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Hypertransaminasemia in a Woman Diagnosed with Anorexia Nervosa Under Day Hospital Therapeutic Intervention

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Abstract

Introduction: Eating Disorder (ED) is one of the central chronic pathologies in adolescents, noted for its high morbidity and mortality rates. Within the spectrum of EDs, anorexia nervosa presents a high mortality rate due to medical complications or suicide. This disorder, in addition to its psychological impacts, involves physical complications such as alterations in liver enzymes and non-alcoholic fatty liver disease, often associated with malnutrition.

Materials and Methods: An 18-year-old Caucasian female with a previous history of anorexia nervosa lasting 4 years was referred in January 2021 to the Spiral Therapeutic Center (STC) for a multidisciplinary clinical approach, after being previously hospitalized in the psychiatric unit of the Marina Baixa Regional Hospital during 2020. The therapeutic approach included multidisciplinary treatments spread over two six-month periods, renewable according to the STC protocol, without using enteral or parenteral feeding during her hospital stays.

Results: During her treatment, a gradual improvement in transaminase levels and a reduction in signs of hepatic steatosis were observed. The integration of psychological and nutritional interventions during outpatient treatment allowed for a more effective and sustained recovery, compared to more intensive and less integrated approaches experienced during her previous hospitalizations.

Conclusions: The multidisciplinary management of anorexia nervosa, incorporating medical, psychological, and nutritional aspects, proves to be effective when carried out on an outpatient and continuous basis, rather than through acute or sporadic interventions. This approach not only improves biochemical parameters, such as liver transaminases, but also contributes to a better overall recovery of the patient. Personalization of nutritional and psychological treatment is crucial to effectively address the challenges associated with this disorder.

Keywords: Eating Disorders; Fatty Liver; Psychological Treatment; Paroxetine; Biopsy

Introduction

Eating disorders (EDs) are the third most common long-term pathology among young adolescents, their social and health importance is associated with high morbidity and mortality rates, and they have become highly relevant in recent decades with an estimated 5.1 deaths per 1,000 people/year in adolescents between 15 and 19 years of age [1]. Of all psychiatric disorders, anorexia nervosa has the highest mortality rate due to medical complications or suicide, the data show a standardized mortality rate for anorexia is 5-9, for bulimia 1-9 and for binge eating disorder 2-3 [2,3].

Global statistics report that eating disorders reach 2.2% in Europe, 3.5% in Asia and 4.6% in America, evidencing the complex synergy between biological, sociocultural and environmental factors. In Spain, the incidence ranges between 4.1% and 6.4% in women aged 12 to 21, while in men it remains close to 0.3% [4], the Association Against Anorexia and Bulimia (ACAB) in 2020 reported receiving three times as many requests for help during confinement in families affected by the disorder as a result of the negative impacts of the pandemic. They are also the third most common chronic pathology among adolescent patients [3,4].

Anxiety disorders are one of the most common psychiatric pathologies among children and adolescents, with an estimated prevalence of 6 to 20% in developed countries. This high incidence places them among the most common mental disorders in these regions. According to data provided by the American Anxiety and Depression Society (ADAA), only one-third of individuals affected by anxiety or depression access appropriate support and treatment services [5].

Anorexia nervosa (AN) is characterized by extreme restriction of food intake associated with distortion of self-image and personal dissatisfaction [6], research suggests that 45-60% of cases could be of genetic cause during the evolution of the disorder; there may be physical, metabolic, behavioral, cognitive and emotional dysfunctions, highlighting the need for comprehensive and specific therapeutic approaches for this population [7-9].

In the context of anorexia nervosa (AN), it is common to observe a slight to moderate increase in liver enzymes, a phenomenon fre-

quently associated with states of protein-energy malnutrition [10]. In addition, non-alcoholic hepatic steatosis arises as a consequence of an imbalance between the production and release of triacylglycerol in the liver, together with a decrease in lipoprotein synthesis due to the scarcity of available amino acids. Hepatic dysfunctions are common in patients with AN, with increases in serum liver enzyme levels during hospital stays. However, it is less common to observe these feedback processes in outpatient treatments that effectively integrate therapeutic practices into patients' daily routines, within the framework of daytime hospitalization. Hepatic steatosis is frequently observed in obese women with long-term hyperglycemia and hyperlipidemia stages [11,12].

