons in the hippocampus and could facilitate memory consolidation by potentiating synaptic transmission. At the same time, both hormones promote social cognition. Oxytocin has parasympathetic activation leading to anti-anxiety and antidepressant effects, while vasopressin activates sympathetic response resulting in stress response activation and regulation. (13)

Lastly, another important factor in this case is the effect of obesity on depression. In normal individuals, the anorexigenic substance leptin produced by adipocytes decreases appetite, while its counterpart, ghrelin, increases appetite. In obesity, due to other factors such as diabetes, hypothyroidism, or hypercortisolism, there is a significant effect on the appetite overriding the leptin-ghrelin control of appetite. The overriding of this system leads to increased macronutrient accumulation, increasing and enlarging the abdominal adipocytes.

This leads to a further increase in leptin instead of further decreasing appetite, which results in leptin resistance. Elevated leptin levels cause an inflammatory response in the CNS. Leptin

inhibits the conversion of tryptophan to serotonin, adding to the development of depression. (14) Relating this to the patient's case, his obesity could be reflective of abnormal leptin levels causing subsequent depressive symptoms.

Aside from the biological causes of depression in this case, we need to analyze the other pillars mentioned earlier. Elaborating on the psychosocial domain, we utilize the Erik Erikson's theory of psychosocial development. At the age 3 -6 years old in Erik Erikson's psychosocial development, children encounter the crisis of initiative vs guilt. The child's expanding initiative forms the basis of subsequent development of realistic ambition and the virtue of purpose. The patient was able to resolve this conflict as he has been an active student in his early pre-school years. By the age of 7-12-years old, children are met with a crisis of industry versus inferiority. This stage is influenced by both peers and family, and which was the particular stage of conflict for the patient. (15)

At the age of 5, even up to the recent events, the patient had significant peer rejection and social exclusion i.e. bullying experience. He wasn't able to establish and evaluate himself in the context of a group. His attempts to acquire peer encouragement and acknowledgment were in vain regardless of his initiatives. While at home, the absence of his father and the lack of siblings led to the focus of acquiring confidence from his mother. However, his attempts of confiding with his mother were met with subtle invalidating responses, such as questioning his behavior in school and towards his peers. His significant acknowledgment in academics was met with disappointment. The cumulative lack of positive peer and familial influence caused him to see himself as inferior leading to a psychological malignancy called inertia. He lacked self-esteem, often blamed himself and filled with self-doubt, considered himself worthless. Every complaint against him and his complaint about others was ignored, which led to his maladaptation. (15) (Figure 5)

He was bullied by his classmates and was considered a burden by his classmates due to his physical illness. The patient confided to his mother but she felt the patient might have been

the problem and that he should be the one to change his behavior. The patient felt his feelings were invalidated, which led to his feeling depressed and helplessness to the point he considered himself a burden to everyone including his family.

Currently at the age of 15 years old, the patient has a new crisis of Identity versus Role confusion. It will be a challenge for him in adapting to the new changes of his adolescent stage and is still in the process of figuring out who he is. (15)

In the socio-cognitive domain, the main prerequisite, of social interaction, proved to be deficient in the patient's case. Social interaction is essential in developing perspective-taking and cognitive flexibility, to be able to set limits to one's point of view, and to shy away from egocentric thoughts. However, in this case, every advice and attempt to correct his mistakes by his parents, such as his diet, and even assuming the point of view of his parents when he would attempt to hurt himself, was met with resistance. He further developed vast cognitive distortions, only assuming his point of view in every endeavor and conflict and learned helplessness (Figure 6)

CONCLUSION

Biopsychosocial approach was the main framework used to treat this patient with panhypopituitarism. This framework enabled the doctors to comprehend a multifaceted disease and identify the patient's problem. Due

to the multiple deficiencies in the patient's hormones particularly testosterone, the depression of the patient could be considered as having biological causes. The psychosocial factors such as bullying and social exclusion by his classmates contributed to the low self-esteem and feelings of inferiority. From the cognitive perspective, deficient peer interaction led to being egocentric with multiple cognitive distortions. Understanding all of the biological, psychosocial, and cognitive factors that contributed to a child's depression; it is imperative to create a tailor-fit treatment and management for this patient.

