

# Intraoperative Anaphylactic Reaction During Hydatid Cyst Surgery: Report of Two Cases and Review of the Literature

## Kist Hidatik Cerrahisi Sırasında İntraoperatif Anafilaktik Reaksiyon: İki Olgu Sunumu ve Literatürün Derlenmesi

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**ABSTRACT** The incidence of the hydatidosis is still high in some Mediterranean regions. Hypersensitivity reactions mediated by Immüoglobulin E, due to the contamination of the bloodstream with highly antigenic cyst fluid, is a serious but fortunately infrequent complication of hydatid disease surgery. Hypersensitivity reactions vary widely, from benign urticaria and short episodes of shaking chills or fever, to potentially fatal bronchial spasms, angioneurotic edema and anaphylactic shock. The anaphylactic shock symptoms may be unlike routine symptoms under general anesthesia. The possibility of anaphylaxis must be kept in mind whenever a sudden hemodynamic deterioration occurs during surgery for removal of a hydatid cyst. Early diagnosis and appropriate treatment are essential for a favorable outcome of the anaphylaxis treatment. We present two cases of intraoperative anaphylactic reaction in patients undergoing surgery for excision of hydatid cysts.

**Key Words:** Echinococcosis, hepatic; anaphylaxis; anesthesia

**ÖZET** Kist hidatik insidansı, Akdeniz ülkelerinin bazı bölgelerinde hala yüksektir. Yüksek antijenik özelliğe sahip kist sıvısının sistemik dolaşıma geçişi sonucu, immüoglobulin E'ye bağlı ortaya çıkan aşırı duyarlılık reaksiyonları, nadir görülen ama kist hidatik cerrahi tedavisinin ciddi bir komplikasyonudur. Aşırı duyarlılık reaksiyonları benign ürtiker, kısa süreli titreme yada ateşten ölümcül olma potansiyeli taşıyan bronkospazma, anjiyonörotik ödem ve anafilaktik şoka kadar çok büyük değişiklikler gösterir. Genel anestezi altında gelişen anafilaktik şok semptomları normal durumlardaki gibi olmayabilir. Kist hidatik cerrahisi esnasında hemodinaminin aniden bozulması anafilaksi olma ihtimalini akla getirmelidir. Anafilaksi tedavisinde başarı sağlayabilmek için, bu durumun erken tanınması ve uygun tedavi yaklaşımı sergilenmesi gerekmektedir. Biz bu makalede, kist hidatik eksizyonu sırasında intraoperatif anafilaksi gelişen iki olguyu sunmayı amaçladık.

**Anahtar Kelimeler:** Ekinokokkozis, hepatik; anafilaksi; anestezi

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**H** ydatidosis is a zoonotic infection, caused by the parasitic tapeworm of Echinococcus. The larval stage of this parasite can be implanted in many organs of the body, most commonly the liver. The disease and parasite have tight links with allergy because of the immunological characteristics that contribute to maintain the larvae in their human host. The contamination of the bloodstream with highly antigenic cyst fluid triggers an Ig E mediated hypersensitivity reaction.<sup>1,2</sup>

We present two cases developed an intraoperative anaphylactic reaction due to rupture of the hydatid cyst.

## CASE REPORTS

The patients given their informed consent for the case report to be published.

### CASE 1

A 20 year old man (height 170 cm, weight 81 kg) was admitted to our hospital due to abdominal and flank pain, breathlessness and cough. Ultrasonography and computed tomography of the abdomen revealed a giant cyst (190 x 180 x 180 mm) of the right lobe of the liver consistent with the diagnosis of hydatid cyst.

Patient was taken into the operating room for laparoscopic treatment of hydatid cyst of the liver and premedicated with intravenous (IV) midazolam 2 mg, prednisolone 60 mg and chlorpheniramine maleate (H<sub>1</sub> blocker) 10 mg. Anesthesia was induced with lidocaine 0.75 mg/kg, propofol 2.5 mg/kg, fentanyl 1 µg/kg, and vecuronium 0.1 mg/kg. The trachea was then intubated using an 8-mm endotracheal tube. The patient was continuously monitored by electrocardiogram (EKG), invasive blood pressure (IBP) monitor, pulse oximetry (SpO<sub>2</sub>) and end-tidal capnography. The anesthesia was maintained by the mixture of nitrous oxide 49%, and sevoflurane 2% in oxygen intermittent boluses of fentanyl and vecuronium. The patient was hemodynamically stable at the onset of the operation with a blood pressure (BP) of 142/86 mmHg and heart rate (HR) of 83 beat per minute (bpm).

After the pneumoperitoneum was achieved, the needle introduced through the cyst capsule for aspiration of the cyst contents. During this procedure the blood pressure of the patient suddenly dropped from 135/82 mmHg to 50/30 mmHg, with an increase in the heart rate from 81 bpm up to 138 bpm, associated with the facial flushing. A generalized erythema was observed, and breath sounds were decreased bilaterally with wheezing. Airway pressure increased from 16 to 52 mmHg kPa.