In clinical practice, the treatment of AN focuses on a central psychotherapeutic intervention, with a comprehensive approach addressed by medical-psychiatric, nutritional, and psychological. The most severe cases require complete or partial hospitalization modalities, where a multidisciplinary approach is implemented [13]. Although these cases represent only approximately 10% of the total diagnoses destined for psychological treatment. The cognitive-behavioral therapeutic approach has been shown to be effective in the treatment of adults diagnosed with anorexia nervosa (AN), whose objective is to normalize eating habits and associated behaviors, thus facilitating weight gain and addressing the distorted beliefs and thoughts that perpetuate restrictive eating practices and body image problems [14,15]. The deficit in health care shows a significant gap in the provision of care, highlighting the need for improved strategies for the early detection and effective management of these disorders [16].

The present paper examines advanced therapeutic management strategies for the treatment of liver complications in patients with anorexia nervosa. A detailed analysis of medical-care and multidisciplinary approaches is carried out, with the aim of guiding clinical decision-making effectively and without generating disproportionate costs. This study contributes to the development of more efficient and economically viable clinical practices, optimizing resources and improving health outcomes in this group of patients.

Materials and Methods

Localization

The study was carried out at the Espiral Therapeutic Center (CT) during the months of May to August 2021. The clinical analy-

ses were requested from the CTE nutrition unit, carried out in the internal laboratory of the Villa Joiosa Hospital belonging to the Marina Baixa.

Participant

This study was approved for dissemination at the institutional level, and the patient's written approval was requested, respecting the established ethical and regulatory standards.

Anthropometric measurements

Anthropometric measurements of weight, height and blood pressure were obtained.

Weight

The OMRON bioelectrical impedance equipment model HBF-514C was used, it was requested to place the heel and instep on the electrodes in position for the reading of data. With the data obtained, the calculation of the Body Mass Index (BMI) was performed using equation 1.

$$\frac{\text{Current weight (kg)}}{\text{Size (cm)}^2}$$

The BMI values of the population were classified in their respective categories, according to the "National Hear, Lung and Blood Institute" [17].

Blood pressure

Blood pressure was measured with an OMRON M3 digital blood pressure monitor; class 1 accuracy. The results provided by the bracelet were categorized according to the "American Heart Association" [18].

Biochemical measurements.

Biochemical measurements included: Hematimetry, general biochemistry, specific biochemistry and urgent biochemistry. The data were obtained in the internal laboratory of the Villa Joiosa Hospital belonging to the Marina Baixa. on an empty stomach, without having smoked previously for 8 hours. 3 mL blood samples per venipuncture were stored in anticoagulant tubes labeled with each participant's code and centrifuged with a Z-29 digital microcentrifuge kit at a rate of 2500-3000 rpm for (5-10 m) to separate the serum from the clot and incubate at a temperature of 65-85°F ± 5°F (17-30°C ± 2.8°C) per h.

Results and Discussion

Presentation of the clinical case

An 18-year-old Caucasian patient with a history of anorexia nervosa of 4 years was referred to the Espiral Therapeutic Center (CTE), for medical-multidisciplinary approach, in January 2021, with previous hospitalization processes in the psychiatric unit of the regional acute hospital of the Marina Baixa during 2020, in none of the hospitalization processes was enteral feeding by nasogastric or parenteral tube used. The therapeutic approach is comprised of the multidisciplinary treatment of two periods of six months renewable as part of the CTE action protocol, in which the areas of psychology, psychiatry, occupational therapy and nutrition are addressed.

On admission, protocol blood tests were requested, and they were within the inclusion values, however, a few months later the patient reported pain, indigestion and gastric spasms, blood tests were requested again and referral to her family doctor for evaluation was managed.

