Case report

Marked elevation of transaminases and pancreatic enzymes in severe malnourished male with eating disorder

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Abstract

We report a case of a 45 year old Caucasian malnourished male with an history of eating disorder who developed severe liver and pancreatic damage and multiorgan dysfunction. At admission to our department, his body mass index (BMI) was 11.1. Biochemical evaluation showed elevated serum levels of transaminases (AST= 2291 U/L, ALT= 1792 U/L), amylose (3620 U/L), lipase (4102 U/L), CPK= 1370 U/L, LDH= 2082 U/L. No other cause of acute liver and pancreatic damage was evidenced. Haematological disorders (anemia, thrombocytopenia, leukopenia) found on admission seem related to bone marrow hypoplasia and to gelatinous marrow transformation described in severe state of malnutrition. Although a moderate increase in liver and pancreatic enzymes are a common finding in malnourished patients, only a small number of reports describes severe liver injury and multiorgan dysfunction. After a few days of treatment (hydration and nutritional support) a marked decrease of serum transaminases, lipase, amylose, CPK, LDH occurred, despite a transient increase in these levels secondary to refeeding syndrome. The association of chronic malnutrition and a decrease in systemic perfusion may be responsible for multiorgan dysfunction. In our patient the high levels of transaminases and pancreatic enzymes were the most important biochemical abnormalities normalized after refeeding.

Case report

On November 2011, a 45 year old caucasian man with an history of eating disorder was admitted to the emergency department because of collapse. The biochemical analyses showed hypoglycemia associated with a marked increase in pancreatic and liver enzymes. He was transferred to our medical unit with the provisional diagnosis of "collapse and pancreatitis in an anorexic subject." When the patient was 35 years old he weighed 70 kg and his body mass index (BMI) was 24.2 Kg/m². At that time he underwent plastic surgery for pseudo-gynecomastia. Subsequently, he manifested sexual identity disorder associated with drastic changes in his dietary habits with an obsessive-phobic component, reduction of food intake and marked weight loss. For these reasons the patient had undertaken a discontinued diagnostic-therapeutic approach in a psychiatric clinic.

On January 2011, he was hospitalized in an internal medicine department for "severe malnutrition syndrome complicated by caloric-protein deficiency, myopathy and osteoporosis" and was discharged with a note to contact a specialized center in eating disorders, but the patient refused to continue the diagnostic therapeutic process. When the patient was admitted to our department his weight was 31 kg and his height 167 cm (BMI = 11.1 Kg/m²). Physical examination revealed poor trophic-nutritional state, body temperature of 35°C, blood pressure of 90/60 mmHg, heart rate of 54 beats/min, SpO₂ 100%, dry skin and mucous membranes, anicteric sclerae, carotid icterus, scarce body hair, edema on the back of the foot, absence of subcutaneous fat, severe muscle hypotonia-hypotrophy with difficult ambulation, testicular hypotrophy. Cardiovascular, pulmonary and neurologic exams were normal. His chest showed severe kyphoscoliosis. His abdomen was scaphoid, with bowel sounds and without hepatosplenomegaly. Initial laboratory values showed a leukocyte count of 3.04 x 10⁹/
Sinus bradycardia (55 beats/minute). Serum electrolytes showed a natriemia of 132 mEq/L (n.v. 132-146) and potassium of 3.7 mEq/L (n.v. 3.7-5.4). Transaminases were elevated (AST 2291 IU/L - n.v. <37, ALT 1792 IU/L - n.v. <41) associated with a marked increase in α-amylose (3620 IU/L - n.v. 28-100), lipase (4102 IU/L - n.v. 13-60), lactate dehydrogenase (LDH 2082 U/L - n.v. 240-480) and creatine-phosphokinase (CPK 1370 U/L - n.v. <308).

Serum alkaline phosphatase was 257 U/L (n.v. 40-129) and γ-glutamyltranspeptidase was of 171 U/L (n.v. 8-61). Total and conjugated bilirubin were 1.4 (n.v. <1.2) and 0.02 mg/dl (n.v. <0.3) respectively, pseudocholinesterase was 2019 U/L (n.v. 5320-12920) and albumin was of 3.4 g/dl (n.v. 3.4-4.8). INR was 1.31 (n.v. 0.8-1.2); fasting plasma glucose was 33 mg/dl (n.v. 70-100) in absence of clinical symptoms.