ETHICAL CONSIDERATIONS

This study was conducted according to the accepted ethical research practice of the CARE guidelines. Informed consent was obtained using Informed Consent for Case Reports as Part I then Certificate of Consent to Participate as Part II in English, as the patient uses English as the medium of communication and the mother is a college graduate. Documents of the patient in making this case report will be stored for 3 years and will be deleted accordingly. A written consent form was obtained from the patient and parent.

The consent was explained to the patient and parent and co-signed by both as required by our review board. This study was approved by the Research Ethics Committee (REC) of our institution.

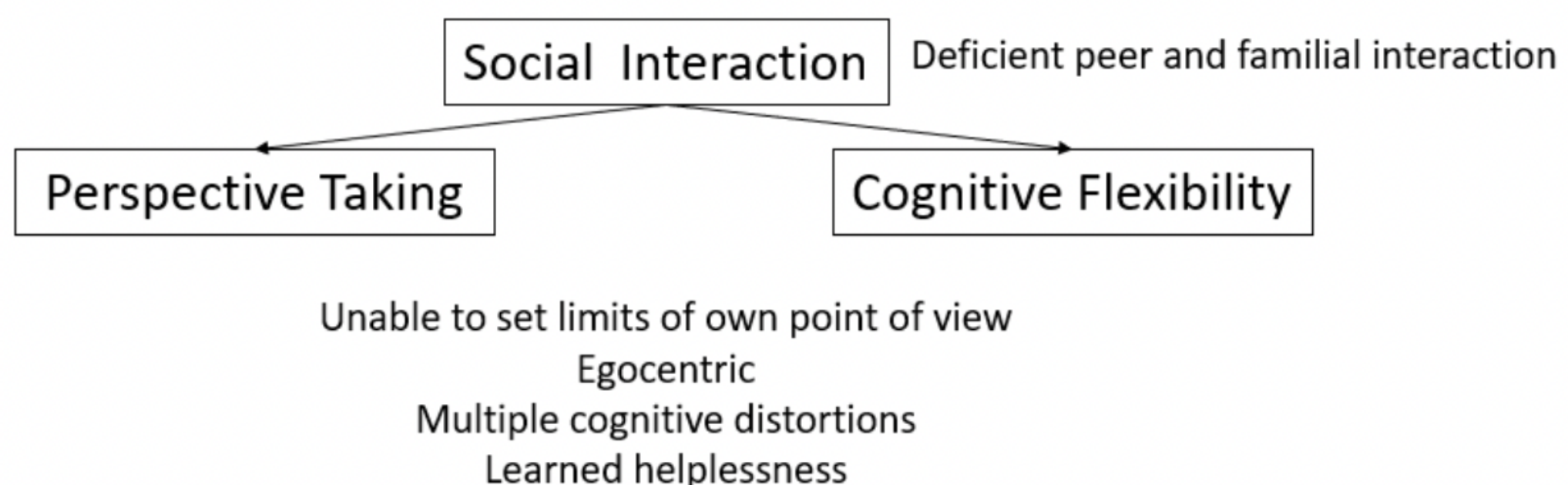


Figure 6. Socio-cognitive Factors

CONFLICT OF INTERESTS

This study was investigator-initiated and not industry-funded or company-sponsored. The attending physician and the principal investigator were directly handling the patient.

PATIENT ANONYMITY, INFORMED CONSENT AND CONFIDENTIALITY

The patient's identity and personal data were not be included in this study, and identifiers were removed from the manuscript. Patient's anonymity and confidentiality was secured by non-disclosure of any personal information that may determine the patient's identity. Data was accessed securely by the principal investigator and protected from illegal or inadvertent access by other people. The written informed consent was directly obtained by the principal investigator from the patient and parent.

RISKS

There were no risks for physical, psychological, social, or economic harm on the subjects due to this case report since the methodology only involved the description of the case itself. No active interventions were done, and no discomfort or injury inflicted on the study patient.

BENEFITS

Since the study was a case report, there was no direct benefit for the patient. All the information gathered about this case will be of great benefit for the welfare of all future patients with this similar presentation.

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