Medical-nutritional approach

As nutritional therapeutic measures, the nutritional objective was to stabilize BMI 19.5, taking into account the severity of the case, a personalized diet plan of closed structure, hypercaloric and hyperproteinic, without oral nutritional supplementation despite its low BMI, was managed in the phase. The patient's anthropometric data at the beginning of their treatment are presented as shown in table 1.

ANTHROPOMETRY	INITIAL PHASE May-2021	FINAL ROUND July-2021
Size (cm)	163	163
Weight (kg)	39	46,3
BMI (kg/m2)	14,8	18,08
Blood Pressure (mmHg)	94/76	103/72

Table 1: Anthropometric values at baseline and three months post-medical-nutritional intervention.

Source: Own elaboration.

Complementary medical studies were requested, such as: electrocardiogram and blood tests provided by the Marina Baixa Hospital as part of the therapeutic approach process. At the time of

taking the blood sample, the patient was emotionally stable and cooperative with a previous 8-hour fast, without pharmacological consumption. The blood biochemistry values are presented below in table 2.

	INITIAL PHASE May- 2021	FINAL ROUND July-2021	Reference values
HEMATIMETRY			
Red blood cells (million/ μ L)	4.98	4.8	(4.2-5.4)
Hemoglobina (g/dL)	16.5	13.4	12-16
Hematocrito (%)	49.8	39.6	37-47
Mean Corpuscular Volume (fL)	100.1	97.1	80-99
Hemoglobina Corpuscular Media (pg)	33.1	32.8	27-33
Mean Corpuscular Hemoglobin Concentration (g/dL)	33.1	33.8	33-37
Erythrocyte Distribution Width (%)	12.6	11.2	11.5-14.5
Platelets (thousands/uL)	195	255	130-400
Mean Platelet Volume (fL)	8.7	10.6	7.2-11.1
Leucocitos (miles/uL)	4.03	5.2	4.1-10.9
Other Types of Neutrophils (%)	47.6	37.7	40-74
Lymphocytes (%)	37.5	39.6	20-48.5
Monocytes (%)	8.3	9.2	3.4-9
Eosinophils (%)	4	12.9	0-7
Basophils (%)	0.6	0.6	0-1.5
GENERAL BIOCHEMISTRY			
Glucosa (mg/dL)	68	81	70-110
Urea (mg/dL)	45	34	10-54
Sodio (mEq/L)	0.9	0.9	0.7-1.2
Potasio (mEq/L)	4.2	4.6	137-145
Proteínas (g/dL)	7.6	7.2	6.6-8.7
Albumina (g/dL)	4.8	4.3	3.5-5.2
Colesterol (mg/dL)	167	157	50-200
Colesterol HDL (mg/dL)	56	48	45-65
Colesterol LDL (mg/dL)	99	93	80-130
Triglicéridos (mg/dL)	62	79	50-200
GOT (AST) (U/L)	257	48	5-37
GPT (ALT) (U/L)	578	100	5-40
LD: Lactatodeshidrogenasa	357	248	135-225
GGT	94	40	5-36
Creatin Kinasa	104	99	20-180
Estimated glomerular filtration rate (CKD-EPI)	>90	>90	>90 (normal)
SPECIAL BIOCHEMISTRY			
TSH (μ UI/mL)	1.59	1.3	0.58-1.64
Vitamina B12 (pg/mL)	658	446	116.6-513.2
25-hidroxi-vitamina D (ng/mL)	44.9	13.9	30-100(sufficient)
Hemoglobin glycosilade (%)	5	5	4-6.5
Urgent Biochemistry			
HBsAG	negative		
Anti-HCV	negative		

Table 2: Biochemical values at baseline and three months after medical-nutritional intervention.

Medical-psychological approach

The American Psychiatric Association (APA), in its guide for the treatment of eating disorders, mentions the cognitive-behavioral technique focused on the disorder as the main therapeutic approach [16]. The patient's Individualized Treatment Plan (ITP) included the following objectives: to reinforce adherence to treatment and the development of a good therapeutic alliance and identification of the processes favoring the development and maintenance of the disorder. These processes include cognitive, emotional, and behavioral factors. Among the contributing and maintaining factors of eating disorders are perfectionism and self-demand [19], an intense desire to achieve unattainably high standards can lead to extreme behaviors of control over eating and weight, along with high levels of self-demand and self-criticism that perpetuate the cycle of maladaptive eating behavior. In addition, low self-esteem and a negative self-concept, characterized by persistent feelings of inadequacy and negative self-worth, can cause individuals to attempt to improve their self-esteem through weight management [20].

