Anaphylaxis Development after Intravenous Injection of Cow's Milk

İnek Sütünün İntravenöz Enjeksiyonu Sonrası Gelişen Anafilaksi

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ABSTRACT

Although rare, intravenous injection of foreign substances during childhood can cause fatal complications. Most of the cases reported in the literature are accidental intravenous administrations of enteral feeding formulas. To the best of our knowledge, this is the first case of intravenous injection of cow's milk. In this report, we discuss the clinical presentation and treatment of a 17-year-old nursing student who injected pasteurized homogenized cow's milk into herself due to curiosity. The girl presented to our emergency department after this injection. During admission, she presented with angioedema, gastrointestinal symptoms, dyspnea, and tachycardia associated with resistant hypotension. She, then, developed leukocytosis and elevated D-dimer levels, as determined in the laboratory. The patient was diagnosed as having anaphylaxis with clinical presentation and cow's milk–specific IgE positivity, based on laboratory findings. The patient was initially treated with adrenaline, corticosteroids, and antihistamines. Inotropes including catecholamines and wide-spectrum antibiotics were added into the therapy for resistant hypotension and sepsis prophylaxis. Low-molecular-weight heparin treatment was given for the elevated D-dimer levels and prevention of embolic events. With these therapeutic interventions, there were no signs of sepsis, thrombosis, embolus, and multi-organ failure. The patient was discharged without any neurological complications or sequelae on the 6th day of hospital admission. Although sepsis and septic shock development is usually expected after the injection of foreign substances such as in this case, interestingly, there was an anaphylactic reaction caused by the patient's subclinical cow's milk allergy.

Keywords: Anaphylaxis, cow's milk, allergy

ÖZ

Çocuklukta nadir olmasına rağmen, yabancı cisimlerin damar içinden verilmesi ölümcül komplikasyonlara yol açabilir. Literatürde bildirilen çoğu olgu enteral beslenme formülalarının kazayla damar içinden verilmesi sonucudur. Bildiğimiz kadarıyla, olgumuz inek sütünün damar içinden yapıldığı ilk vakadır. Bu olgu sunumunda, 17 yaşında kız hemşirelik öğrencisinin, sonucunu merak etmesi nedeni ile kendisine intravenöz pastörize ve homojenize inek sütü enjekte etmesi sonrasında gelişen klinik tablo ve tedavisini tartışmaktayız. 17 yaşında kız inek sütünü damardan kendine enjekte etmesi sonrasında acil birimimize getirildi. Yatışında; anjioödem, gastrointestinal şikâyetler, dispne, taşikardi ve beraberinde dirençli tansiyon düşüklüğü mevcuttu. Daha sonra laboratuar bulgularında, lökositoz ve D-dimer yüksekliği gelişti. Hastamızın klinik görünümü ve laboratuar bulgularında inek sütü spesifik IgE pozitifliği ile anafilaksi geçirdiği teşhis edildi. Olgumuza başlangıçta adrenalin, kortikosteroid ve antihistaminik tedavisi uygulanmıştır. Katekolamin dâhil inotrop ilaçlar ve geniş spektrumlu antibiyotikler dirençli tansiyon düşüklüğü ve sepsis profilaksisi için tedaviye eklendi. Yüksek D-dimer düzeyi ve embolik olayların önlenmesi için, düşük moleküler ağırlıklı heparin tedavisi verildi. Tedaviye yönelik girişimler sonrasında, sepsis, tromboz, emboli ve multi-organ yetmezliğine ait belirtiler gelişmedi. Hastaneye yatışının altıncı gününde, olgu nörolojik komplikasyonsuz ve sekelsiz olarak taburcu edildi. Bu tür bir girişim sonrası normalde sepsis ve septik şok gibi bir tablonun gelişmesi beklenirken, hastamızda daha önceden mevcut olan ancak fark edilmeyen, hafif inek sütü duyarlılığına bağlı anafilâksi tablosunun gelişmesi şaşırtıcı olmuştur.

Anahtar Sözcükler: Anafilâksi, inek sütü, allerji

INTRODUCTION

Intravenous injection of foreign substances in childhood is performed mostly by a caregiver or healthcare worker. Most of the cases reported in the literature are erroneous accidental intravenous administration of enteral feeding formula and maternal breast milk (Table 1) (1, 2). Although rare, intravenous injection of formulas in childhood can cause fatal complications (1-3).

To the best of our knowledge, intravenous injection of cow's milk with the intention to commit suicide or due to curiosity has not been reported earlier in the literature (Table 1). In this report, we discuss the clinical presentation and treatment of a 17-year-old female nursing student who injected pasteurized homogenized cow's milk into herself owing to curiosity.

