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Severe malnutrition and panhypopituitarism

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Summary

Severe malnutrition and panhypopituitarism

The effects of starvation on hormonal pituitary axis is controversial. In former observations on war prisoners performed eight decades ago, a clinical picture similar to Simmond's cachexia was described. Nowadays, in developed countries, severe malnutrition is practically restricted to anorexia nervosa, degenerative neurological disturbances and, rarely, malabsorptive syndromes and terminal neoplastic disease. Especially in anorexia nervosa corticotropin levels are usually raised, and the behavior of the remaining hormones is erratic. On the other hand, several alcoholism may impair secretion of some pituitary hormones. We here present a case of an alcoholic patient with severe malnutrition secondary to chronic pancreatitis, who presented with severe depression of all the pituitary hormones, that recovered "spontaneously" only with pancreatic enzyme replacement and weight gain.

Keywords: Alcoholism. Cachexia. Chronic pancreatitis. Malnutrition. Panhypopituitarism. Starvation.

Resumen

Malnutrición severa y panhipo-pituitarismo

El panhipopituitarismo en relación con la malnutrición fue descrito hace aproximadamente 80 años en prisioneros de guerra, habiendo sido objeto de intenso debate su relación con la denominada caquexia de Simmond. Actualmente en los países desarrollados la malnutrición severa es muy rara, siendo los pacientes con anorexia nerviosa una de las causas más frecuentes. En esta entidad se observa alteración de la secreción de las hormonas hipofisarias pero, por lo general, los niveles de ACTH están elevados, y no todos describen alteración del resto de las hormonas. Por otra parte, en el alcoholismo se han descrito alteraciones hipofisarias especialmente afectando las gonadotropinas. Presentamos el caso de un paciente alcohólico afecto de pancreatitis crónica que acude con una malnutrición muy severa y un panhipopituitarismo que se recupera de forma total con enzimoterapia pancreática y ganancia de peso.

Palabras Clave: Alcoholismo, Caquexia, Pancreatitis crónica, Panhipopituitarismo, Inanición

Introduction

The effects of starvation on hormonal pituitary profile was already pointed out several decades ago, based both on experimental studies and on clinical observations among war prisoners suffering chronic inanition [22]. It was suspected that functional hypopituitarism ensued with severe malnutrition, and efforts were made to establish criteria that allowed separation of this functional hypopituitarism from Simmond´s disease, defined as hypopituitarism related to structural impairment of the pituitary gland [12]. Further observations on patients with anorexia nervosa and other conditions associated with severe malnutrition disclosed that altered nutritional status was associated with reversible alterations of the hypophyseal hormonal profile [10]. However, there are some controversial results, especially among patients with anorexia nervosa [22]. For instance, corticotropin (ACTH) and cortisol levels have been found increased by several authors in this condition [8]. Therefore, the alteration of the hypophyseal-peripheral endocrine axis in non neoplastic adult individuals with severe malnutrition is not clear, given that anorexia nervosa is the most frequent

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cause of non-tumoral malnutrition observed in developed countries.

Multiple factors may provoke malnutrition in alcoholism, including the effects of ethanol itself, associated malabsorption, poor and bizarre feeding habits and the eventual co-existence of cirrhosis, alcoholic hepatitis, or chronic pancreatitis [9]. In alcoholics a reversible decrease in gonadotropins (FSH, LH), co-existing with decreased testosterone has been described several decades ago [19], but, to our knowledge, there are no cases of panhypopituitarism associated with malnutrition in these patients. On the contrary, there are some anecdotical reports of cirrhotics with panhypopituitarism [20], and some authors have proposed that untreated, neonatal panhypopituitarism may cause cirrhosis [4, 18]. We here report the case of a severely malnourished alcoholic patient with chronic pancreatitis who presented with panhypopituitarism that was fully reversible with pancreatic enzyme replacement and weight gain.