Research mentions a pattern in patients associated with the pursuit of perfectionism, contributing as a significant risk factor for the development and maintenance of the eating disorder. This psychological characteristic, marked by the constant search for unattainable standards and critical self-evaluation, can exacerbate vulnerability to harmful eating behaviors such as prolonged fasting or compensatory practices [19]. Perfectionism does not operate in isolation; It interacts with other risk factors such as low self-esteem, sociocultural pressures, and traumatic experiences, creating an environment conducive to the onset or perpetuation of eating disorders [20]. The complexity of perfectionism lies in its ability to intensify these interrelated factors, establishing a cycle that is difficult to break without adequate intervention [21]. This condition manifests itself in a constant and unattainable search for excellence, which can lead to considerable emotional exhaustion [20], low central self-esteem implies a negative and persistent perception of personal value, affecting multiple areas of the individual's life [22]. Mood intolerance reflects the inability to properly manage negative or changing emotions, generating a vicious cycle of psychological distress. In addition to interpersonal difficulties, they can complicate social and professional relationships, increasing isolation and perpetuating emotional problems [23,24]. Together, these factors create a complex environment that requires

comprehensive therapeutic interventions to promote an improvement in the quality of life of the affected individual as a result of inadequate emotional management. Addressing perfectionism is critical to effective and sustainable treatment in patients with eating disorders [20,25]. Several studies have examined two main features of AN, reduced food intake and hyperactivity. Dietary restriction has been associated with reduced dopamine levels in the hypothalamus, hippocampus, and dorsal striatum. Animal hyperactivity following dietary restriction has been linked to an increase in dopamine in the hypothalamus. Dietary restriction (DR) affects the adrenergic, serotonergic, cholinergic, and endocannabinoid systems in mice.

Medical-psychiatric approach

Alterations in serotonin function have been consistently implicated in eating disorders. Previous studies have shown that these alterations not only affect eating behavior, but could also be linked to variations in certain pathological personality traits [26,27]. Abnormal serotonin levels may be related to excessive perfectionism or impulsivity, both of which are common among those with these disorders [28].

Several studies in anorexia nervosa (AN) observed alterations in the functioning of serotonin (5-hydroxytryptamine, 5-HT) compared to healthy controls, patients with AN show reductions in concentrations of 5-hydroxyindoleacetic acid (5-HIAA) in the cerebrospinal fluid indicate that alterations of 5-HT in AN may be related to multiple factors: sequelae of AN, neurobiological causes of AN and variations in personality traits [29]. They found that reductions in monoamine oxidase (MAO) activity were associated with increased impulsivity and decreased persistence in currently symptomatic women with restrictive AN, [26] found that reductions in cortical 5-HT_{2A} binding (a selective ligand 5HT_{2A}) were associated with increased novelty-seeking and decreased thinness desire and avoidance of harm in women recovered from AN of binge eating and purging [30,31].

Olanzapine is an antipsychotic drug widely recognized for its effectiveness in the treatment of mood disorders. Its use is limited due to a number of significant side effects, including weight gain, dyslipidemia, and liver injury. These adverse effects are of concern in the context of obesity, which is considered a risk factor for drug-induced liver injury [32].

Several studies have demonstrated the effective use of Onlazapine and its association with weight gain, suggesting an average weight gain in relation to placebo of 0.67 kg/m², being effective in outpatient treatments of eight weeks [33] it is a priority to implement effective strategies to maximize the therapeutic benefits of olanzapine and minimize its associated risks. Others suggest that its use may have a direct association with the increase in plasma triglycerides (TG), the β -oxidation of fatty acids at the mitochondrial level contributes to the constant balance of hepatic TGs and L-carnitine (L-Carnitine) transfers long-chain fatty acids to the mitochondria for their β -oxidation [34,35].

