



UPON THAT WHICH BINDS ME

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ABSTRACT

The patient is a 36-year-old- male who was bullied by peers and was emotionally abused by his father for being effeminate and preferring to play with dolls. These adverse childhood experiences made him vulnerable to depression. He told himself that he could no longer rely on anyone else but himself and took pride in his independence. He gave his best with his endeavors and did not settle for mediocrity, frequently reviewing his work.

During the pandemic, he experienced several hardships such as disruption of activities, inability to meet the financial needs of his family and unemployment. He found himself struggling but surviving. While in a work-from-home arrangement, he was so frustrated about his internet connection that he complained on social media.

The internet company then threatened him of possible legal charges and felt stuck in a hopeless situation. This affected his day-to-day activities until he felt so overwhelmed that he attempted suicide by ingesting multiple medications. He was then brought to the emergency room and was admitted. He was diagnosed to have Major Depressive Disorder and was started on antidepressants. Psychotherapy focused on identifying stressors and strengthening adaptive coping mechanisms while he was admitted at an isolation facility. He then followed up at the outpatient department of a tertiary government hospital in Mindanao with noted improvement in mood and functionality overtime.

During admission, he was also diagnosed to have Diabetes Mellitus and COVID-19, which added to his burden as these were the biologic factors that were correlated to his depression.

The case highlighted the interplay between the effects of multiple traumatic experiences in a vulnerable individual and thus necessitating a holistic management.

KEYWORDS: *Case Report; Consultation-Liaison Psychiatry; Major Depressive disorder; Psychiatry; Suicide.*

INTRODUCTION

Several studies have shown that adverse early childhood traumatic experiences such as physical, emotional, sexual, or other types of abuse increase the risks of developing psychiatric illness such as depression. This causes dysregulation of the child's developing neurobiological system leading to decreasing resistance to stressful events leading to problems in emotional regulation (1).

Childhood maltreatment has been associated with risk for development of major depressive disorder in adulthood. Although studies would have inconsistent results, it affects the volume of the amygdala and hippocampus owing to their sensitivity to stress (2).

Several types of childhood maltreatment have been correlated with structural changes in the brain. Emotional maltreatment has been associated with abnormalities in the fronto-limbic socioemotional networks. Neglect disturbs the white matter integrity and connectivity or other functions. Overall, reduced frontal cortical volume has been common to all maltreatment types (3).

Children worldwide who were perceived as "different" because of their sexuality suffered from discrimination, intimidation, harassment and violence. This vulnerability increased as they grew older whenever they did not conform to the norms of society. They were exposed to discrimination at school, sports teams and other areas of social life. They were rejected by their family and society; forced into heterosexual marriages; and hate-motivated violence (4).

In the patient's case, he was beaten by his father because he was different and forced to accept his father's ideals and standards. These negative childhood events increased his risk for developing poor health outcomes and mental health problems such as depression, anxiety and suicidal behavior. Although the exact data cannot be determined due to some cases being unreported, it has been said that they are twice likely to experience physical, emotional, and sexual abuse (5).

The pandemic affected almost all aspects of the society; healthcare system became overwhelmed,

schools were closed and several businesses stopped their operation leading to unemployment. It caused overwhelming emotional responses, sudden change in daily routines, and a sense of uncertainty (6-9).

Coupled with the effects of isolation, this led to the development of anxiety and stress symptoms. High number of patients commit violent acts such as homicide and suicide which might be due to increased alcohol consumption or during psychotic episodes. Particularly at risk are those with genetic vulnerability or existing psychiatric patients who had discontinuation or limited access to treatment (10, 11).

CASE PRESENTATION

This is the case of Marvin, a 36-year-old male, call center agent who was admitted under the service of Internal Medicine due to multiple drug ingestion and referred to the Consultation-Liaison Psychiatry service on his second hospital day for evaluation and co-management of depression.

He described himself as a strong, and independent person. He was calm, composed and did not crack under pressure as he figured out the best solution to his problems. If deemed unsolvable, he would vent out his feelings with his friends usually hanging out and drinking alcoholic beverages.

He was organized and planned his daily activities as he would get frustrated if things did not go as expected. However, he also tried his best to find alternative solutions in such situations of unforeseen circumstances. He was more of a leader and directed people, telling them what should be done. He disliked people who were sloppy or those who did not follow what has been previously agreed upon. Despite this, he was described as someone that got along relatively well with people.

History of Present Illness

Ten months prior to admission, during the onset of the pandemic, he experienced several lifestyle changes and restrictions. The rapid spread and novelty of the disease caused uneasiness and he took precautions such as spraying alcohol. Unable to see his loved ones coupled with disruption of his daily routine made him feel he was deprived of his freedom. To ease his apprehension, he regularly called his loved ones.

Eight months prior to admission, as the pandemic ensued, the company where he was working stopped their operation hence, he suddenly became unemployed. He felt sad and worried because of his dwindling finances. He felt ashamed and helpless as he relied on rations from the local government and his relatives.

He celebrated his birthday alone and met his family virtually however it was not enough as there was no human warmth. To him, it was becoming more unbearable each passing day. He started to eat less and could not sleep properly at night as he would frequently think of his own predicament. He felt helpless and became tired of living that he tried cutting his left wrist several times using a blade with the intention to die. Although he survived, he felt relieved as he was still able to feel the pain, which eased the emotional hurt.

Because of the rising number of COVID-19 cases and afraid of being infected, he would just apply pressure and asked his neighbor to help him dress his wound. He sought consult with a private psychiatrist and was diagnosed to have depression. He was prescribed sertraline and diazepam with unrecalled dosage. He was non-compliant as he afraid he would become dependent on it but most importantly, he believed these were the same medications prescribed to his other relatives, which caused long-term side effects such as rigidity, increased salivation, lack of facial expression and other symptoms.

