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Evaluation of ceruloplasmin levels in patients with pulmonary cystic echinococcus

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Abstract

Aim. In this study, we aimed to evaluate serum CP levels in the serum samples before and after the surgical interventions in patients with pulmonary cystic echinococcus (CE).

Materials and Methods. Forty-eight patients with pulmonary CE who underwent surgery and 48 healthy individuals were enrolled to the study. Patients were divided in two groups; group 1 (n=48) consisted of patients with pulmonary CE, and group 2 (n=48) consisted of healthy subjects. Before and after surgical interventions serum CP levels were measured.

Results. Compared to group 2, group 1 had significantly higher CP levels at baseline (p <0.001). In group 1, CP levels were significantly decreased after the surgical intervention (p <0.001).

Conclusions. The present study showed that CP levels increased in patients with pulmonary CE; chronic inflammation may cause these rises, and may be an immune response of the host, and these levels decreased after the surgical intervention. ***Clin Ter 2013; 164(2):e89-92.***
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Key words: *ceruloplasmin, echinococcus granulosis, immune response, inflammation, pulmonary hydatidosis, thoracic surgery*

Introduction

Cystic echinococcosis (CE) is a parasitic disease that is endemic in many parts of the world (1, 2). After the penetration of the parasite, the hydatid cyst secretes and exposes numerous immunomodulatory molecules to the host's immune system. In contrast, the host organism react these molecules by activating complement-depending immune response (3, 4). An acute phase protein, ceruloplasmin (CP) is generally thought to be induced so that its function in host defense. It plays an important role in development and maintenance of the immune system but its exact mechanism of action remains unclear (5-7). Although based on this relationship between immune response and CP mentioned above, no research study has been performed yet to evaluate whether CP levels increases or not in patients with CE. By this way, the present study was undertaken to evaluate the CP levels in the serum samples before and after the surgical interventions in patients with pulmonary CE.

Materials and Methods

Study design and patients

This prospective study was conducted at the Thoracic Surgery Department of Harran University School of Medicine, Sanliurfa, Turkey. Prior to subject recruitment, the study protocol was reviewed and approved by the local Ethics Committee, in accordance with the ethical principles for human investigations, as outlined by the Second Declaration of Helsinki, and written informed consent was obtained from all the patients. From September-2009 to December-2011, consecutively 48 age-gender matched patients with pulmonary CE who underwent surgery and 48 healthy individuals were recruited to the study.

Patients were divided in two groups: group 1 (n=48) consisted of patients with pulmonary CE, and group 2 (n=48) consisted of healthy subjects. The diagnosis of hydatid cyst was based on chest radiography and computed thorax tomography scanning. All patients were examined with abdominal ultrasonography in order to evaluate the liver. The exclusion criteria were as follows: recent acute infectious illness; any evidence of liver, kidney diseases; diabetes mellitus; malignancy; any other inflammatory, or infiltrative disorder; recent use (within 2 weeks) of any systemic drugs; regular alcohol use or alcohol use within the previous 48 hours. The serum CP levels of all CE patients were analyzed before and the after the surgery. Data were also obtained from the healthy subjects at baseline.

Baseline definitions and measurements

Height and weight were measured according to standardized protocols. Body mass index (BMI) was calculated as the weight in kilograms divided by the height in meters squared

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(kg/m^2). Blood pressure was measured using a mechanical sphygmomanometer. For each subject, after being seated comfortably for 15 minutes, the average of three blood pressure measurements was calculated.

Biochemical analysis

All of the blood samples were drawn from a large antecubital vein without interruption of the venous flow using a 19-gauge butterfly needle connected to a plastic syringe. Twenty milliliters of blood was drawn, with the first few milliliters discarded. Ten milliliters were used for baseline routine laboratory tests. The residual content of the syringe was transferred immediately to polypropylene tubes, which were then centrifuged at 3000 rpm for 10 minutes at 10-18°C. Supernatant serum samples were stored in plastic tubes at –80°C until assayed. For the serum markers of CP were measured.

Measurement of ceruloplasmin

The enzymatic activity of Cp was measured according to Erel's method (8). Using this assay, ferrous ion is oxidized to ferric ion via CP ferroxidase activity. The results are expressed as units per gram protein (U/L).

Other variables

Serum urea, creatinine, fasting blood glucose, aspartate aminotransferase, alanine aminotransferase, triglycerides, total cholesterol, and high-density and low-density lipoproteins cholesterol levels were determined using commercially available assay kits (Abbott®, Abbott Park, North Chicago, Illinois, USA) with an auto-analyzer (Abbott®, Abbott Park, North Chicago, Illinois, USA).

Statistical analysis

All statistical analyses were performed using SPSS for Windows version 17.0 (SPSS® Inc., Chicago, IL, USA). Kolmogorov-Smirnov test was used to test the normality of data distribution. The data were expressed as arithmetic means and standard deviations. The chi-square test was used to compare the categorical variables between groups. Independent sample *t* test and Mann Whitney-U test were used for comparison of continuous variables *between two groups.* Paired t-test was used to analyze changes within the CE patients. Two-sided p value ≤0.05 was considered statistically significant.

Results

The clinical, biochemical and demographic characteristics of the study groups are presented on Table 1.

There were no significant differences in gender, age and biochemical values between the control and CE patients (p >0.05 for all).

Compared to group 2, group 1 had significantly higher CP levels at baseline (p <0.001). In group 1; CP levels were significantly decreased after the surgical intervention (p <0.001) (Table 1, 2) (Fig. 1).

Table 2. Comparison of ceruloplasmin levels in Group 1 after the surgical intervention.

