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Acute Liver Damage in Anorexia Nervosa

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Abstract: *We report a case of a 26-year-old White woman with a history of anorexia nervosa who developed severe liver damage and multiorgan dysfunction. At admission to our medical unit, her body mass index (BMI) was 10.8. Biochemical evaluation showed a marked increase in serum levels of aspartate aminotransferases (AST = 9,980 IU/L), alanine aminotransferase (ALT = 3,930 IU/L), amylase (1,002 IU/L), lipase (1,437 IU/L), creatine phosphokinase (CPK; 783 IU/L), and lactate dehydrogenase (LDH = 6,830 IU/L). Glomerular filtration rate was reduced (35 ml/min), reflecting dehydration and prerenal azotemia. No other cause of acute liver damage except malnutrition was evidenced. Hydration and nutritional support were the unique medical treatment. A rapid recovery occurred in few days and all laboratory data were normal at discharge after a 37-day hospitalization.* © *2004 by Wiley Periodicals, Inc.* Int J Eat Disord 36: 114–117, 2004.

Key words: *anorexia nervosa; liver damage; multiorgan dysfunction*

INTRODUCTION

Patients with anorexia nervosa (AN) develop a number of medical complications, due to malnutrition and/or purging behaviors. Although a slight or moderate increase in liver and pancreatic enzymes represents a common finding in patients with AN (Milner, Mc Anarney, & Klish, 1985; Ozawa, Shimizu, & Shishiba, 1998; Sherman, Leslie, Goldberg, Rybczynski, & St Louis, 1994; Umeki, 1998), only one case of severe liver damage has been reported (Furuta et al., 1999). As in other malnutrition states, the slight or moderate elevation of liver enzymes is likely to reflect a fatty liver. The accumulation of triglycerides, characteristic of hepatic steatosis, is the consequence of an imbalance between hepatic triglyceride synthesis and secretion. Carnitine and essential fatty acid deficiencies and a lower antilipolitic effect of insulin are involved in the pathogenesis of fatty liver, by affecting the hepatic biosynthesis of lipoproteins (Fong, Nehra, Lindor, & Buchman, 2000). Laboratory findings associated with steatosis include a slight or moderate increase in serum aminotransferases, γ-glutamyltranspeptidase, and/or serum bilirubin. Other factors, however, have to be invoked to explain the occurrence of acute liver damage resulting in a marked elevation

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of serum aminotransferases. We report a case of a patient with AN who presented with an acute and marked elevation of serum aminotransferases, associated with signs of multi-organ involvement.

CASE REPORT

GB is a 26-year-old woman with a 7-years history of AN. When she was 19 years old, GB weighed 42 kg (body mass index [BMI] = 18.6). At this age, she began to diet, to lose weight, and her menses stopped. She was diagnosed to have restrictive-type AN, according to criteria in the 4th ed. of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV; American Psychiatric Association, 1994). Since she was 21 years old, GB has been treated in the outpatient psychiatric unit of her own town. She periodically required inpatient treatments, both in the psychiatric and medical departments. In the last years, her weight stabilized at about 30 kg (BMI = 13.3). Because she was again losing weight, she was admitted to the gastroenterology unit on June 15th 2002, but she refused nutritional treatment and self-discharged 6 days after admission. Biochemical analyses including levels of liver and pancreatic enzymes were normal. Fifteen days later, she complained of diffuse myalgia and severe asthenia. On July 10th, GB was admitted to the medical department. On admission, her body weight was 24.5 kg (BMI = 10.8). Physical examination showed hypotension (80/45 mmHg), bradycardia (36/min), severe muscle mass depletion, dry skin, lanugo, carotenodermia, acrocyanosis, and atrophy of the breast. Laboratory data at admission are reported in Table 1. Hypertransaminasemia was associated with a marked increase in serum amylase, lipase, lactate dehydrogenase (LDH), and creatine phosphokinase (CPK). A slight increase in international normalized ratio (INR) of the prothrombin time (1.35), total bilirubin (23.2 μmol/L; normal values (n.v.) = 1.7–17 μmol/L), and aldolase (71.9 IU/L; n.v. = 1.0–7.7 IU/L) was also detected. The serum albumin level was normal (42.7 g/L), but decreased after hydration (31.7 g/L). Hormonal parameters showed hypercortisolemia (859 nmol/L; n.v. = 198–695 nmol/L), increased levels of growth hormone (GH; 17.30 μg/L; n.v. = 0.06–10.00 μg/L), low insulin-like growth factor-1 (IGF-1 *z*-score = −2.07), and reduced free-triiodothyronine (FT3 = 1.38 pmol/L; n.v. = 2.85–5.35 pmol/L) with normal free-tyroxine