For several months, his mood gradually worsened. He became sadder and at the same time worried for the safety of his loved ones. He coped by watching movies online and taking care of his plants. He felt slightly better when community lockdowns were partially lifted as he was able to buy basic commodities. He resumed working as a call center agent wherein adjustments were made to accommodate health protocols such as “work-from-home arrangements” and transportation assistance. However, he was absent-minded during conversations with his friends and even at work. It took more effort for him to properly perform his task as he could not focus. He got frustrated and angry at himself because of his inefficiency. He was always in a rush to keep up with deadlines, which was unusual for him. He was

often tired and had an erratic appetite that increased during stressful times.

Despite his difficulties, he managed to hang on until one month prior to admission when he had problems with his internet connection. It was essential to his line of work as a call center agent especially in a “work-from-home” setting. He filed several complaints and paid his bills promptly yet the service he was expecting was not adequately provided. He became so irritated that he made a livestream on social media insulting the repairman and the internet service provider. This prompted the internet service provider to threaten legal action against him unless he made a public apology. He complied yet the company pointed out that his apology was not enough because he continued to point out in his video that he was treated unjustly and was the real victim.

Two weeks prior to admission, he was informed of legal charges filed by his internet service provider. He felt the gravity of the situation and kept on ruminating about the possibility of being incarcerated. His symptoms worsened i.e. he became sadder and more worried as he blamed himself. The image of himself being a strong person was already crumbling. No matter how hard he tried to lift himself up, he still felt down and unmotivated. He would sometimes suddenly cry and preferred to lie in bed most of the time.

He cut off communication with everyone and kept things to himself, not even telling his partner what was going on his life as he did not want to be a burden. He became more inattentive during conversations and kept on committing mistakes during his work as he was constantly thinking about what might happen to him.

Few days prior to admission, he became hopeless, believing it was only a matter of time before he would be arrested. This led to thoughts of escaping such as not being able to wake up or wishing he was dead.

For him, living for another day was agonizing. He talked to his friends who reassured him that everything will be okay, and to call them if he needed someone to talk to.

As days passed, it was becoming more unbearable. On the night he was admitted, he felt he had no other choice, that he wrote a suicide letter and drank 125 ml of isopropyl alcohol, 5 tablets of paracetamol 500mg tab (Biogesic), 5 tablets of phenylephrine with chlorphenamine maleate and paracetamol (Bioflu), as well as 10 tablets of cetirizine and 8 tablets of diosmin and hesperidin (Daflon) 500mg tab. He experienced severe epigastric pain and several episodes of vomiting thus he was then immediately rushed to the emergency room.

At the emergency room (ER), he experienced mixed emotions. He was in pain and felt discomfort. He was also afraid to hear any medical comments about his condition and regretted his suicidal attempt. He was initially seen by the Emergency Medicine service and diagnosed as having a non-accidental multiple drug ingestion. He was referred to the Toxicology service and the following management was started: Fluid resuscitation, baseline laboratory, omeprazole IV and vitamin B complex IM. NGT was inserted wherein gastric lavage was done followed by administration of activated charcoal.

After stabilization, he was transferred to the Cardiopulmonary ward under the service of Internal Medicine. He was initially placed on NPO then eventually on a progressive diet. Pertinent diagnostics of an elevated CBG of 400 mg/dl and Hba1c of 12% were noted. He was started on metformin (on hold while on NPO), insulin (Humulin) 70/30, rescue doses of regular insulin, and D50 water IV for hypoglycemia. Suicidal Precaution was instituted and asked to have a responsible adult to keep him company at all times.

On the second hospital day, the patient was formally referred to Consultation-Liaison Psychiatry for evaluation and co-management of depression. The patient's COVID RT-PCR result showed positive result; thus he was also referred to the Infectious disease service and was transferred to a COVID ward for isolation.

Medical and Surgical History

He had Bronchial Asthma with no known maintenance medications. He had a vehicular accident in college wherein he sustained a

fracture of his left elbow necessitating several consults with an orthopedic surgeon and physical therapist. He has no other known comorbidities.

Family History

A strong familial history of schizophrenia was noted in the maternal side. He is unsure of their outcome but two of his aunts were maintained on psychotropic medications and one died of suicide due to hanging. One of his cousins had a history of methamphetamine use and attempted to hang himself. He only heard he was chained and confined in a separate room. His brother experienced depressive symptoms after his son was forcibly taken away by his ex-partner; he also drinks alcoholic beverages habitually to cope with his problems. Diabetes Mellitus, Bronchial asthma, malignancy (bones and brain tumor), and goiter were also reported in his family. No other heredo-familial diseases were noted.

Psychosocial History

He is the second among three siblings. He and his siblings were under the care of their grandmother because their parents were busy either working or quarreling. They would frequently argue because of their father's problematic behavior i.e. often drunk, poorly supportive, irresponsible and abusive to both his wife and children. His mother eventually became fed up leading to their separation. His mother changed after their separation, she became neglectful and made poor choices in her life. She dated several men and had a series of failed relationships. Marvin felt that his stepfather was a lot worse than his biological father, as he was also abusive and a womanizer.

Marvin had a difficult childhood. He experienced harsh parenting and described being neglected and discriminated as a child. He was effeminate as a child and preferred to play with dolls. His father could not accept him as he claimed that Marvin was smearing his image as a policeman. His father reprimanded and forced him to play with toy guns or cars. His mother on the other hand, would keep silent as she also had her own issues with her husband.

At the age of seven, Marvin's parents separated; so he lived with his maternal relatives. He and his older brother went to live with his mother in

Luzon; while the younger brother stayed with their father. He had trouble adjusting because it was different from his native language, which was Tagalog. Aside from this he was not accepted by his relatives (maternal side) in Luzon and was treated as a disgrace. He experienced being bullied by his peers or seen as a lesser being in the eyes of other people. Later when he was in high school, he was advised by his friends and started to take hormonal pills for him to have a more feminine appearance to look beautiful. He was a consistent honor student and a leader in his class. He participated in and hosted several school events. He was not easily bullied as he would fight back against his bullies.