The psychiatric symptoms and causes of anorexia are multiple and complex, reflecting an intricate interplay between biological, psychological, and social factors. From a biological point of view, various abnormalities in neurotransmitters and hormones have been identified that can predispose a person to develop this disease [36,37]. In addition to personal characteristics such as extreme perfectionism, low self-esteem and anxiety disorders play a significant role in the genesis of anorexia. Social factors should not be underestimated; Cultural pressure to achieve unrealistic aesthetic ideals can exacerbate these underlying problems [26,27]. A comprehensive understanding of these factors is crucial to the development of effective treatments that address all dimensions of the disorder. Ultimately, a multidisciplinary approach that considers these different areas is essential to offer adequate support and promote the patient's complete recovery [25]. The distortion of body image in AN presents a continuous debate about its origin, whether it is a cognitive-emotional problem or if there are neural factors that interfere with the integration or perception of the body.

A significant hereditary component has a significant hereditary component, a first-degree family history with eating disorders increases the probability of developing AN, as well as genetic polymorphisms in serotonin secretion, which are also known for their influence on satiety and emotional well-being, while dopamine is related to reward and pleasure [38]. These genetic alterations could explain why some people are more susceptible to developing anorexia in the face of similar environmental triggers, obsessive-compulsive behaviors reflect a constant attempt to achieve rigid control over various aspects of their lives. [39-41].

Paroxetine is a selective serotonin reuptake inhibitor (SSRI), phenylpiperidine derivative works by inhibiting the reuptake of (5-hydroxytryptamine, 5-HT) used to treat various psychiatric conditions, effective in the management of disorders such as major depression, anxiety disorders, obsessive-compulsive disorder (OCD), post-traumatic stress disorder (PTSD), eating disorders (ED), among others. Regarding endocrine effects, elevations in serum cortisol and prolactin levels have been observed in rats, although there is no evidence of the prolactin effect in humans under four-week treatment [42,43].

Liver biopsy can be used to confirm the diagnosis, stage and grade the disease, predict already diagnosed liver disease, and develop a management plan. The results obtained from the liver biopsy show in the hepatic casts, a mild hepatitis of chronic periportal and lobular predominance with eosinophils compatible with drug-induced hepatitis.

- **Macro:** 4 cylindrical tissue fragments between 0.7 and 0.3 cm. SIT2.
- **Micro:** A cylinder of hepatic parenchyma in which inflammation and significant centrilobular necrosis are observed, some clearly delineated with the presence of occasional eosinophils and histiocyte aggregates that, in turn, are arranged in isolation forming an image that seems to suggest a granuloma. At the level of portal spaces, a moderate lymphocyte and polymorphonuclear inflammatory infiltrate is observed.

Sinusoidal vascular dilation and congestion and occasionally enlarged hepatocytes with a granular pale cytoplasm, with variable, pygnotic, and some binucleate nuclei are observed.

This procedure, while good practice and can provide valuable information, is not necessarily essential in the context of complications arising from eating disorders, such as anorexia nervosa (AN). It should be noted that between 40 and 60% of AN cases present liver dysfunction due to caloric-protein autolysis. Therefore, it is crucial to consider that, although the performance of this procedure implies an expense for the health system, its need must be carefully evaluated so as not to incur insufficient or misallocated resources, especially when the complication arises from an eating disorder.

Discussion

Several studies have examined two main features of AN, reduced food intake and hyperactivity. Dietary restriction has been associated with reduced dopamine levels in the hypothalamus, hippocampus, and dorsal striatum. Animal hyperactivity following dietary restriction has been linked to an increase in dopamine in the hypothalamus. Dietary restriction (DR) affects the adrenergic, serotonergic, cholinergic, and endocannabinoid systems in mice.