Table 1. Laboratory data at admission and during hospitalization

	Day 1	Day 2	Day 3	Day 4	Day 8	Day 13	Day 20	Day 27	Day 37
BW (kg)	24.5	25.0	25.0	26.0	26.4	28.0	28.3	29.6	28.8
AST (IU/L) (10–35)	9,980	5,600	2,440	1,470	202	47	27	22	21
ALT (IU/L) (5–40)	3,930	4,240	3,070	2,700	935	390	144	71	39
LDH (IU/L) (190–380)	6,830	3,910	1,916	1,377	785	712	587	402	378
Lipase (IU/L) (10–280)	1,437		944	724	500		149		
Amylase (IU/L) (<220)	1,002		782	766	532		165		
CPK (IU/L) (10–160)		783			300				97

Note: Normal values for our laboratory are in parentheses. BW = body weight; AST = aspartate aminotransferase; ALT = alanine aminotransferase; LDH = lactate dehydrogenase; CPK = creatine phosphokinase.

and thyroid-stimulating hormone (TSH). Urine analysis and levels of serum glucose, serum creatinine, and electrolytes were in the normal range, but creatinine clearance was reduced (35 ml/min). Electrocardiogram showed sinusal bradycardia (heart rate = 33–36/min) and one supraventricular beat.

The principal causes of acute liver injury were excluded. Anamnestic data for alcohol abuse or drug assumption were negative, as well as serologic tests for hepatotropic viruses (hepatitis A, B, and C viruses, cytomegalovirus, and Epstein-Barr virus) and blood and/or urine analysis for alcohol, cannabis, cocaine, and hepatotoxic drugs (paracetamol, amphetamine, benzodiazepine, methadone, opiates). The morphology of the liver, gallbladder, and biliary tree was normal at ultrasound examination. Histologic examination was not performed because the patient refused to undergo a liver biopsy.

Medical treatment during the first days included hydration (5% dextrose in water, 1,500 ml/day) and plasma volume expansion (isotonic saline, 500 ml/day). Starting on the third hospital day, parenteral nutrition was initiated, followed after 6 days by enteral nutrition through a nasogastric tube. The total energy intake progressively increased from 20 kcal/kg body weight to 50 kcal/kg body weight. The energy distribution of nutritional solutions was glucose 48%, fat 35%, and protein 17%. The usual recommended amounts of vitamins and trace elements were added to nutritional solutions. During the first week of treatment, additional phosphate and magnesium were given intravenously according to biochemical monitoring. Enteral tube feeding was supplied using a standard polymeric formula (Novasource Standard, Novartis Nutrition, Origgio (VA), Italy). Oral feeding was combined with artificial nutrition starting on Day 8.

A marked and rapid decrease in levels of serum aminotransferases and other biochemical parameters occurred after a few days of treatment (Table 1). A temporary mild edema of the lower extremities occurred at the end of the second week. No other signs of a refeeding syndrome were noticed. When GB was discharged after a 37-day hospitalization, her body weight was 28.8 kg (BMI = 12.8). She continued her rehabilitation program in an outpatient psychiatric unit.

DISCUSSION

After a review of the literature, we found only one report describing the occurrence of severe liver damage and multiorgan dysfunction in AN (Furuta et al., 1999). In our patient, serum levels of aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were 285 and 112 times higher than normal, respectively, and pancreatic enzymes, LDH, and CPK were also markedly increased, indicating multiorgan dysfunction. The serum creatinine level was normal, whereas creatinine clearance was reduced, reflecting prerenal azotemia, due to dehydration and plasma volume depletion. As in other conditions associated with severe muscle mass reduction, the serum creatinine level may be normal in spite of a marked reduction in the glomerular filtration rate (GFR). In these situations, the serum creatinine level does not represent a reliable indicator of renal function, whereas creatinine clearance has been found to be a more accurate measure of GFR (Caregaro et al., 1994). The reduction in the serum level of triiodothyronine with normal TSH is a characteristic finding in AN, whereas the pattern of hypercortisolemia, increased serum GH, and low IGF-1 reflects a hypercatabolic state (Caregaro et al., 2001).