He was performing well even during his college years as a nursing student until he had an accident during his last academic year. He sustained a fracture on his left elbow necessitating several consults with an orthopedic surgeon and physical therapist to regain mobility. Although he was able to finish his degree, he realized that he could not use his arm in the same way as before hence he decided not to pursue nursing as a career. Initially, it was hard and disheartening as he was not able to practice his profession. Later he worked as a call center agent which offered higher compensation that somehow made up for his disappointment in his inability to work as a nurse. He gave his best and took pride in his work. He was considered a good and organized leader.

Marvin was attracted to the same sex although he tried courting girls during his teenage years; yet it became clearer to him when he was fifteen that his preference were men. He had a total of three romantic relationships, two of which were with married men. Both were older than him by about 8- 10 years as he preferred matured men. Those relationships did not last as the men were unable to leave their respective families. He denied having problems with his sexuality and accepted who he was. Currently, he is living together with his longtime boyfriend of more than five years. He is his confidant and support whenever he has problems.

After he was hospitalized, he reconnected with his father and other paternal relatives via video call. His father now accepts him and told Marvin that he was proud of him. Marvin had mixed feelings regarding this.

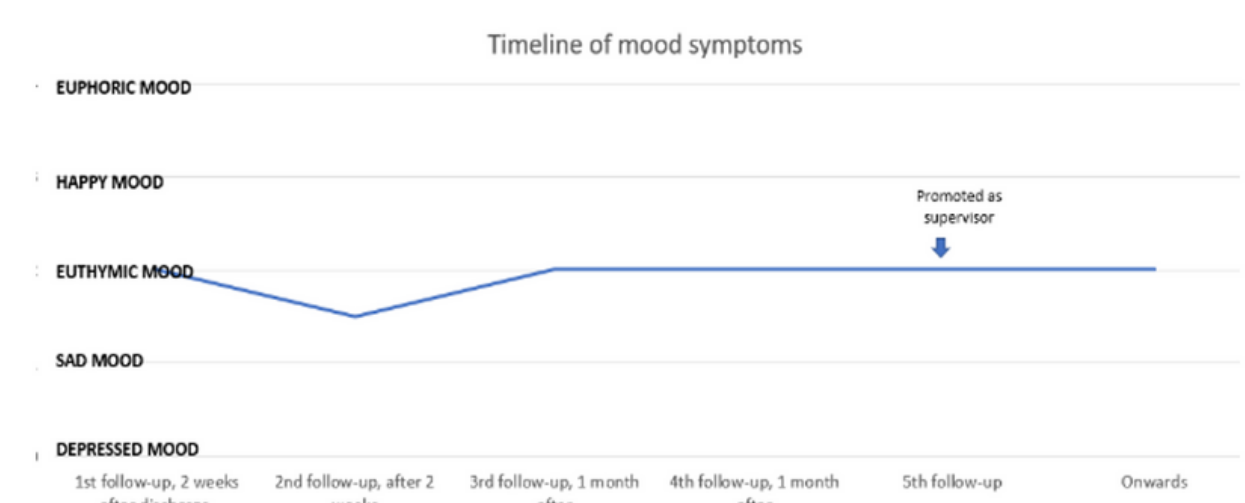
He felt anger and regret; frequently asking “Why now?”, if only his father had changed earlier, their family would not have broken apart. At the same time, he also learned his mother did not accept their father despite the several attempts he made in trying to make amends. Contrary to how he was treated by the relatives of his mother, he now felt warmth and acceptance from the paternal side, frequently showing enthusiasm and verbalizing that they were excited to meet him in person.

Clinical Findings

Physical examinations revealed unremarkable results.

While he was in the Isolation ward, he was co-managed and seen by the CL-Psychiatry service via telephone consultation. He was then diagnosed to have Major Depressive disorder; Multiple drug ingestion, (Intentional); COVID-19 infection, confirmed, mild; Diabetes Mellitus type II- Insulin requiring, and managed accordingly.

Timeline



Differential Diagnosis:

The following conditions were considered in our patient and as follows:

First, Depressive disorder due to another medical condition (Diabetes Mellitus) was considered due to symptoms of depressed mood and markedly diminished interest in almost all activities. Diabetes increases prevalence or risk for depression likewise, depression increases the prevalence or risk for future diabetes.

The patient had a history of oral contraceptive use, which may affect glycemic regulation or causes insulin resistance as well the noted influence of estrogen and progesterone to brain function, and alteration in the activity of neurotransmitters such as GABA, dopamine, serotonin (12-14). However, this was ruled out because the onset of symptoms started after exposure to multiple stressful events and prior to the diagnosis of diabetes. Furthermore, the symptoms of the patient can be explained by a primary psychiatric disorder.

Second, Adjustment disorder with Depressed mood was considered due to the development of an emotional or behavioral symptoms due to an identifiable stressor (effects of pandemic, legal charges) occurring within 3 months of onset of the stressor: marked distress out of proportion to the severity or intensity of the stressor; and significant impairment in functioning. However in adjustment disorder, it doesn't involve as many of the physical and emotional symptoms of clinical depression (such as changes in sleep, appetite, and energy) or high levels of severity (such as suicidal thinking or behavior), hence ruled out (14).

Third, Obsessive Compulsive personality disorder as comorbid condition was considered due to a pervasive pattern of orderliness, perfectionism, and inflexibility with symptoms of preoccupation with details, rules, lists, order, organization, or schedules; perfectionism; rigidity and stubbornness. More frequent in men and history of harsh discipline/parenting. This was ruled out as the patient was not able to fulfill the diagnostic criteria however traits are considered for the patient (14).

Fourth, Persistent Depressive disorder with intermittent major depressive episode, with current episode was considered due to symptoms of Depressed mood; sleep disturbances; fatigue; feelings of poor self-worth; diminished ability to think or concentrate; and appetite changes. Although he experienced multiple adversities since childhood, he had good adaptation did not manifest any symptoms until 10 months prior to his admission hence ruled out (14).