Bu çalışma 11. Uludağ Pediatri Kış Kongresi'nde sunulmuştur, 15-18 Mart 2015, Bursa, Türkiye.
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Table 1. Different cases related to intravenous injection of foreign substances reported in the literature

Features	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Age	10-day-old	6-week-old	60-year-old	50-year-old	5-day-old	17-year-old
Gender	Female	Male	Female	Male	Male	Female
Substance	MCT formula	Breast Milk	Enteral Feeds	Enteral Feeds	Breast Milk	Cow's Milk
Amount of Substance	4 mL	5 mL	25 mL	100 mL	10 mL	5 mL
Complete Blood Count	Mild transient trombocytopenia	Normal	Leukocytosis	Leukocytosis	Leukocytosis, thrombocytopenia	Leukocytosis
Blood Culture	Negative	Negative	Klebsiella spp, Enterococcus spp.	Klebsiella spp	Group , Streptococcus Staphylococcus Epidermidis	Negative
Substance Culture	Negative	Negative	N/A	Klebsiella spp	Group G Streptococcus, Anaerobes	Negative
Vital Signs	N/A	SpO_2↓HR↑RR↑	SpO_2↓HR↑RR↑BP↓ Fever+	SpO_2↓HR↑RR↑BP↓ Fever+	N/A	HR↑RR↑BP↓ Fever+
Sign of Embolism	Superficial trombophlebitis, trombosis of greater saphenous vein	No	No	No	No	No
Organ Failure	Brain	No	Pulmonary Oedema	Respiratory Failure	Respiratory Failure	Angioedema
Antibiotics	Vancomycin, Imipenem	Ampicillin	Piperacillin-Tazobactam	Antibiotics	Broad-spectrum antibiotics	Meropenem, Vancomycin
Ionotrops, Vasopressors	No need	No need	Noradrenalin, Vasopressin, Dobutamine	Dopamine, Norepinephrine	No need	Dopamine, Adrenaline
Other treatments	O_2, IV fluid, LMWH	O_2	O_2, IV fluid, LMWH, hydrocortisone, furosemide, Pheniramine, Pethidine, Promethazine	Mechanical Ventilation, IV fluid, plasmapheresis	Mechanical Ventilation	O_2, IV fluid, LMWH, pheniramine, prednisolone
Neurological Outcome	Leukomalacia	Good	Good	Good	Good	Good
Reference	3	1	5	16	7	Our Case

MCT: medium-chain triglycerides; BP: blood pressure; HR: heart rate; LMWH: low molecular weight heparin; N/A: not available; RR: respiratory rate; SpO_2:oxygen saturation

CASE PRESENTATION

A 17-year-old female patient presented to our emergency department with a history of intravenously injecting 5 ml of pasteurized homogenized cow's milk into herself because of curiosity 2 h prior to presentation. She reported that seconds after injection, she experienced dizziness and swelling of lips, eyes, face, and hands, followed by palpitation, cyanosis of lips and face, shivering, dyspnea, and abdominal pain within minutes. Approximately 40 min after injection, she was first brought to the emergency service of a state hospital with complaints of vomiting, angioedema, and persistent hypotension (80/50 mmHg at home and the ambulance). In the emergency room of this state hospital, 1 mg adrenaline (0.5 mg × 2 doses from 1/1000), 8 mg dexamethasone (1 ampul), and 45.5 mg pheniramine (1 ampul) were given intravenously due to the suspicion of anaphylaxis and referred to our research/training hospital. When she and her family were questioned, there was nothing significant in her past medical and family histories.

On arrival to our emergency department, the physical examination revealed a conscious, alert, and oriented patient with a body temperature of 38 °C. The initial blood pressure was 108/35 mmHg (109/50 mmHg: systolic and diastolic blood pressure at the 5th percentile for her age) and the heart rate was mildly tachy-

cardic at 139 beats/min with regular sinus rhythm: the respiratory rate was 36 breaths/min. Physical examination revealed edema of lips, face, and periorbital area (Figure 1). The rest of the systemic examination showed normal physical findings.

Complete blood count, urine analysis, blood glucose, electrolytes, prothrombin time (PT), activated partial thromboplastin time (aPTT), international normalized ratio (INR), calcium (Ca), phosphorus (P), total protein, arterial blood gas analysis, troponin I, creatinine kinase (CK), creatinine kinase myocardial band (CK-MB), myoglobin, renin, and total IgE test results were within normal ranges. Skin prick tests were done a few months later and found to be negative for classical food and inhalant allergens. Although specific IgE for inhalant and food allergens were negative, cow's milk–specific IgE were moderately positive (0.94 kU/L). Blood cultures and cultures from injected milk itself showed no growth. Pulmonary function test parameters were within normal limits 2 months after the reaction. Postero-anterior chest radiograph, echocardiography, abdominal ultrasonography, and renal Doppler ultrasonography did not show any pathology.