In spite of the repeated intravenous doses of 10 mg ephedrine HCl, with a total dose of 30 mg blood pressure further decreased to 45/ 25 mm Hg

and heart rate increased to 147 bpm. After the administration of repeated intravenous bolus doses of 100 µg adrenaline (total dose of 2 g) with prednisolone 250 mg and chlorpheniramine maleate 10 mg, and rapid fluid administration (1000 ml of lactated Ringer's solution and 500 ml gelatin [Haemaccel® (Hoechst, Behring-Werke, Marburg Germany)]), the blood pressure increased to 80/50 mm Hg, and the heart rate decreased to 115 bpm. Infusion of adrenaline (2 µg/kg/min) was started. The patient progressively improved with continuous fluid loading and adrenaline infusion. The blood pressure and heart rate gradually returned to normal ranges in 20 minutes later (the blood pressure to 130/70 mmHg and the heart rate to 90 bpm). Following hemodynamic stabilization, the adrenaline infusion was dropped to 0.5 µg/kg/min and surgery was continued. However, laparoscopic procedure was converted to open surgery. Cyst excision was performed, followed by careful and prolonged peritoneal lavage with chlorhexidine and normal saline. Adrenaline infusion was stopped, but after then blood pressure decreased to 75/45 mm Hg and heart rate increased to 117 bpm. So, an intravenous bolus of 200 µg adrenaline was administered and continued with the infusion of adrenaline at 0.5 µg/kg/min. The blood pressure and the heart rate returned to normal ranges. The surgery was completed and trachea was extubated without any problem and the adrenaline infusion weaned off. Total fluid loading was 70 ml/kg [2000 ml lactated Ringer's solution, 1000 ml gelatin [Haemaccel® (Hoechst, Behring-Werke, Marburg Germany)] and 2500 ml saline 0.9%]. The patient was observed in the post anesthetic care unit for 24 hours. As the hemodynamic parameters of the patient sustained stable, he was discharged to the ward without any complication.

### CASE 2

A 35 year old man (height 182 cm, weight 86 kg) was admitted to emergency department with acute abdomen symptoms. Ultrasonography and computed tomography of the abdomen revealed multiple cysts in the liver and intraperitoneal fluid collection. The patient was planned to be operated.

There were no specific findings in preoperative evaluation of the patient except fever (38°C) and leucocytosis (WBC; 14.000/mm<sup>3</sup>).

After monitoring by ECG, SpO<sub>2</sub> and non-invasive blood pressure (NIBP), the patient was premedicated with dexamethazone 8 mg and pheniramine maleate 45.5 mg intravenously. Preoperative hemodynamic findings were; heart rate: 115 bpm, NIBP: 146/90 mmHg and SpO<sub>2</sub>: 95%.

Anesthesia was induced with thiopental sodium 4 mg/kg, fentanyl 1 µg/kg, and vecuronium 0.1 mg/kg. The trachea was then intubated using an 8-mm endotracheal tube. The anesthesia was maintained by the mixture of inhalation agents (O<sub>2</sub> 49%, N<sub>2</sub>O 49%, and sevoflurane 2%). The patient was hemodynamically stable at the onset of the operation.

After surgical laparotomy, a ruptured cyst was seen on the right lobe and multiple cysts on the left lobe of the liver. Also infected cyst content had been spilled into intraperitoneal cavity.

Until to the 145<sup>th</sup> minute of the operation, the hemodynamic findings continued stable. After puncturing one of the cysts on the left lobe of the liver, the blood pressure suddenly dropped from 143/73 mmHg to 47/30 mmHg. The heart rate of the patient increased to 163 bpm. Then, flushing occurred and angioneurotic edema was developed. Airway pressure increased from 15 to 40 mmHg kPa with the clinical finding of bilateral pulmonary wheezing.

When the blood pressure began to decrease, we administered a total dose of 25 mg ephedrine HCl (10 mg + 15 mg) intravenously with rapid fluid replacement, but there was no improvement. Then, a total dose of 200 µg adrenaline (100 µg + 100 µg) administered intravenously. The blood pressure gradually increased to 140/71 mmHg and the heart rate decreased to 90 bpm. Also, 250 mg prednisolone and 45.5 mg pheniramine maleate was added to the treatment process.

The hemodynamic parameters continued stable until to the end of the operation. Trachea

was extubated without any problem. The patient was observed for two hours in the post anesthetic care unit. The flushing and the angioneurotic edema regressed gradually. As the hemodynamic parameters of the patient continued stable, the patient was discharged to ward.