The ammonia value was 13 umol/L (n.v. 11-35), cyanocobalamin 2001 pg/ml (n.v. 180-900), folates 20 ng/ml (n.v. 3-18), total vitamin D 11 ng/ml (n.v. 15-80), ferritin 1045 ng/ml (n.v. 30-400) and serum iron 54 mcg/dl (n.v. 58-158).

Fecal haemoccult was negative. The hormonal parameters showed mild hypercortisolism (cortisol at 8:00 am was 26 mg/dl n.v. 6.2-14.4 and cortisol at 06:00 pm was 13 mg/dl n.v. 2.3 - 11.9). GH was at the upper limit (5.23 mg/dl n.v. 0.9-6.2) and cortisol at 06:00 pm was 13 mg/dl n.v. 2.3 - 11.9).

The clinical course was characterized by anorexia nervosa with low BMI, especially in young men. Transaminase levels were elevated in 50% of the cases. Incidence and severity of hypertransaminasemia are greater in patients with low BMI, especially in young men. Transaminase levels were elevated in 50% of the cases. Incidence and severity of hypertransaminasemia are greater in patients with low BMI, especially in young men.

**Discussion**

On admission the patient showed an eating disorder which was secondary to a schizotypical personality with erroneous beliefs about the somatic self, obsessive ideas, somatization and absence of DSM-IV criteria for the anorexia nervosa diagnosis. The latter can not however be excluded because of the absence of anamnestic data about the onset of the psychiatric disorders. However, for the state of severe malnutrition and the organ complications, our patient is similar to subjects with anorexia nervosa. Chronic malnutrition and anorexia nervosa are often complicated by endocrine dysregulation (hypogonadism, hypercortisolism, GH-resistance, altered regulators of hunger), fluid and electrolyte imbalances, cardiovascular and hemodynamic abnormalities (bradycardia and arrhythmia, hypotension, heart failure), haematological disorders, osteopenia and osteoporosis, increased serum levels of transaminases, amylase and lipase which return within the normal range after an adequate nutritional and volaemic support. Anorexia nervosa is associated with a mortality rate of 5.6% per decade (1-3).

High serum levels of amylase and lipase are often found in the absence of clinical and instrumental evidence of pancreatic damage (4-6). However, in patients with chronic malnutrition have also been found cases of idiopathic acute recurrent pancreatitis (7). After a review of the literature, we found a small number of reports describing severe liver injury and multiorgan dysfunction in anorexia nervosa. In 12.2% of patients with anorexia nervosa, a moderate increase in transaminase levels was observed; other reports showed transaminase elevation in 50% of the cases. Incidence and severity of hypertransaminasemia were greater in the patients with low BMI, especially in young men.
>200 U/L were observed in 76% of patients with anorexia nervosa and a BMI <12 Kg/m²; however rare cases of severe hepatic impairment was reported (8-9). Despite a probable multiorgan injury, in our patient the high levels of transaminases and pancreatic enzymes were the most important biochemical abnormalities found which normalized after refeeding. The mechanism of hypertransaminasemia is unclear. According to several studies, it is probably caused by ischaemic hepatitis secondary to liver hypoperfusion. Chronic malnutrition is in fact associated with dehydration, hypovolemia, decreasing in cardiac output, marked hypotension and arrhythmias secondary to electrolyte imbalance which may be exacerbated during refeeding. Our patient showed no signs of cardiac dysfunction, but severe dehydration and hypotension may have been responsible for the reduction in the liver perfusion. Other hypothesis which might lead to liver injury involves changes in hepatocyte lipid metabolism (increased production of triglycerides associated to decreased beta-oxidation of fatty acids), the selenium deficiency followed by the reduction of glutathione-peroxidase activity and increased oxidative stress and iron accumulation in hepatic cells. In some cases, imaging and histologic studies have detected a fatty liver. The largest series of liver biopsy have showed glycogen depletion, trabecular atrophy, sinusoidal fibrosis, autophagosomes or the presence of aggregates of Kupffer cells. It has been reported that steatohepatitis similar to NASH can occur in patients during total parenteral nutrition (9-14).

