Comorbid pulmonary aspergillosis as a justifier for weight loss in anorexia nervosa

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Dear Editor,

Anorexia nervosa

Anorexia nervosa (AN) is a psychiatric disease with a high standardized mortality rate, ranging from 5.9 to 6.2, which means that a person with AN has a six times greater risk of dying than the general population. Annual mortality is reported in 5.1 per 1000 person-year[1]. Women with AN, between the ages of 15-24 years of age have a mortality 12 times higher than the rest of the women with the same characteristics[2], finally, AN has the highest mortality rate (3-40%), among psychiatric diseases. Being its main causes of death, suicide (one in five deaths) and electrolyte imbalances, because of the latter cause lethal cardiac changes, leading to death in most cases[3,4].

The criteria to make the diagnosis of anorexia nervosa, more current are those of the DSM5[5]. Among the less frequent complications of this condition, are resistant hypoglycemia, tuberculosis, and the rarer entities, Aspergillus infection.

Aspergillus

Aspergillus is a ubiquitous fungus, with several species, is considered the Aspergillus fumigatus-complex the most frequent agent, this fungus in immunocompromised patients can produce a wide spectrum of clinical presentations, ranging from aspergilloma in lung caverns, to chronic necrosis by Aspergillus[5].

The diseases most frequently associated with pulmonary aspergillosis are tuberculosis, neoplasms, ankylosing spondylitis, sarcoidosis, bronchiectasis, cystic fibrosis, and invasive aspergillosis. Tuberculosis is the most frequent cause of pulmonary cavities, later an aspergilloma develops in the caverns, a phenomenon classically described in the literature[6].

His most frequent symptom is hemoptysis, other less frequent symptoms are precordial pain, dyspnea, and general malaise. The diagnosis is made by first assessing the risk of colonization and contamination, microbiological documentation, galactomannan, and complementary imaging tests. The treatment of choice is with antifungals such as amphotericin B, voriconazole, itraconazole, posaconazole, and echinocandins. In current treatment guidelines, there is controversy over the response to antifungals of certain Aspergillus species due to the difficulty these antibiotics have in entering the cavities, which is why surgical intervention is the first option[7].

Anorexia nervosa plus Aspergilloma

So far in the international literature, four cases of anorexia nervosa plus aspergilloma have been reported.

Three of these reports, of anorexia nervosa associated with pulmonary aspergilloma, were successful, after a thoracotomy, reaching recovery in the postoperative period, it is worth mentioning that in none of these the evolution of the psychiatric condition was followed.

In the fourth case report, the result was fatal for the patient due to the presence of resistant hypoglycemia in addition to pulmonary aspergilloma[8-13].

Case report

Female 23-year-old psychology student, single, lives with her parents. In 2014, he was diagnosed with Acquired Pneumonia in the Community, treating it in a conventional way, leaving as a sequel, Pulmonary fibrosis and supplemental oxygen dependence 2 to 3 Lt/min. A probable case of pulmonary tuberculosis is diagnosed and strictly supervised treatment is initiated.

In 2017, secondary to a cough with expectoration and hemoptysis, new studies were performed, obtaining a diagnosis of pulmonary aspergilloma, from chest tomography with evidence of left subsegmental pulmonary atelectasis, multiple apical predominance cavitations, bronchoscopy with bronchial lavage -alveolar, reports positive galactomannan and the culture is positive for Aspergillus Fumigatus. Beginning treatment with Voriconazole with partial response, in its other laboratory and cabinet studies, it presents a hormonal profile compatible with hypogonadism hypogonadotrophic, hypochromic microcytic anemia, and osteopenia. In this hospitalization, the entire study protocol for weight loss and immunosuppression was performed, looking for differential diagnoses, such as sarcoidosis, HIV, primary immunodeficiency, all being negative, being graduated with antibiotic scheme and weight restitution plan.

A year later, she was admitted again for hemoptysis and with a BMI at the beginning of her hospitalization of 13, this time consultative psychiatry was made to the psychiatry service, which performed the diagnosis of Anorexia nervosa, because it presents: chronic food restriction (documented from childhood), which has led to a significant loss of weight; being under the lower weight percentile, for his age, besides evidencing alterations in behavior, standing out, bad attachment in the management schemes for weight gain, the family corroborates a story since childhood, with a great refusal to food intake , eating only small portions, referring to sensation of fullness, heaviness and drowsiness, if fed more, all these factors that justified their difficulty in reaching weight.

In the mental examination highlights a coherent language, congruent, denies fear of gaining weight, is accepted thin and on the contrary, refers to the desire to gain kilos, initially, as it continues to interview the patient, we emphasize, an absence of concern, about his health, he wants to be discharged to return to school, mild affective symptoms are detected, of approximately four years of evolution that have not received treatment. The patient also uses a counter-discourse, based on denying the eating disorder systematically, minimizing its symptoms and with no capacity for introspection. The self-criticism he makes about his patterns of eating behavior is totally inappropriate, trying to give a front of tranquility and "normality" about his physique and his weight.