Lastly, Major Depressive disorder (MDD) was primarily considered due to the following symptoms: Depressed mood in most the day,

nearly every day; diminished interest or pleasure in almost all activities; sleep disturbances; fatigue; feelings of worthlessness; diminished ability to think or concentrate; recurrent thoughts of death; suicide attempt and significant impairment in functioning. Onset of symptoms usually occurs between 20-50 years old which is seen in our patient. Hence the diagnosis of Major Depressive disorder is considered in our case (14).

Hence, based on the above-mentioned findings our Final Diagnosis for our patient are as follows:

1. Major Depressive disorder,
2. Obsessive compulsive personality traits,
3. Diabetes Mellitus type II-controlled,
- and 4. COVID-19 infection, mild- recovered

Diagnostic Tests

The diagnostic tests requested were as follows: Complete Blood Count, Serum creatinine, BUN, FBS, HbA1c, lipid profile, SGPT, SGOT, Ferritin, LDH, Chloride, CRP, Na, K, Ca, Mg, PT, APTT, INR, UA, CXR PA, ECG 12L and COVID-19 RT-PCR.

Pertinent diagnostic test includes a FBS of 11.2, HbA1c of 12%, Glucosuria of 3+, and a positive COVID-19 RT PCR. While rest of the diagnostic tests requested were unremarkable.

During his consult at the Outpatient service of Psychiatry, Neuropsychological test was requested and administered by the psychological service which revealed an IQ of 91 and findings suggestive of Persistent Depressive Disorder.

Therapeutic Intervention

During his admission, he was under the care of Internal Medicine and referred to other services including toxicology and CL- Psychiatry.

After initial management at the ER, his diabetes was then controlled by giving insulin glargine; regular insulin, and D50W IVTT in case he had hypoglycemia. While for his COVID-19 Infection, vitamin C and zinc were given, and was isolated from other patients.

For his depression, escitalopam, aripiprazole and clonazepam were given. Supportive psychotherapy and later during his follow-up consultations at the Outpatient service of

TABLE 2 MEDICATION COST AS OF OCTOBER 2015

CHARITY					PAY				
Meds	Dose/Day (mg)	Length of Stay (wks)	Drug Cost (PhP)	Total (PhP)	Dose/Day (mg)	Length of Stay (wks)	Drug Cost (PhP)	Total (PhP)	
Risperidone	2	1	8	56	2	1	8	56	
		2	8	112		2	8	112	
		3	8	168		3	8	168	
		4	8	224		4	8	224	
	4	1	16	112	4	1	16	112	
		2	16	224		2	16	224	
		3	16	336		3	16	336	
		4	16	448		4	16	448	
	Olanzapine	5	1	34.5	241.5	5	1	34.5	241.5
			2	34.5	483		2	34.5	483
			3	34.5	724.5		3	34.5	724.5
			4	34.5	966		4	34.5	966
20		1	138	966	20	1	138	966	
		2	138	1,932		2	138	1,932	
		3	138	2,898		3	138	2,898	
		4	138	2760		4	138	2760	
50		1	8.5	59.5	50	1	8.5	59.5	
		2	8.5	112		2	8.5	112	
		3	8.5	178.5		3	8.5	178.5	
		4	8.5	238		4	8.5	238	
600	1	102	714	600	1	102	714		
	2	102	1,428		2	102	1,428		
	3	102	2,142		3	102	2,142		
	4	102	2,856		4	102	2,856		
Quetiapine	200	1	152.25	1,065.75	200	1	152.25	1,065.75	
		2	152.25	2,131.5		2	152.25	2,131.5	
		3	152.25	3,197.25		3	152.25	3,197.25	
		4	152.25	4,263		4	152.25	4,263	
	800	1	609	4,263	800	1	609	4,263	
		2	609	8,526		2	609	8,526	
		3	609	12,789		3	609	12,789	
		4	609	17,052		4	609	17,052	
Amlisulpride	100	1	42.5	297.5	100	1	42.5	297.5	
		2	42.5	595		2	42.5	595	
		3	42.5	892.5		3	42.5	892.5	
		4	42.5	1,190		4	42.5	1,190	

	400	1	136	952	400	1	136	952
		2	136	1,904		2	136	1,904
		3	136	2,856		3	136	2,856
		4	136	3,808		4	136	3,808
Aripiprazole	5	1	58	406	5	1	58	406
		2	58	812		2	58	812
		3	58	1,218		3	58	1,218
		4	58	1,624		4	58	1,624
	30	1	202	1,414	30	1	202	1,414
		2	202	2,828		2	202	2,828
		3	202	4,242		3	202	4,242
		4	202	5,656		4	202	5,656
Chlorpromazine	200	1	13	91	200	1	13	91
		2	13	182		2	13	182
		3	13	273		3	13	273
		4	13	364		4	13	364
	600	1	39	273	600	1	39	273
		2	39	546		2	39	546
		3	39	819		3	39	819
		4	39	1,092		4	39	1,092
Haloperidol	5 mg/ml + 50mg/ml	At least 1 Dose	277	277	5 mg/ml + 50mg/ml	At least 1 Dose	277	277
Fluphenazine	25mg/ml	q 2-4 wks	55/dose	55	25mg/ml	q 2 - 4 wks	55/ dose	55

possible food cost for two people was assumed. (cheapest possible sandwich at the outpatient cafeteria: PhP 25.00, average price of rice meal: PhP 50.00) Table 4& 5 lists these other expenses below.

Transport expenses were reported based on the assumption that majority the hospital's patients are from the immediate Metro Manila area hence the cheapest fare for public transportation extending about 2 kilometers was used and multiplied for 2 (jeepney base fare of 8.5x2). Relapse for known patients was reported to occur from a minimum of 0/year to about 4/year, especially for charity patients who were reported to be non-compliant to their medication.

Psychiatry underwent Cognitive Behavioral Therapy.