With her resistant hypotension, decreased urine output, and cow's milk-specific IgE positivity, the patient was thought to be suffering from anaphylactic reaction. During the initial course of management, bolus intravenous fluid was given at 20 mL/kg using normal saline. Dopamine (10 mcg/kg/min) was administered continuously to maintain blood pressure. Ceftriaxone (50 mg/kg/day), gentamicin (5 mg/kg/day), and clindamycin (30 mg/kg/day) treatment were initiated because of resistant hypotension and suspicion of sepsis with fever and elevated C-reactive protein (CRP). Since an anaphylactic reaction could not be ruled out, prednisolone (2 mg/kg/day) and pheniramine (1 mg/kg/day) were continued, and ranitidine (1 mg/kg/day) was initiated, too. Despite increased dopamine dosage (up to 20 mcg/kg/min), hypotension persisted; therefore, 0.2 mcg/kg/min adrenaline infusion was initiated. Follow-up laboratory investigations revealed elevated D-dimer and leukocytosis on day 1. In view of these findings, disseminated intravascular coagulation and sepsis were suspected, and the antibiotic treatment was changed to meropenem (60 mg/kg/day), vancomycin (40 mg/kg/day), and low-molecular-weight heparin (50 U/kg/dose, bid) treatments and used for 5 days. On the 3rd day of admittance, her blood pressure normalized (110/65 mmHg) and adrenalin infusion was discontinued. Facial edema of the patient was resolved on the 4th day of the hospital stay (Figure 2). The patient was discharged with cure on the 6th day in the pediatric intensive care unit. According to the psychiatric evaluation performed in the outpatient clinic, her action was not interpreted as a mood disorder and suicide attempt; it is thought to be in agreement with adolescence behavioral pattern. Written informed consent was obtained for this case report.

DISCUSSION

In childhood, inadvertent intravenous administration of enteral feeding formulas may lead to a wide spectrum of clinical presentations, and even death. Most of the cases reported in the literature are medication errors (1, 2, 4-7). Probably due to the shortage of reporting, there has not been a similar case of milk injection reported before from Turkey as well as the rest of the world.

Intravenous infusion of enteral feeding may lead to sepsis, acute respiratory distress, cardiovascular collapse, liver and renal failures, thrombosis, microembolism, hypersensitivity, seizures, multiple organ failure, and death (1, 3, 7-9). Seizures and permanent neurological impairment was described in preterm infants (Table 1) (1). In our case, anaphylactic reaction was diagnosed on the basis of clinical findings such as angioedema, resistant hypotension, and respiratory and gastrointestinal findings, as well as specific IgE positivity. Enteral feeding formulas have a base of milk proteins; therefore, inadvertent injection of these formulas may lead to anaphylaxis even in mildly sensitized persons. Enteral feeding formulas have high osmolarity, which contributes toward organ dysfunction (5, 10). Symptom severity depends on the type of substance, amount of substance given, and rate of infusion (1). After injecting cow's milk, there was an anaphylactic reaction clinic that developed immediately in the patient. This anaphylactic reaction was mediated through an immune response to the cow's milk proteins. Despite being unaware of her sensitization, mild hypersensitivity of the patient could explain this anaphylactic reaction.

Any hypotension develops secondary to sepsis or anaphylaxis; it should be treated with aggressive fluids, vasopressors, and inotropes (5, 8, 10). In our case, adrenalin, anti-histamines, and corticosteroids were given in the beginning. Further, fluid bolus, inotropes, and catecholamines had to be given for resistant hypotension. We think that late administration (after the 1st hour) of adrenalin in our patient was thought to be responsible for resistant hypotension, particularly in the diastolic component.

Enteral feeding formula injection may lead to sepsis, which is related to bacterial overgrowth in its content (5, 11). In the reports from literature, multi-organ dysfunction was not directly related to septic shock but the osmolarity of the product (1, 8). The patient in this report, who did not develop multi-organ dysfunction, was treated prophylactically to prevent sepsis with broad-spectrum antibiotics until the blood and milk cultures turned negative.

Badran et al. (3) reported a 34-week-old neonate who developed leukocytosis, thrombocytopenia, transient metabolic acidosis, superficial thrombophlebitis, and thrombosis of greater saphenous vein after accidently receiving formula milk intravenously for over 2 h through the central catheter. Our case developed only leukocytosis at the 9th hour of admission, which persisted for 4 days; this was thought to be related to an anaphylactic reaction, systemic steroids given, or adrenalin infusion.