Among the signs of multiple organ dysfunction, the elevation of liver enzymes was the most severe biochemical alteration in our patient. Serum levels of aminotransferases were

lower in the case reported by Furuta et al. (1999). In that study, aggressive support therapy (hemodialysis, mechanical ventilation, and drug therapy) was required for the treatment of liver dysfunction and its complications.

In our case, the acute onset of liver damage, the marked elevation of serum levels of aminotransferases, and the association with an involvement of other organs are consistent with the hypothesis of acute hypoperfusion. Cardiac arrhythmias, heart failure, and severe hypotension, which are known complications of AN, may critically impair the perfusion of the liver and other organs. In our patient, there were no signs of cardiac failure, but severe hypotension and dehydration may have been responsible for a critical reduction in the perfusion of various organs. The rapid recovery after intravenous hydration and plasma volume expansion supports such an interpretation. Malnutrition-related deficiencies may constitute a predisposing factor for multiple organ dysfunction (Brass, 1994). Other factors, such as dehydration, marked hypotension, arrhythmia, or cardiac failure, may act as precipitating events by critically impairing organ perfusion.

Although active nutritional intervention is mandatory in severely malnourished patients with AN, the risk for refeeding syndrome should be taken into account (Khon, Golden, & Dhenker, 1998). Starting nutrition with low energy intake, as in our patient, and gradually increasing intake are critical to avoid the life-threatening complications of refeeding. Careful clinical and biochemical monitoring is the second clever device. Monitoring should include the assessment of vital signs (cardiac rate, blood pressure), presence of edema, fluid intake and output, and serum electrolytes.

The current study illustrates the clinical course and medical treatment of a life-threatening episode of severe acute multiorgan dysfunction in a patient with AN. The combination of malnutrition and a critical reduction in the perfusion of the liver and other organs was most likely responsible for acute liver damage and multiorgan dysfunction. A treatment strategy aimed at correcting both fluid disturbances and malnutrition resulted in a favorable outcome.

REFERENCES

American Psychiatric Association. (1994). Diagnostic and statistical manual of mental disorders (4th ed.). Washington, DC: Author.

Brass, N.J. (1994). Predisposition to multiple organ dysfunction. Critical Care Nursing, 16, 1–7.

Caregaro, L., Favaro, A., Santonastaso, P., Alberino, F., Di Pascoli, L., Nardi, M., Favaro, S., & Gatta, A. (2001). Insulin-like growth factor (IGF-1), a nutritional marker in patients with eating disorders. Clinical Nutrition, 20, 251–257.

Caregaro, L., Menon, F., Angeli, P., Amodio, P., Merkel, C., Bortoluzzi, A., Alberino, F., & Gatta, A. (1994). Limitations of serum creatinine and creatinine clearance as filtration markers in cirrhosis. Archives of Internal Medicine, 154, 201–205.

Fong, D.G., Nehra, V., Lindor, K.D., & Buchman, A.L. (2000). Metabolic and nutritional consideration in non-alcoholic fatty liver. Hepatology, 32, 3–10.

Furuta, S., Ozawa, Y., Maejima, K., Tashiro, H., Kitahora, T., Hasegawa, K., Kuroda, S., & Ikuta, N. (1999). Anorexia nervosa with severe liver dysfunction and subsequent critical complications. Internal Medicine, 38, 575–579.

Khon, M.R., Golden, N.H., & Dhenker, I.R. (1998). Cardiac arrest and delirium: Presentation of the refeeding syndrome in severely malnourished adolescents with anorexia nervosa. Journal of Adolescent Health, 22, 239–243.

Milner, M.R., McAnarney, E.R., & Klish, W.J. (1985). Metabolic abnormalities in adolescent patients with anorexia nervosa. Journal of Adolescent Health, 6, 191–195.

Ozawa, Y., Shimizu, T., & Shishiba, Y. (1998). Elevation of serum aminotransferase as a sign of multiorgan-disorders in severely emaciated anorexia nervosa. Internal Medicine, 37, 32–39.

Sherman, P., Leslie, K., Goldberg, E., Rybczynski, J., & St Louis, P. (1994). Hypercarotenemia and transaminitis in female adolescents with eating disorders: A prospective, controlled study. Journal of Adolescent Health, 15, 205–209.

Umeki, S. (1998). Biochemical abnormalities of the serum in anorexia nervosa. Journal of Nervous and Mental Disease, 176, 503–506.