Follow-up & Outcomes

He was discharged after eight days of admission and continued another week of home quarantine. He was then first seen in the outpatient department after his quarantine. In the subsequent follow-up consults, he had trouble sleeping after one of his friends died of suicide and his aunt was intubated because of severe COVID. He was also concerned about the possible legal consequences of his previous actions on social media. He coped with grieving by attending his friend's wake, was able to process feelings of guilt, and addressed his worries about his case by seeking legal advice. He had regular consultations with Medical Internist (IM) who maintained patient on his medications for Diabetes. He had frequent follow-ups, although irregular due to the restrictions of the pandemic; He practiced what he has learned in therapy sessions.

During his course of treatment, he had resolution of symptoms and improvement of both interpersonal and work relationships. He also had regular consultations with IM and maintains his medications for Diabetes with good glucose control.

Although it became irregular due to the pandemic, he had frequent follow-up visits and practiced what he has learned in the therapy sessions. He was even designated as their company's advocate for mental health.

Patient Perspective

Despite having experienced depression and committed suicide, he considers himself as a survivor and views himself in a new light. He used to have negative beliefs and several "what ifs", which caused hindrances to his improvement but now he considers himself as someone who has emerged from his comfort zone.

He learned more about mental health and recognized that it's okay to feel sad. What's important is how he deals with and adapts to the negative situations he encounters. He also provided help to his coworkers by giving advice while keeping in touch with his emotions. He tells them honestly if he is uncomfortable and tells

them to seek consultation with a mental health professional as it is beyond his expertise.

CASE DISCUSSION

Summary of the Case

To briefly summarize Marvin's trauma and stressful experiences across his developmental years made him vulnerable to depression. Marvin, for the majority of his childhood, was subjected to emotional, psychological and physical abuse by his father, who was strict yet neglectful. While his mother who also had her own share of problems because of marital discord could not attend the needs of her children. Later this resulted in his parents separating and splitting up the children from each other. Furthermore, during his adolescence, his high school classmates and schoolmates bullied him; then during his adulthood, he had an accident that incapacitated him from working as a nurse, for which he strove to achieve throughout his college years.

The experiences he encountered when he was a child influenced how he is as an adult and developed a fragmented sense of self. His parents especially father was not able to act as his role model for him to feel a sense of likeness and to make him calm and comfortable hence idealizing did not take place. While his mother was not able to act as a mirror to reflect back a sense of self and value hence mirroring did not take place. He had no one to turn to for affection or security and was placed in a helpless situation.

He used to be a victim and in order to overcome this, he strived to the best of his abilities, focusing on his strengths instead of his weaknesses. He persevered and excelled in his academics to avoid being helpless and being a victim again. Because of his accident, all his efforts in college came to naught. He lost his dreams of working as a nurse and initially became sad. Because he learned to be strong, he looked at his situation from another perspective and did not consider defeat.

Despite the numerous problems he faced, he was able to adapt by planning just like the way he did before. The hardships he encountered during the pandemic - including losing his job, contracting COVID and receiving legal threats as a result of his own provocation caused him to lose control of the situation. He once again became a helpless victim and eventually gave up the fight, committing suicide

to escape it all.

Neuro-biologic effects of Trauma

Marvin experienced several stressful events since childhood predisposing him to the development of depression. These Childhood adversities would in turn lead to both neurobiological and structural changes in the developing brain such as: alteration of the Hypothalamic Pituitary Adrenal (HPA) Axis, decreased hippocampal volume, hypertrophy of the amygdala, inflammatory responses, and impaired gene interactions.

Brain Imaging studies of Individuals with traumatic experiences

The structural changes in the different areas of the brain would differ depending on the type of abuse encountered. Sexual abuse leads to deficits in the reward circuitry and genito-sensory cortex, while sad autobiographic memory recall is caused by amygdalar hyperreactivity. While emotional abuse causes widespread abnormalities in the fronto-limbic activity, and connectivity especially networks involved in emotional processing of social contexts (3).

As the child grows, synapses that are no longer needed are pruned. However because of constant stimulation, these synapses neuronal synapses continue to grow and become permanent. This is seen in children who are victims of bullying as they are observed to have thicker cortex in the fusiform gyrus. This area is part of Brodmann 37 which has been implicated in facial and emotional processing, language, and theory of the mind. Aside from this, chronic stress leads to dysregulation of the HPA axis causing the developing brain to be exposed to high levels of glucocorticoid. Hence causing both structural and functional brain abnormalities that further increases the risk for the development of psychopathologies which persists to adulthood (2,3).

Effects of Trauma in Childhood

For the emotionally neglected child, like Marvin, there is usually a decrease in size in the anterior cingulate cortex (ACG). The ACG which surrounds the frontal part of the corpus callosum is involved in higher levels of function including attention, reward anticipation, decision making, impulse control and others. It is linked to the experience of pain and is involved more in emotional reaction rather than perception of pain itself (3).

different types of abuse resulted in a myriad of brain abnormalities affecting four (4) major components: 1) limbic irritability manifested clinically by a markedly increased prevalence of symptoms suggestive of temporal lobe epilepsy and by an increased incidence of clinically significant electroencephalogram (EEG) findings; 2) deficiency in the development and differentiation of the left hemisphere manifested throughout the cerebral cortex and hippocampus which is involved in memory retrieval; 3) deficient left to right interaction indicated by mark shifts in hemispheric activity during memory recall and by the underdevelopment of middle portions of the corpus callosum which is the primary pathway connecting the two hemispheres; and 4) abnormal activity in the cerebral vermis which appears to play a major role in emotional and attentional balance, and regulates the electrical activity within the limbic system. Thus a child who experience abuse before the age of eighteen whose brain is still rapidly developing would have greater impact on limbic irritability (15).

For the hippocampus, that is located on each side of the hemisphere; it was shown to reduce in volume in the presence of abuse. There is also a suppression of neurogenesis in the dentate gyrus and dendritic remodeling in the cornu ammonis. It can be noted that most glucocorticoid sensitive hippocampal subfields identified are the most sensitive subfields among maltreated individuals (16).