However the cause of hypertransaminasemia is not only due to liver injury but to a multiorgan injury, as suggested

Fig. 1. Evolution of biological parameters during hospitalization.
by the elevated CK and LDH levels found in this patient and in several other cases described in literature in which increased levels of non-hepatic isoforms of LDH have also been shown (15). A transient increase in transaminases also occurs after refeeding. An inadequate nutritional treatment may cause the refeeding syndrome. This syndrome is defined by a severe and potentially fatal fluid and electrolyte imbalance, associated with metabolic abnormalities occurring in malnourished patients undergoing refeeding, whether orally, enterally, or parenterally (16). It is characterized by neurological symptoms (delirium, lethargy, coma), nausea, respiratory and heart failure, hypotension, arrhythmias, hematologic disorders (anemia, thrombocytopenia, abnormal leukocyte function). Hypophosphatemia is the most frequently observed abnormality in association with hypomagnesemia, hypokalaemia, vitamin deficiencies (thiamine) and hypoalbuminemia. Once the subjects at risk of refeeding syndrome are detected, it is advisable to start with a caloric intake of 5-10 kcal/kg per day and to increase slowly. Vitamin supplements (thiamine and vitamin B complex) should be started straight away and fluid balance carefully controlled. In order to prevent the hypophosphatemia a glucose intake of 4-7 mg/Kg/min and a phosphate supplement (31-62 mg/100 kcal) is recommended (17, 18). Mild asymptomatic hypoglycemia is commonly found in anorexia; cases of hypoglycemic coma, often associated with hepatic impairment, are rare. Hypoglycemia is an unfavorable prognostic factor in these patients. The correct pathogenesis of hypoglycemia has not been elucidated but several mechanisms including depletion of liver glycogen, glucagon secretion deficiency and decreased gluconeogenesis have been proposed (19). In our patient haematological test showed thrombocytopenia, leukaemia (with lymphocytopenia), anemia and increased levels of ferritin and vitamin B12. Anemia and leukaemia are found in approximately one-third of the anorexic subjects while thrombocytopenia in 11.5%. The reticulocyte count is usually normal or reduced. Iron deficiency is an uncommon finding in these patients, especially in males. The ferritin levels, elevated in 30% of cases, are reduced to the normal range after refeeding. Vitamin B12, folate and erythropoietin levels are usually normal; the latter increase significantly during the refeeding with weight gain. Leukopenia was observed in 29-36% of the cases. Granulocytopenia, lymphopenia and normal lymphocytes T/B ratio are frequent (20), although the exact pathogenic mechanisms of these features remain unclear. In the 50% of patients with anorexia nervosa and hematological changes in the peripheral blood count, signs of bone marrow hypoplasia and less frequently a complete atrophic transformation with deposition of amorphous material were observed. This alteration has been described as “gelatinous degeneration”. It would be secondary to a chronic deficit of carbohydrates and it regresses rapidly after an adequate refeeding to which the use of hematopoietic growth factors have been associated (21, 22). Altered levels of inflammatory cytokines (IL-1, IL-6, TNF-α) and leptin may also contribute to the genesis of hematopoietic disorders (23). In our case the haematological disorders found on admission seem to be the result of the severe state of malnutrition. Anemia, treated with red blood cell transfusion and erythropoietin, could depend on the refeeding syndrome. After the nutritional treatment, a normalization of the blood platelet count associated with a slightly increase of the leukocyte has been observed. Osteopenia and osteoporosis are further complications of chronic malnutrition. In a group of adult women with anorexia the prevalence of osteopenia would reach 92%. A reduction in bone mineral density (BMD) was observed in 41% of female adolescents and in 35% of anorexic young males. Possible causes involve the hypogestrogenism and the hypoandrogenism, the hypercortisolism, the reduction of IGF-1 associated with GH-resistance, the high levels of appetite regulators such as ghrelin and peptide YY (24). Our patient showed severe osteoporosis, low levels of vitamin D3 and testosterone, increased levels of PTH and cortisol.

Conclusions

In this case the association of chronic malnutrition and the decrease in systemic perfusion, secondary to dehydration and hypotension, may be responsible for multiorgan injury. In our patient the high levels of transaminases and pancreatic enzymes were the most important biochemical abnormalities normalized after refeeding.

A treatment strategy aimed at the nutritional support and at the correction of the electrolyte imbalance associated with the supplement of thiamine and erythropoietin was helpful in achieving a favorable outcome.

References