At baseline, plasma values of total protein (7.6 mg/dL) and albumin (4.8 mg/dL) were within normal ranges, despite his initial BMI of 14.8. This can be explained by the fact that the body tries to maintain body fluids as an adaptive effect of energy deficit, thus avoiding edema caused by protein deficiency, characterized by an evident loss of muscle mass [44]. At the end of the intervention, protein values were 7.2 mg/dL and albumin at 4.3 mg/dL, with a BMI of 18.8, close to normal. This shows that the hypercaloric diet provided, with a meal plan of 2500 kcal slightly hyperprotein at 18%, has been effective in nutritional intervention [45].

AN is a common eating disorder among young women, characterized by body image distortion and excessive preoccupation with thinness, under conditions of stress or food restriction, 80% of body lipids are capable of autophagy as a survival strategy. This mechanism is responsible for providing nutrients and energy to cells in times of need. In AN, this mechanism can be supportive and protective [46-48].

This process involves multiple sequential adaptations in the cytoplasm, especially in lysosomes. Severe malnutrition results in a significant increase in liver enzymes, a considerable reduction in glycogen, and signs of autophagy on histology. Between 40 and 60% of patients with anorexia nervosa (AN) may experience mild degrees of liver damage. In the case at hand, alanine aminotransferase (ALT) values of 578 U/L and aspartate aminotransferase (AST) of 257 U/L were recorded, both higher than normal values, which is directly associated with the patient's body mass index. Kwashiorkor protein-calorie malnutrition could cause liver damage in cases of AN, although scientific evidence in this regard is still insufficient [48,49]. AN can lead to liver dysfunction, primarily due to autophagy and increased oxidative stress in hepatocytes, suggesting that severe starvation plays a crucial role in liver injury associated with anorexia nervosa [50].

Hemoglobin (Hb) values in the initial phase were 16.5 (mg/dL) and after the nutritional intervention 14.4 (mg/dL), research has reported that the wide distribution of red blood cells (RDW) as markers is a marker of risk for metabolic syndrome and non-alcoholic fatty liver disease (NAFLD). consequence of muscle self-consumption [51,52].

The imaging modality can detect the presence of hepatic steatosis, histological evaluation is suggested, to date this procedure remains an accurate diagnostic tool that includes the severity of hepatic inflammation and fibrosis [52].

Liver biopsy can be used to confirm the diagnosis, stage and grade the disease, predict already diagnosed liver disease, and develop a management plan. The results obtained from the liver biopsy show in the hepatic casts, a mild hepatitis of chronic periportal and lobular predominance with eosinophils compatible with drug-induced hepatitis.

- Macro: 4 cylindrical tissue fragments between 0.7 and 0.3 cm. SIT2.
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This procedure, while good practice and can provide valuable information, is not necessarily essential in the context of complications arising from eating disorders, such as anorexia nervosa (AN). It should be noted that between 40 and 60% of AN cases present liver dysfunction due to caloric-protein autolysis. Therefore, it is crucial to consider that, although the performance of this procedure implies an expense for the health system, its need must be carefully evaluated so as not to incur insufficient or misallocated resources, especially when the complication arises from an eating disorder.

Antidepressant medications including paroxetine have been shown to be safe, with a rare incidence of serious side effects or mortality due to overdose. Research suggests that paroxetine is one of the most commonly prescribed medications to treat depression in children, however, its discontinuation is associated with gastric effects such as nausea and vomiting as severe side effects (orthostatic hypotension) or hypomania [53].

Conclusion

The pathological findings were not consistent with the expected pharmacological side effects, suggesting that the process observed in the patient is attributable to muscle autophagy, a result of caloric-protein anorexia, and does not correspond to the initial diagnosis of drug-secondary hepatitis, as indicated in the pathological report. Interdisciplinary collaboration and effective connection between health professionals are essential and decisive in decision-making on the implementation of invasive procedures in this type of patient. Effective and cost-effective management of the public health service could be achieved through active integration and collaboration with the nutrition professional involved in treatment. Demonstrating that therapeutic management strategies are the most appropriate for liver disorders in cases of anorexia nervosa, from a medical-care and multidisciplinary perspective. The proposed approach facilitates informed decision-making, avoiding incurring excessive or unnecessary expenses for health systems.

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Conflict of Interest

I declare that there is no financial interest or conflict of interest.

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