While for the cerebral cortex, there is an attenuation in the prefrontal cortex and orbitofrontal cortex wherein there is a reduced gray matter volume, blood flow, and thickness. These areas are most sensitive during the age of 14-16 years and play an important role in decision making and emotional regulation (16).

While for the amygdala, it is highly susceptible to stress due to its high density of glucocorticoid receptors on its pyramidal cells. During the postnatal development, there is a rapid growth followed by a more sustained growth to peak volumes between 9-11 years old with gradual pruning thereafter. However in trauma and chronic stress, this causes a stress induced amygdala hypertrophy which endures long after the cessation of the stressor (16).

Moreover, stress activates the HPA axis which stimulates the production and release of glucocorticoids from the adrenals.

hippocampus facilitate the activation of the HPA axis, causing a continuous release of glucocorticoids which leads to atrophy of the hippocampus. Because of this, there is a reduction of the memory resources available to help the individual formulate appropriate reactions to stress (16).

Effects of Trauma in Adolescence

After the separation of his parents, Marvin was initially under the care of his mother who was neglectful of his needs. He had no one to turn to except himself. He strove and did his best in all his endeavors.

Despite the trials he faced, he seemed to bloom when he was in high school as he was excelling in despite of constant bullying he faced. Despite being bullied by some, he had lots of friends and received honors and awards. He started to see his strengths and used it to gain friends and the attention of teachers which is also a form of affection that he didn't receive as a child.

According to studies, exposure to mild to moderate stressors early in life has been shown to enhance HPA regulation and promote lifelong resilience to stress (17). However, in Marvin's case, he was exposed to extreme and prolonged stress which induced a hyperactive HPA axis contributing to lifelong vulnerability to stress.

Marvin, on a positive note, developed resilience after childhood maltreatment. The neurobiology of resilience after childhood maltreatment is complex and there are many factors involved. Resilient functioning in individuals who have experienced childhood maltreatment may be facilitated by larger prefrontal cortex and hippocampal volume and connectivity as well as the ability to regulate emotions and dampen stress responsivity, cortisol and proinflammatory baseline responses and polygenic resilience effects. Social support from the immediate environment i.e. friends and teachers also allowed him some reassurance and affirmation of his inner strength and developed a capacity to be resilient (18).

At the neurochemistry level, the HPA axis is known to be involved in resilience. Chronic stress due to childhood maltreatment would lead to a chronically activated HPA system, which may lead to the following: adrenal fatigue via down

regulation and chronic adrenal stress hypo-reactivity. This suggests that cortisol levels and responses may be related to resilient functioning after childhood maltreatment. In addition, glucocorticoids interact with other adrenal hormones such as steroid androgen dehydroepiandrosterone (DHEA) that acts as the natural antagonist to cortisol and has a protective action against the harmful effects of hypercortisolism and aids resilient functioning, especially against depression (19).

Assuming that the hippocampus of Marvin as a child had decreased in volume, his developing brain was reshaped by the positive experiences he had in his adolescence. These positive experiences encouraged hippocampal neurogenesis. The improved connectivity in his brain was behaviorally manifested by Marvin in his capacity to learn and excel in school, to establish friendships and experience stable emotions or even happiness as a teenager. The mesolimbic reward system seemed to be doing its work on Marvin as well. It has a role in the production of resilience through self-care and seeking social support. As in the case of Marvin's seeking appreciation from his teachers and reaping awards and honors in high school.

Effects of Trauma in Adulthood

Now as an adult, it was noted that he seemed to be doing well until the pandemic when he lost his job, had no money, was faced with the threat of legal action filed against him by the telecommunication network, his admission to a hospital due to COVID and discovery of diabetes. These stressors overwhelmed him leading him to back to the day when he was a child, vulnerable, and a victim once more. These stressors did not directly cause depression but triggered the past traumas that destroyed what he has developed for himself over the years. The type of person who is strong, and someone who solves everything by doing the best logical approach was gone. Hence maladaptation ensued and depression developed.

In the neurobiological aspect, these stressors led to the dysregulation of the HPA axis which is the mediator to physiologic stress and depression. Corticosteroid signaling is impaired which resulted in the increased production and secretion of Corticotrophin releasing hormone (CRH) in various regions.

Persistent increase in glucocorticoids such as cortisol exerts neurotoxic effects on the prefrontal and hippocampus affecting its functions (20). Thus in the case of Marvin, his condition contrary to the belief of others that depression is based solely on psychological aspects but also contributed by the neurochemical changes in the brain that needs to be addressed.

COVID-19 and Depression

The main neuropsychiatric manifestations of COVID-19 have been shown to include anxiety, memory or concentration difficulties and depressive disorder, which may be a consequence of the viral infection. The COVID-19 virus attaches to the Angiotensin 2 Converting Enzyme (ACE2) and then enters the host cell. Once it releases its viral RNA, replication starts causing cell death and migration to another cell. This is mediated by recognition of the antigen-presenting cell, which in turn activates lymphocytes and the subsequent production of cytokines and chemokines (21).

The virus attacks different tissues in the body causing injury by attaching to the ACE-2 receptors. These receptors are abundant and found in the pulmonary, cardiac, and nervous system explaining the ability of the virus to reach different organs and systems. Although this doesn't totally explain the whole phenomenon, it might be an important receptor for penetration. These receptors are present on the endothelium of cerebral capillaries, neurons, and glia cells. Its presence can facilitate the access of the virus to the central nervous system, coupled with the inflammatory reaction caused by cytokines and chemokines resulting in increased permeability of the blood-brain barrier hence further entry to the cells. Thus depression may emerge because of neuroinflammation in susceptible individuals (21).

Depression & Diabetes

Depression has been shown to increase the risk for progressive insulin resistance and incident type 2 diabetes mellitus in multiple studies, whereas the association of stress with diabetes is less clear, owing to differences in study designs and in forms and ascertainment of stress. The biological systems involved in adaptation that mediate the link between stress and physiological functions include the hypothalamic-pituitary-adrenal (HPA) axis and the autonomic nervous and immune system (13).