CASE REPORT

A 58-year-old man was admitted to the Hospital due to unintentional weight loss, malaise, progressive asthenia during the last four months, anorexia, sometimes accompanied by dysphagia. Before arrival to this hospital the patient was diagnosed of bronchial aspiration in another center. The patient reported heavy alcohol consumption (over 100g ethanol/day) during many years, occasional episodes of self-limited diarrhea during these last months and was recently diagnosed of diabetes.

Physical examination at admission was notable for severe malnutrition (45 kg weight and a body mass index of 16), and subjective nutritional score of 10 points (in a scale from 0 to 10, 10 being the worst situation [11], with a total absence of Bichat's fat, temporal excavation and marked sarcopenia. Systolic blood pressure was 90 mmHg, pedal and popliteal pulses were absent. Pulmonary crackles were present in the lower left lobe. Abdominal examination was anodyne. In addition to the suspicion of an underlying neoplastic disease (oesaphagus and/or pancreas), a diagnosis of pneumonia was made, and the patient was placed on ceftriaxone and levofloxacin, with improvement of his general status. At the second day of hospital stay the patient suffered unexplained hypoglycaemia, that was initially attributed to the extreme malnutrition in a septic context. A complete laboratory evaluation was performed, together with a plain X ray film of thorax and abdomen that confirmed the diagnosis of pneumonia and was consistent with chronic calcifying pancreatitis. Also striking calcification of the aortic and iliac arteries vessel walls was observed. The finding of a very low thyroxine levels and a very low thyreotropic hormone (TSH) levels together with the unexplained hypoglycaemia prompted us to perform a laboratory evaluation destined to explore pituitary function (Table I). The general status of the patient markedly improved besides any treatment, so we repeated the analysis destinated to evalute hypophyseal function. Values were still abnormally low, but had improved compared with the first determination. However, the very low cortisol value together with the relative hypotension and the hypoglycaemic episode prompted us to indicate treatment with hydrocortisone 30 mg during 3 days; the excellent recovery of the patient lead us to withdraw hydrocortisone treatment. The next analyses after several days without hydrocortisone revealed marked increased of the pituitary hormone levels. The patient gained appetite, was placed on pancreatic enzymotherapy, gained weight (50,300 kg) and was discharged. One month later, he was attended at the ambulatory unite of our service, with notably improvement of the general status and nearly normalization of the hormonal profile, that was confirmed one month later in another ambulatory appointment (Table I); at this time weight was 55.1 kg. A significant relationship was observed between the gain of weight and pituitary hormones (Figure 1).

During the hospitalization period, the presence of tumor was excluded, performing gastroscopy and total body CT. In addition, we performed a magnetic resonance exploration of the sella. A small image compatible with craneofaryngioma vs cystic macroadenoma was observed, but by no means able to explain a panhypopituitarism. The patient did not complain any visual defects, headache or another neurological disturbances. The neurosurgery service did not recommend any surgical procedure for the aforementioned finding.

Discussion

The case here reported constitutes an example of a severe malnutrition accompanied by hypopituitarism that recovered after adequate feeding and pancreatic enzyme substitution.

As discussed earlier, a great effort was made in the past to differentiate between "organic" hypopituitarism (the so called Simmond´s cachexia) and the functional alterations observed in severely malnourished individuals, especially among war prisoners [21].

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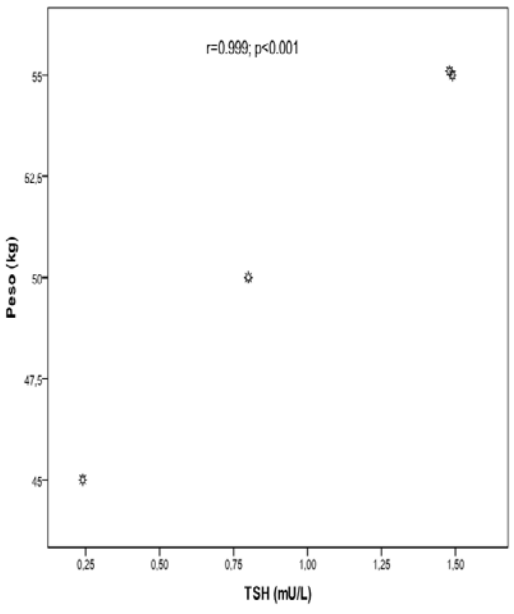
TABLE I – Relationship between gaining weight (kg) and hormone's increase.