Several studies suggested that treatment should basically focus on the regulation of osmolarity, treatment of microembolism, hypersensitivity, and sepsis (5). Patients should be started on broad-spectrum antibiotics and adjustment of antibiotic treatment according to the blood results and injected material cultures should be done (1, 5, 8, 9, 10). In our case, blood cultures were negative; it might be due to single-dose ceftriaxone treatment before admission to our facility. Since injected material cultures and laboratory results were negative after clinical presentation, the diagnosis of sepsis was ruled out and her antibiotic therapy was stopped on the 5th day of admission.

Some of the clinical features of inadvertent intravenous injections may be explained by the microembolism of fat globules, water-insoluble particles, and an immune response to foreign antigens (Table 1) (1, 10). It is reported that a particular structure of enteral feeding may lead to pulmonary embolism (5). During treatment, oxygen therapy should be initiated and the patient should be watched closely for pulmonary edema and pulmonary throm-

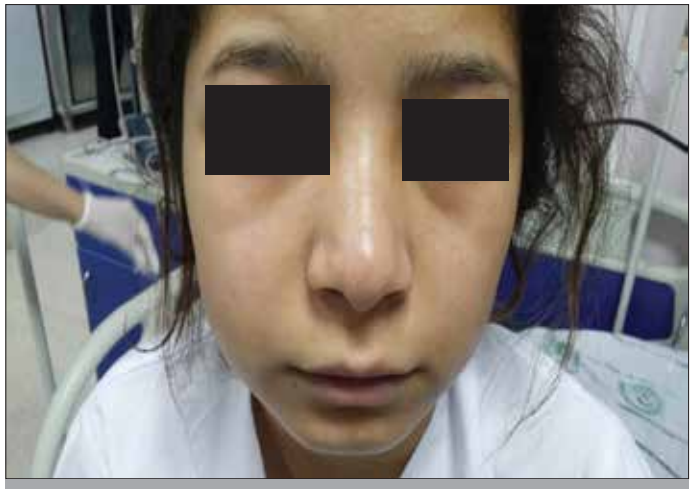

Figure 1. Facial angioedema of our patient 1 day after admission into intensive care unit

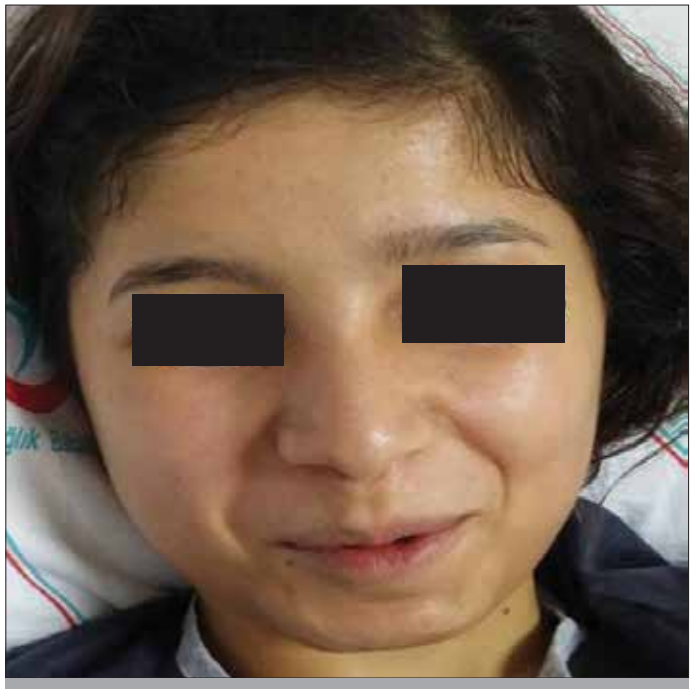

Figure 2. Normal facial appearance of the patient at the 4th day of admission

boembolism. Heparin was administered, in some cases, as prophylaxis to prevent thromboembolic events (1, 5). In our patient, there were no radiological findings and clinical presentation of pulmonary embolism. In the 20th hour of follow-up, since our patient's D-dimer level was elevated, low-molecular-weight heparin treatment was initiated. The D-dimer level returned to normal at the 45th hour of admission.

Management of most cases in the literature was supported by oxygen supplementation and mechanical ventilation, diuretic therapy, peritoneal dialysis, and steroid administration (Table 1). Plasmapheresis and exchange transfusion in an adult and a preterm infant was reported to improve oxygenation and stabilize hemodynamics (1). Our patient did not need plasmapheresis and exchange transfusion. A comparison of our patient with the cases reported in the literature is shown in Table 1.

CONCLUSION

Although sepsis and septic shock presentation is usually expected after the injection of foreign substance, interestingly, there was a clinical presentation of anaphylaxis in which angioedema and systemic symptoms involving 4 organs caused by the patient's mild, subclinical cow's milk allergy.

Informed Consent: Written and verbal informed consent was obtained from patients' parents and the patient who participated in this study.

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