The evolution of the patient has been torpid, not to be possible to perform surgery for the cavities and aspergilloma, the Pneumology Service indicates that the patient is not a candidate because of the serious risk of surgical complications that she has at this moment.

The pharmacological treatment is based on nutritional nutrition rehabilitation, antibiotics, olanzapine 5 mg, with an increase up to 12.5 mg per day (art 2018), zinc 25 mg daily, phosphorus substitution 2.5 mg per day and required a transfusion by Hemoglobin of 8.5 mg.

Diagnostic challenges

for adult hospitalized patients, weight loss is not an unusual event and represents between 33-60% of patients in hospitalization services, considering it a challenge for the clinician[12,13]. This loss of weight is clinically important when it supposes a reduction> 5% with respect to the habitual one in a period of 6 months, although the majority of authors consider up to 1 year[14].

Its importance is that it is associated with an increase in morbidity and mortality, although this varies according to the follow-up period[15-17]. It is considered in a classic way, three main causes: Organic (malignant and non-malignant neoplasms), psychiatric and idiopathic.

In many cases the etiology is multifactorial. The variability of recent articles shows a wide range: organic (cancer 6-38%, non-tumoral gastrointestinal 6-37%), psychiatric 9-42% and idiopathic 11-36%. In people older than 65 years, the most frequent cause is psychiatric pathology and specifically, depression[18-20]. In a more recent study they show an increase in the oncological causes, Parkinson's and dementia, in people under 65 years, highlights tuberculosis, HIV, and depressive, anxious and obsessive-compulsive disorders[21].

In our experience, other psychiatric causes of malnutrition are somatic disorders, dementia, factitious disorders, and simulation. In the diagnostic algorithms of weight loss under study, the psychiatric illness must always be included, as a high diagnostic suspicion.

Discussion

Aspergillus is an opportunistic fungus that when infecting human beings, is capable of producing syndromes that cover a wide clinical spectrum from allergic bronchopulmonary aspergillosis to more serious entities such as pulmonary aspergilloma or fulminating aspergillosis, mainly attacking patients with chronic diseases. and immunosuppressed, as in this case, a patient with a severe eating disorder of long evolution, the damage was extensive covering the entire left lung and most of the right lung, only retaining the upper part of the right lobe, which complicates both its prognosis and its therapeutic surgical approach, considered the treatment of choice[23].

Our patient presented chronologically: malnutrition, pneumonia, tuberculosis and later aspergilloma. Infectious disorders (tuberculosis and aspergilloma) were the "justifiers" of the chronic weight loss associated with the eating disorder. It is currently observed that patients with eating disorders are informed on web pages (pro-ana, pro-mia), about how to confuse the doctor, so that they are not diagnosed, denying the disease, minimizing their symptoms, even expressing the desire to gain weight[24].

On the other hand, the medical services that attended her, directed their diagnostic and treatment efforts, in both infectious entities and they did not pay attention to the basic nutritional disorder, being AN a solid base in which the infection was generated by opportunistic agents. In the current medical literature, the wide stigmatization that eating disorders entail is known, in addition to the misconceptions that have been maintained for decades in health personnel, family members, patients and people in general, producing

a significant delay in the diagnosis of these disorders and complicating their treatment[25].

Conclusions

When studying weight loss, clinicians are mainly focused on differential diagnoses (malnutrition, immunological, oncological and infectious), without considering psychiatric illness.

In this specific case, the patient diverted the doctors' attention to the infectious diseases she suffered, feeling comfortable in attributing her emancipated state (BMI: 13) to the chronic malnutrition caused by her infectious diseases.

The treatment for patients with severe Anorexia nervosa is multimodal, according to the particular needs of each patient in terms of medical, nutritional and psychological-psychiatric management[26]. Based mainly on rapid nutritional rehabilitation[26,27], as well as the use of psychotropic drugs such as the second generation antipsychotic Olanzapine, for its potential decrease in obsessions and ruminations around food, weight gain due to its antihistaminic effect, control of anxiety and sleep problems[28,29].

The ideal treatment based on the literature´s review of this case consists of

- Olanzapine increased a gradual dose of 2.5 mg until reaching a dose of 10 mg per day.
- Zinc 25 mg per day (30) and replacement of phosphorus if less than 2.5 mg.
- Domperidone 10 mg per day.
- The psychotherapeutic approach based on the Maudsley model or cognitive restructuring therapy[31].
- Fractional diet and in fifths.
- Absolute rest.

In addition to daily monitoring of BMI and Electrolyte, together with weekly electrocardiographic monitoring.

The therapeutic difficulties presented by this patient are listed below:

- Pending thoracic surgery for lack of weight necessary to ensure adequate intervention.
- Voriconazole antibiotic scheme, with limited response.
- No parenteral nutrition due to a risk of over-aggregated infection.

The treatment offered in our institution was: fractionated and supervised diet, antibiotic scheme according to clinical practice guidelines, Zinc restitution 25 mg per day, Metoclopramide 10 mg per day, absolute rest and by the psychiatric service, of psychopharmacological treatment: Olanzapine 10 mg per day. Along with a broad psychoeducation to family and patient, in terms of maintenance of treatment and quality of life focused on health[32].