## DISCUSSION

Echinococcosis is endemic in Mediterranean countries, the Middle East, south-eastern Africa, South America, New Zealand and Australia.<sup>3-5</sup>

Dogs are the most important definitive hosts of the parasite. The intermediate hosts are usually sheep or camels. Humans are accidental intermediate hosts.<sup>6</sup> The intermediate host digests eggs of the parasite. Proteolytic enzymes digest the protective coating of the egg, releasing embryos which attach to the jejunal mucosa by hooklets and suckers. Embryos then enter both the veins and travel to the capillary bed of the liver or the lymphatics, bypassing the liver and reaching the brain, lungs, kidneys, bones, etc.<sup>7</sup> In humans, the liver is the most common site of cyst development (60%), followed by the lungs (20%), and much less commonly, the kidney, spleen, brain, and soft tissue.<sup>8,9</sup>

In most patients, the clinical findings are unapparent for a long period of time and the disease can be detected incidentally in asymptomatic patients undergoing abdominal ultrasonography for unrelated reasons.<sup>10</sup> Symptomatology, when present, depends on the anatomic location, size, and phase of development of the hepatic cysts.<sup>11</sup>

The cutaneous manifestations of the disease are either specific as skin hydatidosis and hepatic-cutaneous fistulae or non-specific as pruritus, flushing, urticaria.<sup>12</sup> The severe anaphylactic reactions, develop due to hydatid cyst disease, generally occurs after spilling of the cyst fluid accidentally, during surgical or laparoscopic treatment of the disease or posttraumatic rupture of the cyst.<sup>13</sup> The specific IgE plays a major role in the anaphylactic shock, while IgG and IgG1 antibodies are also important.<sup>14</sup>

The immune system to respond to allergens is dependent on factors including the type and load of allergen, behavior and type of antigen-presenting cells, innate immune response stimulating substances in the same micromilieu, the tissue of exposure, interactions between T and B lymphocytes, costimulators, and genetic propensity known as atopy. Antigen-presenting cells introduce processed allergens to T-helper lymphocytes, where a decision of developing different types of T-cell immunity is given under the influence of several cytokines, chemokines, costimulatory signals and regulatory T cells. Among Th2-type cytokines, interleukin (IL)-4 and IL-13 are responsible for class switching in B cells, which results in production of allergen-specific IgE antibodies that bind to specific receptors on mast cells and basophils. After re-exposure to the sensitized allergen, this phase is followed by activation of IgE Fc receptors on mast cells and basophils resulting in biogenic mediator releases responsible for the symptoms and signs of anaphylaxis. Since the discovery of regulatory T cells, the concepts of immune regulation have substantially changed during the last decade. Peripheral T-cell tolerance is a key immunologic mechanism in healthy immune response to self antigens and non-infectious non-self antigens. Both naturally occurring CD4<sup>+</sup> CD25<sup>+</sup> regulatory T (Treg) cells and inducible populations of allergen-specific, IL-10-secreting Treg type 1 cells inhibit allergen-specific effector cells and have been shown to play a central role in the maintenance of peripheral homeostasis and the establishment of controlled immune responses. On the other hand, Th17 cells are characterized by their IL-17 (or IL-17A), IL-17F, IL-6, tumor necrosis factor-alpha, and IL-22 expressions, which coordinate local tissue inflammation through upregulation of proinflammatory cytokines and chemokines.<sup>15</sup> Measurement of serum tryptase and specific IgE levels should be undertaken for possible anaphylaxis.<sup>16</sup>

Spontaneous anaphylactic phenomena in asymptomatic patients with hydatid disease,

however, are extremely rare, and only a few cases have been reported in which an anaphylactic reaction was the initial manifestation of hydatidosis.<sup>17</sup> In one of our cases above, the patient had no complaint before the rupture of the cyst and the rupture developed spontaneously. However the patient applied the emergency department with acute abdomen symptoms, not with anaphylactic reaction signs.

Hypersensitivity reactions vary widely, from benign urticaria and short episodes of shaking chills or fever, or both events, to potentially fatal bronchial spasms, angioneurotic edema and anaphylactic shock.<sup>18</sup> The latter occurs most frequently after the accidental rupture of the hydatid cyst or during surgery.<sup>19,4</sup>

The anaphylactic shock symptoms developing under general anesthesia may not be evident as normal conditions. Khoury and coll.<sup>13</sup> reported a sudden drop in the blood pressure, with a significant increase in the heart rate, associated with facial flushing and edema in a case of hydatid disease of the liver which was treated by laparoscopic evacuation. The symptoms seen in our cases match with the reported symptoms, but, these can be seen due to many reasons under general anesthesia.

Minor hypersensitivity symptoms as fever, urticaria or hypotension may develop during either surgical or laparoscopic treatment of hydatid cyst disease.<sup>20</sup> Also, Schiller has reported that two of three cases occurring anaphylaxis died in 48 hours in a study of 30 cases with ruptured cyst.<sup>21</sup> For this reason, preoperative administration of antiallergic drugs as antihistaminics and corticosteroids are recommended in these cases.<sup>2,22</sup>

In two different cases, it has been reported that, intravenous adrenaline and appropriate fluid replacement with steroids and H<sub>1</sub> and H<sub>2</sub> blockers have administered for the treatment of anaphylaxis and the vital parameters have returned to normal ranges.<sup>10,13</sup> We had affirmative response to similar treatment for anaphylaxis occurred in our cases.

## CONCLUSION

The present report describes the occurrence of a serious anaphylactic reaction during surgical treatment of a liver hydatid cyst. The probable allergic reactions during invasive treatments of

echinococcosis are rare. Therefore, it seems to be underestimated. But, it should be stressed that, simple precautions and close follow up with appropriate therapy may decrease morbidity and mortality of such cases.

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