The HPA axis is a tightly regulated system that represents one of the body's mechanisms for responding to acute and chronic stress. Depression is associated with cross-sectional and longitudinal alterations in the diurnal cortisol curve, including a blunted cortisol awakening response and flattening of the diurnal cortisol curve. Flattening of the diurnal cortisol curve is also associated with insulin resistance and type 2 diabetes mellitus (13).

So, in Marvin's case, the activation of the HPA Axis, the COVID-19 effect on serotonergic systems, and the effects of insulin resistance to HPA axis, ANS, and immune systems contributed to developing depression.

Legal Aspects

Protecting a child against abuses is vital because the experience of abuse as a child predisposes the individual to develop psychiatric disorders later in life. Just like Marvin who became vulnerable to depression. However, he is not alone as there are many others as reported by the statistics of Women and Children Protection Unit (WCPU) from Department of Health (DOH) retained and government hospitals, Local Government Units (LGUs), and other government health facilities all over the Philippines (22). In order to protect their welfare, the following are some of the laws that have been passed in our country.

Republic Act 9262 known as the Anti-Violence Against Women and their Children Act of 2004 or VAWC is a law passed for the protection of women and children from violence committed against them with the fundamental freedoms guaranteed under the constitution. Included are physical i.e. acts including bodily and physical harm, and psychological harm i.e. that causes emotional suffering (23).

Another is Republic Act 7610 known as the Special Protection of Children Against Abuse, Exploitation, and Discrimination Act; under this act, the head of a public or private hospital, medical clinic, or similar institution as well as the physician and nurse who attended to the needs of the abuse child should report cases of abuse within forty-eight (48) hours from the knowledge of the event (23,24). Section 31 of RA 7610 lists some of the institutions on where to report child abuse cases:

1. Department of Social Welfare & Development or to the Child Health and Intervention and Protective Service (CHIPS) Tel. No. 8-734-4216
2. Anti-Child Abuse, Discrimination, Exploitation Division (ACADED) National Bureau of Investigation Tel. Nos. 8- 525-6028/ 8-525-8231 loc. 403 & 444
3. Commission on Human Rights Child Rights Center Tel. No. 8- 927-4033 (Mon-Fri during office hours)
4. Philippine National Police Operation Center Tel. Nos. 8-712-8613/ 8-722-0540 & 8-724 8749 or nearest police station
5. DOJ Task Force on Child Protection, Tel. Nos. 8-523-8481 to 89 or contact the nearest Provincial, City or Regional Prosecutor
6. Local Barangay Council for the Protection of Children.

Role of Metabolomics in Major Depressive Disorder

Major depressive disorder (MDD) is a common mental disorder. However, no robust objective laboratory test is available for the diagnosis of MDD, evaluation of the severity of depression or response to treatment. Research frontiers in MDD in terms of diagnosis and improvement in treatment are along the lines of genomics, transcriptomics, proteomics, and metabolomics (25).

A metabolomics-based approach can be employed to identify products of a given biochemical system and metabolic substrates thus this approach has emerged as a method, by which to increase our understanding of diseases and biological systems in a large-scale manner. In metabolomics, enzyme kinetics, degradation, interconversion, transport, secretion, accumulation, and exogenous intake of metabolites are being measured. The technology of metabolomics offers significant potential as a tool to investigate the diagnosis of diseases and responses to medications (26).

Metabolomics has been used in MDD-related research, such as to evaluate the severity of depression, identify biomarkers of MDD, for predictive diagnosis of MDD, identify metabolic profiles post-antidepressant treatment, pinpoint biomarkers of metabolites for drug response disorder (26). In a study from drug-naïve patients with MDD indicated that their glucose levels have been higher than those of healthy controls when first diagnosed. Thus it has been

concluded by researchers that dysfunction of glucometabolic pathway may result from MDD from hypercortisolemia (27).

Accumulating evidence suggested that the HPA-axis may play a critical role in the onset of depression, and its abnormalities could contribute to metabolic syndromes in depressed individuals. A previous study have indicated disturbances in amino acid metabolism in depression including high levels of glutamate, lysin, aspartate, serine and so on. Moreover, a number of metabolic disturbances have been reported to be associated with depression such as dysfunction of tryptophan pathway, kyurenine pathway, and other pathways except the classic metabolic pathways of neurotransmitters. Nevertheless, until now findings on metabolic dysfunction are not consistent for many reasons such as pleomorphisms of this disease, and defects in methodological sources. Therefore, the existing evidence is hardly applicable to investigating the function of metabolic disorder in MMD pathogenesis (27).

Aside from mentioned above, metabolomics have also been used in assessing differences in treatment responses. Therapeutic response to selective serotonin (5-HT) reuptake inhibitors in Major Depressive Disorder (MDD) varies considerably among patients, and the onset of antidepressant therapeutic action is delayed until after 2 to 4 weeks of treatment (27).

In pharmacometabolomic studies they analyzed changes within methoxyindole and kynurenine (KYN) branches of tryptophan pathway to determine whether differential regulation within these branches may contribute to mechanism of variation in response to treatment. Metabolomics approach was also used to characterize early biochemical changes in tryptophan pathway and correlated biochemical changes with treatment outcome (27).

The tryptophan, tyrosine and purine pathways were investigated in metabolomic studies regarding depression. Within the tryptophan pathway, there were significant reductions in serotonin (5HT) and increase in indoles that were known to be influenced by human gut microbial co-metabolism. 5HT, 5-hydroxyindoleacetate (5HIAA), and the ratio of 5HIAA/5HT showed significant correlations to

temporal changes in Hamilton Depression Rating Scale (HDRS17) scores (27).