Currently, the patient continues to follows her treatment with internal medicine and our service, with gradual weight gain and aspergilloma control through immunotherapy and antibiotics.

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Energy drinks and mental health, reasons to be alarmed?

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Dear Editor,

Energy drinks (ED) are those beverages marketed with stimulant purpose and that usually contain caffeine. They differ from other caffeinated drinks because of ED also include ingredients such as taurine, glucuronolactone, guarana, ginseng or ginkgo biloba, among others. However, caffeine is considered the main stimulant substance of the ED and its interaction with the other ingredients remain unknown[1]. Since its creation in Austria in 1987, through the brand Red Bull™, the variety and consumption of ED has exponentially increased[2]. In 2014, the World Health Organization warned about the increasing use of ED, reflecting worrying data from a study conducted by the European Food Safety Authority (EFSA): 68% of adolescents between the ages of 10-18 years old, 30% of adults and 18% of children under 10 years old consumed these drinks[3,4]. Concomitantly, there has been growing concern about the potential health consequences of ED consumption and the need for more severe marketing regulation, especially on children and adolescents because they are a vulnerable subgroup of the population with a higher prevalence of ED consumption[5]. In fact, in England has been forbidden the sale of ED to minors and in Spain has been presented a non-law proposal addressing this issue in the Congress of Deputies recently[6,7].

The EFSA consider safe caffeine intakes up to 400 mg per day for healthy adults and 200 mg per day for pregnant and lactating women. For children and adolescents, available information is insufficient, considering as basis the adults recommendations[8]. Nevertheless, it is easy to exceed these recommendations if some ED cans are consumed because many of them have between 200-400 mg caffeine per can, even existing some marketed ED that have more than 500 mg caffeine per can[5]. Some institutions have notified the possible health effects. The U.S. Poison Control Center (2000–2012 period) reported 552 adverse events related to ED consumption[9] and the FDA's Center for Food Safety and Applied Nutrition (2004–2012 period) notified 166 adverse events, including 18 deaths[10].

Cardiovascular adverse effects of ED are the most reported consequences, showing that it consumption can cause increase in QTc interval, supraventricular arrhythmias or sudden death, among others. In addition to this, it has been reported possible neurologic effects (epileptic seizures, reversible cerebral vasoconstriction and intracerebral hemorrhages), gastrointestinal effects (gastrointestinal upset, elevated transaminases), renal effects (acute renal failure, rhabdomyolysis and metabolic acidosis) and endocrine-metabolic effects (obesity, hyperinsulinemia)[3,11–13].

In mental health there are evidence, mainly through case reports, about the possible harmful consequences of ED consumption. The causal effect of ED consumption has been reflected in psychotic relapses of schizophrenia patients[14–17] and, even, its influence on *de novo* psychotic disorders[18]. Likewise, there are scientific articles in which ED consumption is related to anxious disorders, affective decompensation in patients with bipolar disorder and suicidal behavior in people with no previous psychiatric history[19–26]. The underlying mechanism that could be involved in psychopathological effects observed is the antagonism exerted by caffeine on adenosine receptors, mechanism that can potentiate the effects of dopamine on D_2 receptors[27].

Additionally, there is concern about the possible association of ED use with the consumption of other substances. The Spanish Observatory on Drugs and Drug Addiction (2016) showed that 40.4% of young Spanish aged 14-18 had consumed ED during the last month and that 14.3% had consumed them mixed with alcohol. It also warned of a higher consumption of ED among those young people who consumed illegal substances such as cannabis and cocaine (prevalence of consumption of 63% and 65%, respectively)[28]. Likewise, a prospective observational study conducted with 1099 students, who were followed up from 21 to 25 years, showed that those who maintained an intermediate and persistent ED consumption had significantly increased risk of cocaine, stimulants and alcohol consumption[29]. In addition, there is more and more data about the risk and negative consequences of combined ED consumption with other substances, such as alcohol[30,31].

Nowadays, there is evidence about the potential adverse effect of ED consumption as well as data that reflect that visits to emergency services related to these drinks have been doubled in recent years. In contrast to this, it is claimed that in 42% of emergency visits there was a concomitant consumption of other substances, that more robust longitudinal studies are lacking and that the level of toxicity is low considering the billions of consumed cans annually[32].

Despite the debate, it is advisable to make some recommendations on this issue. It would be recommendable to incorporate data on the pattern of ED consumption (along with other sources of caffeine) in the anamnesis of patients, inform about the convenience of their responsible use and the possible consequences of their abusive intake, and warn of their counterproductive combination with other substances. Furthermore, it would be advisable to pay special attention to some subgroups of population population that may be more vulnerable, such as children and adolescents as well as people with cardiovascular disease and / or severe mental disorder. Finally, it would be necessary to conduct more studies on the effects of ED consumption on mental health to clarify and specify the risk.

Conflict of interest

The authors declare no conflict of interest regarding this manuscript.

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