	Before surgery (n=48)	After surgery (n=48)	p^{α}
Ceruloplasmin, U/L	668.99±105.90	590.29±90.20	0.001

All measurable values were given with mean ± standard deviation. By Paired sample *t* test$^{\alpha}$

Table 1. Comparison of the demographic and biochemical characteristics of all patients.

	Group 1 (n=48)	Group 2 (n=48)	p
Gender, male/female	26/22	23/25	NS[a]
Age, years	31.13±11.56	32.98±9.13	NS[b]
BMI, kg/m^2	24.76±3.21	23.84±2.33	NS[b]
Systolic BP, mmHg	111.24±9.38	114.25±8.54	NS[b]
Diastolic BP, mmHg	71.20±9.35	73.46±8.58	NS[b]
Glucose, mg/dL	83.66±8.29	80.71±9.91	NS[b]
Urea, mg/dL	25.67±5.12	24.72±4.83	NS[b]
Creatinine, mg/dL	0.70±0.16	0.68±0.10	NS[b]
ALT, U/mL	26.53±5.87	25.81±4.79	NS[b]
AST, U/mL	26.36±4.37	25.81±4.62	NS[b]
Total cholesterol, mg/dL	209.65±18.05	202.43±22.42	NS[c]
LDL cholesterol, mg/dL	132.16±33.45	137.56±27.37	NS[c]
Triglyceride level, mg/dL	193.58±42.64	198.34±48.39	NS[c]
Ceruloplasmin, U/L	668.99±105.90	591.72±109.65	0.001[b]

All measurable values were given with mean ± standard deviation. NS: non-significant, ALT: alanine aminotranferase, AST: aspartate aminotransferase, LDL: low density lipoproteins, By Chi-square[a], Independent sample T test[b] and Mann Whitney-U[c] tests .

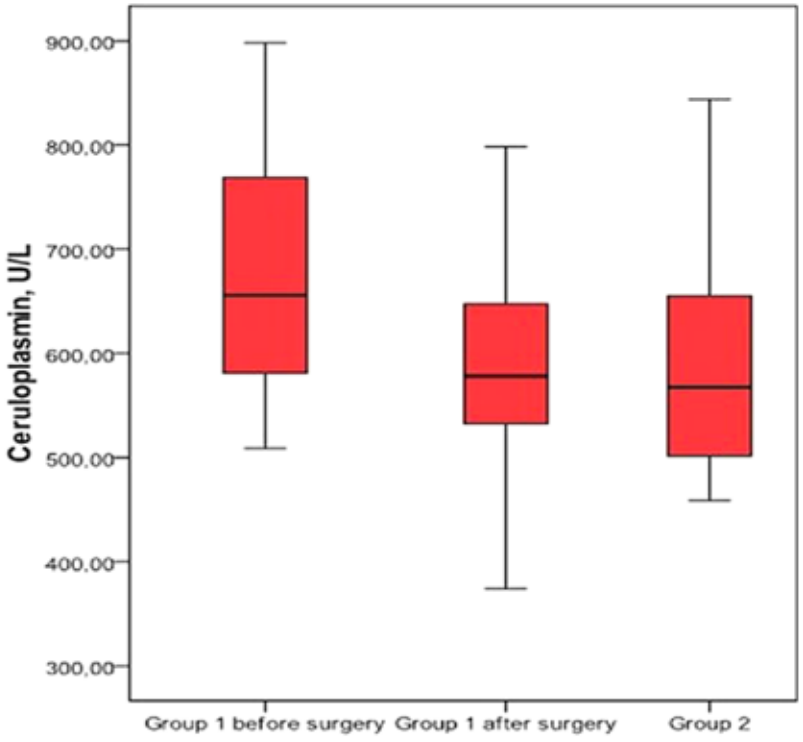

Fig. 1. Graph demonstrating the ceruloplasmin levels among study groups.

Discussion

To the best of our knowledge, this is the first report to evaluate the CP levels in patients with pulmonary CE. The main findings of the present study showed that (i) the CP levels increased in patients with pulmonary CE, and (ii) these levels decreased after the surgical intervention.

The host-parasite relationship is interactive and the outcome of infection depends on the balance achieved by the combination of the different variables involved with the host immunity and the parasite avoidance strategies (9). The main feature of this relationship is the coexistence of the chronic infection with detectable humoral and cellular responses against the parasite (10-12). Helminths penetrate and establish themselves in the host tissues, incorporate metabolites from the host, and modulate the host immune response by developing a variety of effective strategies (13, 14). Some of these strategies are passive, whereas others involve active manipulations of the host's defensive responses. Namely, parasite-derived substances play an important role in initiating or maintaining the parasite's advantage, directly suppressing the function of certain subsets of immune cells as well as stimulating other cell populations related to immunopathology (15-19).

Little is known about parasitic molecules that behave as immunomodulatory antigens and the mechanisms that they use to evade the host's immune response (20). Some studies demonstrated that hydatid cyst produces and secretes significant quantities of molecules that modulate the immune responses; these include both humoral and cellular immune response against the parasite (21, 22). On the other hand, copper is known to play an important role in development and maintenance of the immune system (6). The rise in serum copper is primarily due to the hepatic synthesis and release of CP. The increases in serum copper and CP parallel one another (23). Numerous studies have demonstrated that CP deficiency impairs both innate and acquired immunity. Besides, higher levels have been shown with inflammatory conditions and infectious diseases (24-26). However, the rises of these levels have been poorly understood. In our study, compared to healthy subjects, CP levels were increased in patients with pulmonary CE, and these levels were reversed after the surgery.

In conclusion, findings of the present study demonstrate that CP increased in patients with pulmonary CE. Although not definitively, chronic inflammation may cause these rises, and may be an immune response of the host. Relatively small sample size is a major limitation of the present study. Therefore, future large-scale prospective cohort studies are needed to clarify this issue.

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