Overall, exposure to escitalopram/citalopram results in shifts in metabolism through noncanonical pathways, which suggest possible roles for the gut microbiome, oxidative stress, and inflammation-related mechanisms (27). Thus Pharmacometabolomics remains a new frontier of research that leaves much to be explored. However, the benefits from these studies are promising in all aspects in management of patients with Major Depressive Disorder (25,26).

ETHICAL CONCERNS

Informed Consent

The patient gave consent and agreed in writing that his case be presented and published for as long as it is anonymized. It was emphasized to him that his name, complete address, and other identifying details would remain confidential as it would be substituted to a pseudonym.

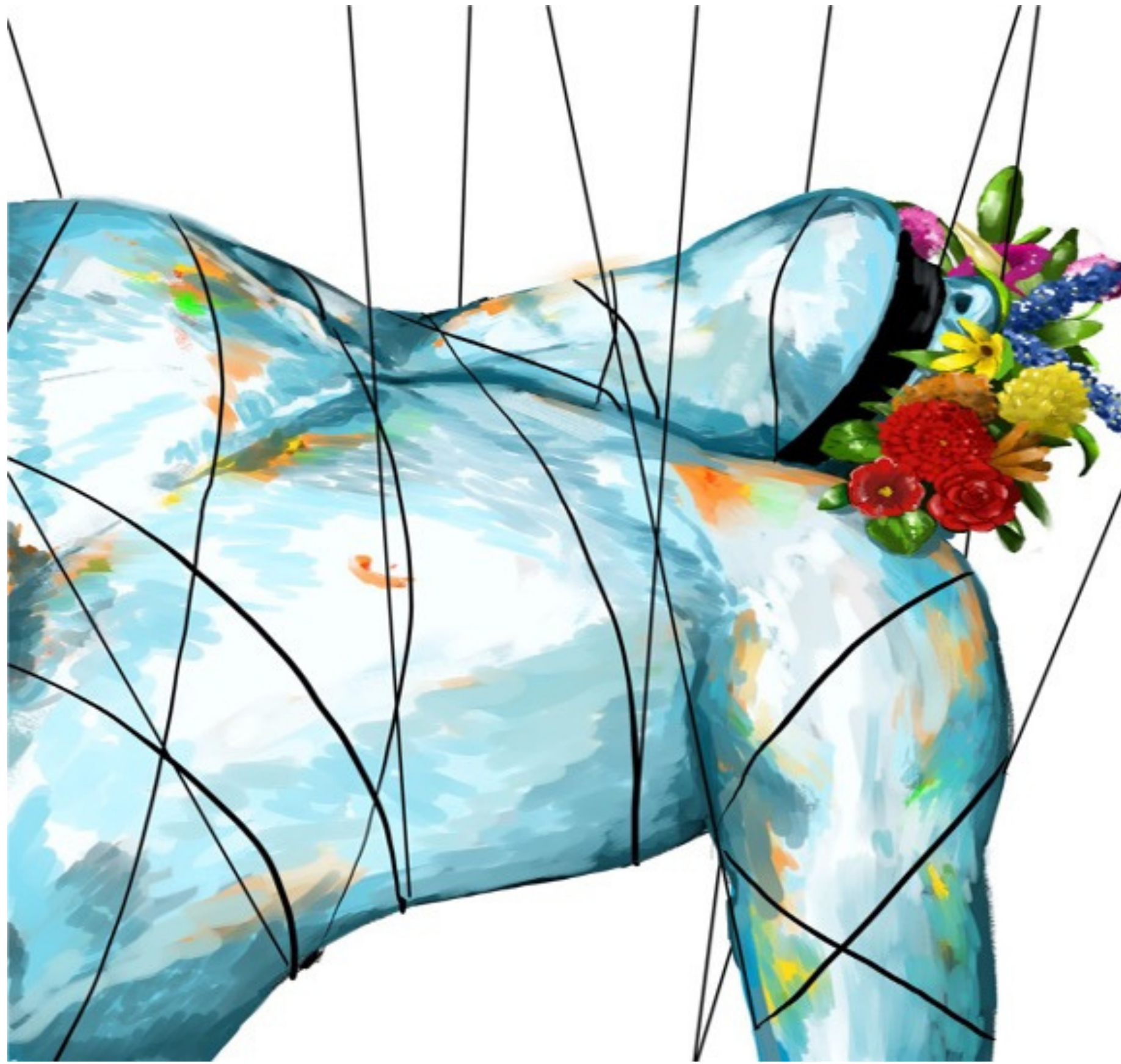
Ethics Review

The internal review board of the hospital was consulted and advised to acquire written consent from the patient prior to publication. A written consent for presentation and publication was procured prior to the publication of this case report.

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UPON THAT WHICH BINDS ME
MICHAEL ADAM AQUINO, MD

This piece symbolizes the biologic, psychologic and social vulnerabilities of our patient, Marvin i.e. how past traumas are intertwined to his struggles during the pandemic but also, the hope for patients like Marvin.

The mouth is gagged to symbolize the trauma Marvin experienced when he was forced to suppress his femininity and sexuality due to abuse by his father, rejection by his relatives and bullying by his classmates.

The strings that are interlaced around the body are representations of regret, abuse and trauma that are deeply connected and bind the patient. Each of these represents the binding trauma he suffered that is interwoven with the regrets of decisions in the past that led to painful experiences. The unresolved trauma and pain became the net of strings that binds him like a trap wherein the more he struggled, the more he felt unable to escape.

The bare torso shows that no matter how Marvin attempted to show a tough exterior, he was still vulnerable to depression, not just psychosocially but also biologically, with the factors of not just adverse childhood experiences but additionally with the covid19 infection and diabetes.

Despite these symbols, this piece does not only present dark motifs but also of hope and recovery. The strings, though intertwined, can be slowly and carefully unbound through holistic help from his medical team, his loved ones, and Marvin himself thus allowing Marvin to be free. With proper love and care, the vivid flowers grow in the same way that hope in our treated patients do, beautiful and radiant. They are placed on the eyes, to represent seeing a future wherein the patient not only survives, but blooms and thrives resiliently.