	23/10 /18	29/10 /18	06/11 /18	13/11 /18	21/11/ 18	09/01/ 19	21/01 /19	Units	Normal values
Serum TSH	0.383	0.244	0.381	0.766	1.08	1.49	1.48	μU/mL	0.4-4 μU/mL
Serum T4	0.38	0.30	0.30	0.35	0.46	0.37	0.63	ng/dL	0.71-1.85 ng/dL
Serum testosterone		0.22	0.21		0.22	0.57		pg/mL	14.20-43.40 pg/mL
Serum PRL		1.22	1.21	1.45	1.25	2.17		ng/mL	2.5-17 ng/mL
Serum cortisol		2.27			1.16	9.12		μg/dL	5-25 μg/dL
Serum FSH		1.42	2.10	3.44	2.46	2.70		mUI/mL	1.5-15 mUI/mL
Serum GH		0.53	0.31		0.49	0.54		ng/mL	<2 ng/mL
Serum LH		0.33	0.43	1.17	1.03	1.79		mUI/mL	1.4-7.7 mUI/mL
Weight	45				50.300	55.100	55.100	kg	

Currently, such severe cases of malnutrition are very uncommon, and cases of malnutrition associated with hypophyseal dysfunction are scarcely reported. Panhypopituitarism and decreased growth hormone (GH) secretion is an important cause of short stature in children, especially in middle or low-income countries [16], or in patients affected by inflammatory bowel disease [11], but it is very uncommon in adult patients. Schuetz et al [15] described a case of panhypopituitarism in a patient subjected to bariatric surgery, who also showed a cystic adenoma, as in the case here described. A 22-year-old male suffered from hypopituitarism due to severe malnutrition, with significantly low values of basal metabolic rate, 24-hr 131 iodine uptake, serum T4, serum T2-RU and plasma TSH [10]. In the case of Ogura et al. [11], the patient improved pituitary function when placed on glucocorticoids (Crohn's treatment). In Nakashima et al's [10], the patient gained weight, height, pubic and axillary hair, and improved after surgery. In another instances, panhypopituitarism was attributed to a (possible) vasculitis, although the patient was severely malnourished [17].

Partial deficiency of pituitary hormones have been described more frequently. TSH may become totally suppressed in severe starvation [2] and rats on starvation show reduced prolactin (PRL) levels [14]. In monkeys, starvation and severe malnutrition leads to a decrease in PRL-, FSH-, LH-, GH-, TSH-secreting cells [13], but not corticotrophs. Herbert and Carrillo [6] described higher levels of corticosterone and an increase in ACTH secreting cells in protein-calorie malnourished rats, but Herbert et al. [7] found a reduced number of corticotrophs, with smaller cell and nuclear areas in malnourished rats (8% protein vs 27% protein containing diet). Generally, the effect of starvation on ACTH is controversial, because increased levels have been reported in anorexia nervosa [8]. On the contrary Aumaitre et al [1] described decreased ACTH in a malnourished alcoholic patient, as was the case of the patient presented here.

FIGURE 1 – Relationship between weight gain and serum TSH levels.



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Alcoholics is a subgroup of patients in whom pituitary function may become altered by the effect of ethanol itself. This was described already nearly 4 decades ago by Van Thiel et al [20], who found that, in relation with gonadal hormones, alcoholics showed a transient double defect. A study performed by our group in rats showed that protein malnutrition affected gonadal function and histology, but pituitary hormones were not assessed [5].

Conclusions

Given the intense relationship between ethanol and malnutrition, it is tempting to speculate that perhaps malnutrition might play a role in the pituitary alterations observed in alcoholics. This seems to be the case in the patient reported here: pituitary function was severely impaired and recovered with weight gain, but the patient also stopped ethanol ingestion. Therefore, an open question remains regarding the pituitary function in alcoholics, and the relative and combined effects of ethanol or malnutrition on these changes.

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